IL-17/23 IN THE TRANSITION FROM AUTOIMMUNITY TO INFLAMMATION

Pfeifle R.1,2, Rothé T.1,2, Scherer H.U.1, Wuhrer M.1, Rombout Y.1, Koeleman C.A.1, Toes R.1, Holmåhl R.1, Herrmann M.1, Blüml S.1, Nimmerjahn F.1,2, Schett G.1, Krönke G.1,2
1Dept. of Internal Medicine 3 and Institute for Clinical Immunology, University Hospital Erlangen, Erlangen; 2Nikolaus-Fiebig Center for Molecular Medicine, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany; 3Dept. of Rheumatology, Leiden University Medical Centre, Leiden, The Netherlands; 4Medical Inflammation Research, Dept. of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden; 5Division of Rheumatology, Internal Medicine 3, Medical University Vienna, Vienna, Austria; 6Institute of Genetics at the Dept. of Biology, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany

Checkpoints and mechanisms contributing to autoantibody-driven disease are yet incompletely understood. By dissecting and analyzing different murine arthritis models, we demonstrate that the IL-23/Th17 axis acts as a decisive factor that triggers the clinical onset of autoimmune arthritis rather than contributing to a break of self-tolerance. Analysis of human rheumatoid arthritis (RA) patients confirms that similar changes occur during the transition from asymptomatic autoimmunity to symptomatic RA.

IL-17 AS A TRIGGER FOR ARTHRITIS AND JOINT DESTRUCTION

Lubberts E.
Dept. of Rheumatology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

Interleukin (IL-)17A is a proinflammatory cytokine and its signaling has a role in inflammatory arthritis, in particular in orchestrating tissue inflammation and destruction. IL-17 is a T cells cytokine and is produced by the newly identified Th17 helper subset, the Th17 cells. However, also other T cell subsets, innate immune cells and even tissue specific cells can produce IL-17A, which may be dependent on the type of the disease. The discovery of Th17 cells and the newly identified IL-23–IL-17 immune pathway has changed immunology and our view on autoimmune-mediated diseases. The current view is that IL-23 receptor positive T cells becomes more pathogenic after exposure to IL-23. Neutralizing IL-17A or IL-23 might be a promising approach to control the development of immune-mediated inflammatory arthritis.

However, neutralizing IL-23 in the early stage of autoimmune arthritis is beneficial but not during the effector stage. IL-17 receptor A signaling is critical in the downstream IL-23 induced autoimmune arthritis as mice lacking IL-17 receptor A were completely protected against the development of autoimmune arthritis. Here I will discuss the fundamentals how IL-17A and the IL-23/IL-17 axis works in the pathogenesis of inflammatory arthritis with focus on tissue inflammation and joint destruction.

IS THE T2T CONCEPT APPLICABLE TO SPA?

van der Heijde D.
Leiden University Medical Centre, Leiden, The Netherlands

An international task force of expert physicians and patients has published recommendations for the management of SPA according to a target (‘treat-to-target, T2T’) in 2014. These recommendations were based on results of a systematic literature review and expert opinion. Although the literature review did not reveal trials comparing a treat-to-target approach with another or no strategy, it provided indirect evidence regarding an optimised approach to therapy that facilitated the development of recommendations. The group agreed on 5 overarching principles and 11 recommendations; 9 of these recommendations related commonly to the whole spectrum of SPA and PsA, and only 2 were designed separately for axial SPA, peripheral SPA and PsA. The main treatment target, which should be based on a shared decision with the patient, was defined as remission, with the alternative target of low disease activity. Follow-up examinations at regular intervals that depend on the patient’s status should safeguard the evolution of disease activity towards the targeted goal. Additional recommendations relate to extra-articular and extramusculoskeletal aspects and other important factors, such as comorbidity. The task force defined the treatment target as remission or, alternatively, low disease activity, being aware that the evidence base is not strong and needs to be expanded by future research.

The T2T concept is borrowed from internal medicine based on diseases that have a clear relationship between ‘process’ measures (e.g. glucose level, HbA1c in diabetes mellitus) and outcome (cardiovascular disease) which can be influenced by treatment: insulin and oral drugs reduce the level of HbA1c and patients with a lower HbA1c have fewer cardiovascular events. Using HbA1c as a target is resulting in fewer cardiovascular events. This has been successfully applied to rheumatoid arthritis too. The question is if this is also applicable to SPA. The first question to answer is the definition of remission and the ultimate goal for the treatment of a patient. Secondly, if this can be achieved by treatment. And finally if this indeed leads to a better outcome in comparison to patients who are not treated according a T2T principle.

CAN FIBROMYALGIA BE AN OBSTACLE FOR T2T?

Mease P.
Rheumatology Research Division, Swedish Medical Center; University of Washington, Seattle, WA, USA

Introduction/Aim. Fibromyalgia (FM), also known as “central sensitization syndrome” (CSS) presents as a syndrome of chronic widespread pain, fatigue, sleep disturbance, and dyscognition (1, 2, 3). It is present as a concomitant illness in 10–30% of rheumatologic disease patients, depending on the disease in question and the population sample. States of chronic pain and/or inflammation, as in rheumatoid arthritis (RA), spondyloarthritis (SpA) (including anklyosing spondylitis (AS)/axial spondyloarthritis (AxSpA) and psoriatic arthritis (PsA)), osteoarthritis (OA), and lupus are a setting in which central sensitization (CS) can arise, influenced by genetic as well as psychosocial factors (4, 5, 6, 7). CSS is characterized by dysregulation of nociceptive and anti-nociceptive neuronal pathways and neural signaling, evidenced by advanced neuroimaging, quantitative sensory testing, and CS-discriminatory patient reported outcome measures (PROMs) (1, 2, 3). Concomitant FM (CSS) alters rheumatologic disease presentation, natural history, disease severity assessment, and treatment outcomes, including the ability to achieve ideal goals of treatment of remission or low disease activity (4, 5, 6, 7). Concomitant FM may worsen disease activity measures and blunt ability to achieve low disease or remission criteria.

Materials and Methods. This review will be constituted by a literature review of studies on FM (CSS) in rheumatologic disease including RA, AS/AxSpA, and PsA. Data on impact of concomitant FM on rheumatologic disease presentation, natural history, disease severity assessment, and treatment outcomes, including treatment to-target of remission or low disease activity is analyzed.

Results. Concomitant FM (CSS) has been demonstrated to occur in 10–20% of patients with RA and SpA, depending on method of ascertainment, geographic/cultural and gender variation. Initially most clearly described in RA, current studies document the impact of concomitant FM in the spectrum of SpA, including AS, AxSpA, and PsA (4, 5, 6, 7). SpA patients with concomitant FM are more likely female, have a greater likelihood of enthesis, and display worse disease activity measures than SpA patients without FM, including BASDASL, BASFI, ASQL, which are wholly patient reported outcome measures, and to a lesser extent ASDAS (4, 5, 6, 7). SpA patients with FM cycle through a greater number of treatment options in a shorter period of time (4).

Discussion. These results suggest that SpA patients with concomitant FM have worse disease activity measures and may have greater difficulty achieving ideal targets of treatment such as remission or low disease activity as measured by outcome measures heavily weighted with patient reported outcome measures. Approaches to deal with this issue and a research agenda are outlined.

Conclusions. Concomitant FM (CSS) occurs in at least 10–20% of patients with SpA. Concomitant FM influences disease presentation, natural history, assessment of disease severity and outcomes of treatment. The presence of concomitant FM should be investigated when assessing patients with SpA and taken into account when assessing disease severity and impacts of treatment. This has significant implications for disease monitoring and the ability to use a treat-to-target strategy in achieving remission or low disease activity.

References
INV10
PATHOPHYSIOLOGY AND TREATMENT OF PSORIASIS
Di Meglio P.
The Francis Crick Institute, Mill Hill Laboratory, London, UK

Psoriasis is a chronic inflammatory skin disease with a complex etiopathogenesis, resulting from the interplay of genetic, environmental, and immunological factors. In the last two decades, a large and integrative research approach, combining the analysis of clinical samples and animal models of disease, has resulted in the elucidation of many underlying pathogenic mechanisms. More importantly, many of these discoveries have been translated into novel targeted therapies already in the clinic, or in advanced stage of clinical trials. Genome-wide association studies and subsequent meta-analysis have identified a fast-growing number of psoriasis susceptibility genes (>40), uncovering critical immunological and skin-specific pathways involved in the disease. A pathogenic cross talk between innate and adaptive immune cells, and keratinocytes in the skin, underpins the dysregulated cutaneous immune responses. Although still in its infancy, the mechanistic investigation of environmental triggers holds the promise to uncover additional pathogenic mechanisms and novel potential therapeutic strategies.

I will give an update on the more recent genetic and immunological findings, and discuss the current therapeutic portfolio for psoriasis, spanning from local to systemic therapies, from old fashioned drugs discovered by serendipity, to innovative targeted therapies, already approved or under evaluation. Finally, I will identify and discuss research gaps which need to be filled, and future directions to be taken, to further enhance our understanding of the disease and ultimately provide better patient’s care.

INV11
UVEITIS: CLINICAL IMPLICATIONS AND PATHOGENESIS IN SPONDYLOARTHRITIS
Rosenbaum J.T.1,2, Asquith M.3
1Oregon Health & Science University, Portland, OR; 2Legacy Devers Eye Clinic, Portland, OR, USA

Introduction. Uveitis is the most common, clinically apparent extra-articular manifestation of spondyloarthritis.

Methods. Literature review and studies in HLA B27/β2-microglobulin transgenic rats.

Results. As many as 50% of patients with ankylosing spondylitis develop acute anterior uveitis. The phenotype of the uveitis is typically sudden onset, unilateral, anterior, and recurrent. The recent DUET and SENTINEL studies indicate that many individuals with acute anterior uveitis have an associated spondyloarthritis which is most often undiagnosed. We have reported that HLA genotype shapes the incidence of uveitis in patients infected by global alterations in the peptidome. Genome-wide association studies and subsequent meta-analysis have identified a fast-growing number of psoriasis susceptibility genes (>40), uncovering critical immunological and skin-specific pathways involved in the disease. A pathogenic cross talk between innate and adaptive immune cells, and keratinocytes in the skin, underpins the dysregulated cutaneous immune responses. Although still in its infancy, the mechanistic investigation of environmental triggers holds the promise to uncover additional pathogenic mechanisms and novel potential therapeutic strategies.

I will give an update on the more recent genetic and immunological findings, and discuss the current therapeutic portfolio for psoriasis, spanning from local to systemic therapies, from old fashioned drugs discovered by serendipity, to innovative targeted therapies, already approved or under evaluation. Finally, I will identify and discuss research gaps which need to be filled, and future directions to be taken, to further enhance our understanding of the disease and ultimately provide better patient’s care.

INV18
THE PATHOGENETIC ROLE OF THE HLA-B27 PEPTIDOME
López de Castro J.A.
Centro de Biología Molecular Severo Ochoa, Consejo Superior de Investigaciones Científicas y Universidad Autónoma de Madrid, Spain

Introduction. The joint association of HLA-B*27 and the endoplasmic reticulum aminopeptidases ERAPI and ERAP2 with ankylosing spondylitis (AS) suggests a role of the HLA-B*27 peptidome in this disease, since these enzymes are involved in the final processing of MHC-I-bound peptides. Genetic studies indicate that ERAPI variants with high enzymatic activity and ERAP2 expression predispose to AS. Thus, our study addressed the influence of natural ERAPI polymorphism and ERAP2 expression on shaping HLA-B*27-bound peptide compositions.

Methods. HLA-B*27 ligands were isolated from human lymphoid cell lines with distinct ERAPI/ERAP2 backgrounds by affinity chromatography and acid extraction. ERAPI and ERAP2 expression was characterized by genomic sequencing and Western blotting. Peptides were identified and quantified by mass spectrometry. The relative amounts of shared peptides among cell line pairs, were estimated from the respective ion peak intensities. The susceptibility of N-termini to ERAP2 trimming was scored, based on published studies, from 0 to 100. The theoretical affinity of the peptidome was estimated with standard algorithms. Statistical analyses were performed with various methods depending on the particular comparisons. In vitro digestions were carried out with recombinant enzymes and synthetic peptides.

Results. 1) ERAPI polymorphisms associated with increased risk to AS shaped an optimized HLA-B*27 peptidome with increased abundance of nonamers, peptides with ERAPI-resistant N-terminal residues, distinct internal sequences and higher affinity. 2) Analysis of HLA-B*27 subtype-bound peptidomes indicated that peptides found only among AS-associated subtypes showed an increased frequency of ERAPI-resistant N-terminal residues compared to peptides found only among non-AS-associated subtypes. 3) ERAPI expression also resulted in an increased abundance of nonamers, and in the selective destruction or lower abundance of HLA-B*27 ligands with N-terminal basic residues, without altering the global affinity of the peptidome.

Discussion. Both ERAPI and ERAP2 have significant effects on the HLA-B*27 peptidome, affecting the expression levels of many natural ligands. The mechanism of ERAPI/HLA-B*27 interaction consists in altering the peptide generation/destruction balance in a way that depends on the sequence of each peptide and the particular ERAPI variant. This leads to an optimized, higher affinity, peptidome in AS-predisposing ERAPI contexts. The pattern of N-terminal residue usage among HLA-B*27 subtype-bound peptides suggests that AS-associated subtypes may be more influenced by ERAPI polymorphism than non-AS-associated ones. The effects of ERAP2 on the N-terminal residues of HLA-B*27 ligands are consistent with the known preference of this enzyme for basic residues and are best explained by direct trimming. Yet, the influence on peptide length might point out to an additional effect on increasing ERAPI activity, from 0 to 100. The theoretical affinity of the peptidome was estimated with standard algorithms. Statistical analyses were performed with various methods depending on the particular comparisons. In vitro digestions were carried out with recombinant enzymes and synthetic peptides.

Results. 1) ERAPI polymorphisms associated with increased risk to AS shaped an optimized HLA-B*27 peptidome with increased abundance of nonamers, peptides with ERAPI-resistant N-terminal residues, distinct internal sequences and higher affinity. 2) Analysis of HLA-B*27 subtype-bound peptidomes indicated that peptides found only among AS-associated subtypes showed an increased frequency of ERAPI-resistant N-terminal residues compared to peptides found only among non-AS-associated subtypes. 3) ERAPI expression also resulted in an increased abundance of nonamers, and in the selective destruction or lower abundance of HLA-B*27 ligands with N-terminal basic residues, without altering the global affinity of the peptidome.

Conclusions. The significant influence of ERAPI and ERAP2 on the HLA-B*27 peptidome strongly supports a peptide-mediated mechanism as the basis for the association of all three molecules with AS. The precise pathogenic effect remains unclear and may have a complex basis, since the presentation of specific epitopes, but also HLA-B*27 folding, stability and NK recognition, may be affected by global alterations in the peptidome.

INV19
THE ROLE OF ERAPI IN SPONDYLOARTHRITIS IN HLA-B27 TRANSGENIC RATS
Tran T.M., Hong S., Bennett J., Colbert R.A.
National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, Maryland, USA

Introduction/Aim. Common variants of the HLA class I B gene (predominantly HLA-B*2705) predispose to spondyloarthropathies, and in particular ankylosing spondylitis. Endoplasmic reticulum (ER) aminopeptidase 1 (ERAP1) trims peptides in the ER, and alters the quantity and quality of peptide cargo available for loading onto HLA class I heavy chain-β2-microglobulin (β2m) complexes. Common variants of ERAPI that affect its function and expression impact the risk of developing several immune-mediated inflammatory diseases, including ankylosing spondylitis, Behçet’s disease, and psoriasis, all of which have HLA class I associations suggesting epitope presentation. In spondyloarthropathies, there are conflicting data on how gain/loss-of-function of ERAPI affects the risk of ankylosing spondylitis, and how altered function affects the biology of HLA-B*27. To address these questions, we developed an animal model to examine the role of ERAPI loss-of-function on the development of spondyloarthropathies using HLA-B27/human β2m transgenic (B27-Tg) rats.

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Materials/Methods. Genome editing in fertilized embryos was used to delete 29 nucleotides in the first exon of ERAP1 (ERAP1<sup>del29/</sup>) resulting in a frame shift, premature stop codons, and complete loss of ERAP1 protein expression in cells from ERAP1<sup>del29/</sup> animals, with approximately 50% expression in ERAP1<sup>+/+</sup> cells. We generated cohorts of ERAP1<sup>+/+</sup>, ERAP1<sup>+/del29</sup>, and ERAP1<sup>del29/del29</sup> rats expressing HLA-B27/hβ<sub>2</sub>, HLA-B7/hβ<sub>2</sub>, or no transgene (wild type, WT) by breeding to evaluate effects of ERAP1 deficiency on arthritis and colitis.

Results. B27-Tg males with either ERAP1<sup>+/+</sup> or ERAP1<sup>del29/</sup> genotypes developed arthritis with a frequency of 52% (12/37), and 26% (10/38), respectively, with comparable arthritis severity scores (1.6) and age of onset (4.1 months). In contrast, only 12% (4/34) of rats with an ERAP1<sup>+/del29</sup> genotype developed arthritis (p<0.05) with an average arthritis severity score of 1.3 (p<0.05). CT scans of affected limbs revealed less bone erosion in representative B27-Tg ERAP1<sup>+/del29</sup> or B27-Tg ERAP1<sup>del29/del29</sup> rats compared with B27-Tg ERAP1<sup>+/+</sup> rats. Twelve percent (2/17) of B27-Tg ERAP1<sup>+/del29</sup> females developed arthritis (average arthritis score 0.75), while B27-Tg ERAP1<sup>+/del29</sup> and B27-Tg ERAP1<sup>del29/del29</sup> females remained healthy. Persistent arthritis was not seen in 49 B7-Tg and 48 WT rats of various genotypes. All B27-Tg rats developed gut inflammation with no differences in clinical colitis determined by stool scores, although average colon histology scores were slightly higher in the complete absence of ERAP1<sup>+/del29</sup> compared to ERAP1<sup>+/+</sup> (5.0 vs 0.05). No B7-Tg or WT rats developed colitis.

Discussion/Conclusions. The absence of ERAP1 (loss-of-function) protects B27-Tg rats from the development of arthritis, but not from gut inflammation, suggesting tissue-specific contributions of ERAP1 to pathogenic mechanisms. Ongoing studies are examining how loss of ERAP1 affects the expression of various forms of HLA-B27 that have been implicated in disease. This novel model provides a system to determine how ERAP1 impacts inflammatory arthritis and whether functional interaction with HLA-B27 is responsible.

INV22

WILL THERE BE ANYTHING CLINICALLY USEFUL OTHER THAN HLA-B27 FOR AXIAL SPONDYLOARTHRITIS?

Van Gaalen F.A.
Leiden University Medical Center, Dept. of Rheumatology, Leiden, The Netherlands

Although most common inflammatory rheumatic disease have a complex genetic background, genetic testing is generally not used in the diagnosis of these diseases. The major exception is axial spondyloarthritis (axSpA) where HLA-B27 testing has become an essential part of the diagnosis of early axSpA. In recent years, many new genetic risk factors for axSpA have been discovered. However, despite these discoveries and the dramatic drop in costs of genetic testing in the past decades, HLA-B27 is still the only genetic risk factor used in clinical practice. The main reason for this is that the new genetic risk factors (e.g., HLA-B<sup>*4001</sup>, ERAP1, IL-23R) are typically not as strong a risk factor as HLA-B<sup>*27</sup> for ankylosing spondylitis in two major genetic studies. Adenine, acting at its receptors (A<sub>1</sub>R, A<sub>2</sub>A<sub>R</sub>, A<sub>2</sub>B<sub>R</sub> and A<sub>3</sub>R), has a plethora of effects including anti-inflammatory actions. Adenosine, acting at its receptors (A<sub>1</sub>R, A2A<sub>R</sub>, A2B<sub>R</sub> and A3R), has a variety of effects on both the immune system and osteoblastic cells. Osteoclast differentiation depends, in part on A1R function whereas A2AR and A2BR stimulation inhibits osteoclast differentiation. In contrast, A2AR and A2BR stimulation promotes osteoclast function. The role of A3R in bone homeostasis is not well established. In responsive individuals methotrexate therapy diminishes bony erosions and destruction and recent observational studies suggest that methotrexate therapy provides better protection against development of endstage joint disease requiring total joint replacement than TNF antagonists. We will discuss the efficacy of adenosine receptor agonists in the treatment and prevention of inflammatory bone disease.

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O1
ANTI-IL-17A TREATMENT BLOCKS INFLAMMATION, DESTRUCTION AND NEW BONE FORMATION IN EXPERIMENTAL SPONDYLOARTHRITIS IN HLA-B27 TRANSGENIC RATS
van Tok M.N.1,2, van Duivenvoorde L.M.1,2, Kramer I.1, Ingold P.1, Taurog J.D.4, Kolbinger F.1, Baeten D.J.1,2,3,4
1Dept. of Clinical Immunology and Rheumatology/Experimental immunology, AMC, Amsterdam; 2Amsterdam Rheumatology and Immunology Center, Amsterdam, The Netherlands; 3Novartis Institutes for Biomedical Research, Basel, Switzerland; 4Rheumatic Diseases Division, Dept. of Internal Medicine, UT Southwestem Medical Center, Dallas, TX, USA

Background. Recent data indicates that Secukinumab can halt new bone formation after two years of treatment in ankylosing spondylitis patients. However, due to a relatively short follow up and lack of appropriate control groups more evidence is needed to prove that IL-17A affects new bone formation.

We aimed to assess the impact of anti-IL-17A on new bone formation in a validated animal model for spondyloarthritis.

Methods. HLA-B27/huβ2m tg rats (23-1x283-2) were immunized with M. tuberculosis/iLFA and weekly treated with 15mg/kg anti-IL-17A or IgG2a isotype, treatment continued for five weeks. Rats were clinically assessed for spondylitis, arthritis and hind limb swelling. Micro-CT analysis and histology were performed at the end of the study.

Results. In the controls, spondylitis and arthritis was observed in all treated rats 31 and 19 days after immunization, respectively. In contrast, only 8% and 33% of the anti-IL-17A treated rats developed spondylitis and arthritis at these time points. Additionally, there was a significant delay in mean appearance of spondylitis (day 28 vs day 14; p<0.05) and arthritis (day 27 vs day 14; p<0.05) in treated versus control animals. Arthritis severity was lower in the anti-IL-17A-treated group compared to controls (p=0.05). Quantitative analysis of structural damage by micro-CT of ankle joints showed a 17% higher total bone volume in anti-IL-17A treated rats (p=0.05), suggesting decreased bone loss.

Moreover, the volume of low density bone, reflecting newly formed bone, was lower in the anti-IL-17A treated rats than in controls (p=0.05). In the axial joints there was a tendency towards less inflammation, destruction and new bone formation in anti-IL-17A treated rats.

Conclusion. IL-17A blockade significantly suppressed clinical spondylitis and arthritis and could impact structural damage, including pathological new bone formation.

O2
EFFECT OF COMEDICATION WITH CONVENTIONAL SYNTHETIC DMARDs ON RETENTION OF TNF INHIBITORS IN PATIENTS WITH SPONDYLOARTHRITIS: A PROSPECTIVE COHORT
Sepehrnoori A.1,2,3, van der Heijde D.2, Ávila-Ribeiro P.1, Fonseca R.4, Borges J.1,4, Teixeira L.1, Carvalho P.1, Cerequiera M.1, Neves J.1, Meirinhos T.1, Barcelos A.1,2,3, Sequeira G.5, Canhão H.6, Branco J.C.7, Vieira-Sousa E.3, Teixeira L.4, Salvador M.J.5, Bernardes M.1, Vieira-Sousa E.3, Canhão H.6, Branco J.C.7, Pimentel-Santos F.1,2,3, Landewé R.1
1CEDOC, NMS, Lisboa, Portugal; 2LUMC, Leiden, The Netherlands; 3Lisbon Academic Medical Center, Lisbon; 4CH São João, Porto; 5IPR, Lisboa; 6Hospital Garcia de Orta, Almada; 7CH Universitário Coimbra; 8ULSAM, Ponte de Lima; 9CH Baixo Vouga, Aveiro; 10Hospital de Faro; 11IMM, Lisboa; 12HEM-CHLO, Lisboa, Portugal; 13ARC, Amsterdam, The Netherlands

Introduction/Aim. The effects of comedication with csDMARDs on TNFi-retention in SpA are inconclusive. We aimed to evaluate if comedication with csDMARDs influences TNFi-retention in patients with SpA.

Methods. Patients with SpA from the Rheumatic Diseases Portuguese Register (Reuma.pt), with first TNFi started between 2001 and 2014 were included in this prospective, multicenter, cohort-study. Cox-regression was used to estimate the effect of csDMARD comedication on TNFi-retention in two types of models, one including baseline (time-fixed) variables and the other with time-varying variables. To control for possible “confounding by indication”, the effect of csDMARD comedication was also tested after propensity score (PS)-adjustment.

Results. In total, 954 patients were included and 289 (30.3%) discontinued their first TNFi after a median of 2.5 years (range: 0.08-13). Inefficacy was the most common reason for TNFi-discontinuation (56%). In the multivariable analysis co-medication with csDMARDs had no measurable effect on TNFi-retention, neither in the baseline model (HR: 0.83; 95% CI: 0.59; 1.16) (figure A) nor during follow-up adjusting for time-varying covariates (1.07; 95% CI: 0.68; 1.68). The effect of csDMARDs remained non-significant after PS-adjustment (figure B).

Conclusion. Comedication with csDMARDs does not prolong TNFi-retention in SpA patients in clinical practice suggesting no benefit in the concomitant use of these drugs.
O4

EFFICACY OF GOLIMUMAB IN PATIENTS WITH ACTIVE, VERY EARLY PERIPHERAL SPONDYLOARTHRITIS: FIRST RESULTS FROM THE CRESPIAL TRIAL

Carron P.1, Varkas G.2,3, Cybes H.2, Van Praet L.1, Elewaut D.1,2, Van den Bosch E.1  
1Ghent University Hospital, Dept. of Rheumatology, Ghent; 2Ghent University, VIB Inflammation Research Center, Ghent, Belgium

Objective. To evaluate the efficacy of golimumab in patients with active peripheral Spondyloarthritis (pSpA) in a very early stage of the disease.

Methods. CRESPIAL (Clinical REmission in peripheral SpondyloArthritis) is an ongoing prospective, open-label, single center study of golimumab treatment in pSpA patients. Eligible patients were ≥18 years and fulfilled the ACR classification criteria for pSpA. At randomisation, all patients had a symptom duration of ≤12 weeks. Integration with RNA expression data will allow the functional analysis of interesting miRNAs whose deregulation might contribute to the pathogenesis of the disease. From week 12 onwards, there was an option to start rescue medication with golimumab 50 mg every 4 weeks or switching placebo for 24 weeks. The primary endpoint was the percentage of patients achieving clinical remission at week 24. Clinical remission was defined as the absence of arthritis, enthesitis and dactylitis on clinical examination.

Results. In total 60 patients were randomized of whom 20 to the placebo group and 40 to the golimumab group. Baseline demographics and disease characteristics were generally similar between the 2 groups. At week 24 a significant higher percentage of patients receiving golimumab achieved clinical remission compared to patients receiving placebo (75% [30/40] versus 20% [4/20]; p<0.001). At week 12 similar results were observed (75% [24/32] versus 25% [6/25]; p=0.001). Overall, improvement in other outcomes were significantly greater in the golimumab group compared to the placebo group (Table 1). In the placebo group 10 out of 20 patients (50%) entered the rescue arm, compared to only 4 of 40 (10%) patients in the golimumab arm.

Conclusion. In patients with active, very early peripheral spondyloarthritis, treatment with golimumab led to high percentages of clinical remission and significant improvement in all secondary efficacy outcomes, compared to placebo, with a safety profile consistent with that observed in other anti-TNF trials in AS and PsA.

O5

KILLER IMMUNOGLOBULIN-LIKE RECEPTORS ARE ASSOCIATED WITH ANKYLOSING SPONDYLITIS

Hanson A.L.1, International Genetics of Ankylosing Spondylitis Consortium, Lè Cao K.A.1, Kennu T.J.2, Brown M.A.2
1The University of Queensland Diamantina Institute, Brisbane; 2Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia

Introduction. Killer immunoglobulin-like receptors (KIRs) are arranged in variable content haplotypes of 4 to 20 genes that differ substantially in composition across the human population. Specific HLA subtypes act as KIR ligands, and the repertoire of HLA and KIR alleles carried has been shown to alter risk for autoimmune inflammatory diseases by shifting activation thresholds of cytotoxic NK cells. We aimed to interrogate patterns in, and statistical interactions between, KIR gene and HLA alleles in a large population of individuals with ankylosing spondylitis (AS).

Methods. Gene dosages across KIR loci were imputed from Illumina human OmniExpress genotyping arrays for 10464 AS cases and 15329 control HLA-typed individuals using the statistical package KIR*IMP. Differences in KIR gene content and haplotype composition were assessed, with additional consideration of HLA type used to investigate gene-gene interactions and co-occurrence patterns in cases and controls.

Results. We identified a statistical interaction between the HLA-Bw4 recognising KIR genes KIR3DL1 and KIR3DS1 and HLA-B27 (a Bw4 type allele). Presence of the NK cell activating receptor KIR3DS1 increased risk of AS in HLA-B27 positive individuals, but was protective in HLA-B27 negative individuals (p interaction = 0.007). In contrast, inhibitory receptor KIR3DL1 exhibited the opposite pattern of association, with presence of the gene being protective in HLA-B27 positive individuals but risk predisposing in HLA-B27 negative individuals (p interaction = 0.002). We observed a suggestive disease association with KIR locus variant rs775859 (p=2x10^-4) and a significant interaction between the variant used to tag the presence of the KIR2DL5 gene and HLA-B27 (p=3x10^-4), with carriage of both KIR2DL5 and HLA-B27 increasing disease risk. Intriguingly, a significantly lower frequency of KIR2DL5 was also seen in HLA-B27+ve controls relative to HLA-B27+ve controls (p=0.001, OR=0.81), indicative of evolutionary pressure against this co-occurrence.

Conclusion. Interactions between HLA-B27 and specific KIR genes may contribute to AS by altering the inflammatory activity of NK cells.

O6

WHICH IS THE MOST RELIABLE IMAGING METHOD FOR DETECTION OF STRUCTURAL CHANGES IN THE SIJ IN AS? COMPARISON OF MRI, CT AND RADIOGRAPHS

Baralikos X., Hoffmann F., Deng X., Wang Y., Huang F., Braun J.

Background. Erosions, sclerosis and ankylosis assessed by conventional radiographs (CR) or CT are characteristic for AS. Direct reliability comparisons of CR, CT and MRI for detection of structural changes in SJJs of AS patients have not been performed to date.

Methods. Complete sets of MRI, CT and CR of 69 AS patients and 49 age- and sex-matched controls were analyzed. Two blinded readers evaluated the images independently. Assessment of lesions was performed based on SJJ-quadrate (SQ).

Results. The mean age of AS patients was 44.6 years, 72.5% were male, the mean time since diagnosis was 4.8±5.8 years. In total, 552 SQ were analyzed. Erosions were found in 131 (23.7%) SQ by CR, 141 (25.5%) by CT and in 167 (30.3%) SQ on T1-MRI. Agreement for erosions was seen for 64 SQ assessed by CT/MRI and 70 SQ by CR/MRI, with 48.9% of SQ detected by MRI and 72.8% by CT. Complete sets of MRI, CT and CR of SIJs of 69 AS patients and 49 age- and sex-matched controls were analyzed. Two blinded readers evaluated the images independently. Assessment of lesions was performed based on SJJ-quadrate (SQ).

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Discussion. Erosions and ankylosis are more common than sclerosis in AS and rarely seen in controls. The agreement between methods was limited. Compared to CT, less erosions were detected by MRI and CR. CT and MRI were more reliable than CR for the detection of ankylosis.

O7 ADDING MRI OF THE SPINE TO THE ASAS CLASSIFICATION CRITERIA FOR AXIAL SPONDYLOARTHRITIS, REDUNDANT OR BENEFICIAL?

Ez Zaitouni Z., Bakker P.1, de Hooge M.1, van den Berg R.1, van Lunteren M.1, Reijnierse M.1, Fagerli K.1, Landewé R.1, van Oosterhout M.1, Ramonda R.3, van Gaalen F.1, van der Heijde D.1
1LUMC, Rheumatology, Leiden; 2LUMC, Radiology, Leiden, The Netherlands; 3Diakoniecentrum Hospital, Rheumatology, Oslo, Norway; 4AMC, Rheumatology, Amsterdam; 5GHZ, Rheumatology, Gouda, The Netherlands; 6University of Padova, Rheumatology, Padova, Italy

Aim. To describe the prevalence of spinal inflammation on MRI (MRI-spine+), in patients with chronic back pain (CBP) at baseline and one-year follow-up, and to evaluate the yield of adding MRI-spine as imaging criterion to the ASAS classification criteria for axSpA.

Methods. The SpondyloArthritis Caught Early (SPACE)-cohort includes patients with CBP (>3 months, ≤2 years, onset <45 years). All available baseline and one-year follow-up MRI-SIJ+ and MRI-spine were scored by 2 well-calibrated readers. MRI-SIJ were scored according to the ASAS definition. To define MRI-spine+, two cut-off values were used: ≥3 inflammatory lesions (ASAS consensus definition) and ≥5 inflammatory lesions.

Results. Patients with both MRI-spine+ and MRI-SIJ+ available at baseline (n=329) and follow-up (n=168) were included in the analyses. At baseline 43/329 (13.1%) patients had MRI-SIJ+, of which 7/43 (16.3%) patients had MRI-spine+ (ASAS definition, ≥3 inflammatory lesions) and 2/43 (4.7%) if defined by ≥5 inflammatory lesions, respectively. In total, 4 patients had MRI-spine+ and ≥5 inflammatory lesions, respectively. At baseline 2 patients according to ASAS-definition of whom 1 also fulfilled the alternative definition. At follow-up this was 2 (different patients than at baseline) and 0 patients, respectively. Addition of MRI-spine to the ASAS-criteria by the ASAS definition of ≥3 inflammatory lesions would lead to 2 patients than at baseline) and 0 patients, respectively. Addition of MRI-spine to the ASAS-criteria by the ASAS definition of ≥5 inflammatory lesions resulted in 2 patients and 0 patients, respectively. Addition of MRI-spine to the ASAS criteria by the ASAS definition of ≥5 inflammatory lesions would lead to classification of 3 additional patients via imaging arm, with 1 patient already fulfilling the clinical arm.

Conclusion. In this cohort, MRI-spine+ in the absence of sacroiliitis on MRI was rarely seen. Addition of MRI-spine+ as imaging criterion to the ASAS-criteria had low yield in number of classifications. Therefore, performing MRI-spine at either baseline or one-year follow-up is of little value in patients with short duration CBP and suspicion of axSpA.

Fig. 1. Prevalence of positive MRI-AS1 according to ASAS definition and positive MRI-Spine at baseline and one-year follow-up using two different cut-off values, ≥3 inflammatory lesions (ASAS consensus definition) and ≥5 inflammatory lesions, respectively.

08 IL-7 PRIMES IL-17 IN MUCOSAL-ASSOCIATED INVARIANT T (MAIT) CELLS, WHICH CONTRIBUTE TO THE TH17-AXIS INankylosing Spondylitis

Gracey E., Quiyum Z., Inman R.
University of Toronto, Canada

Objective. Ankylosing spondylitis (AS) is a chronic inflammatory disease of unknown origin in which IL-17 has been genetically and therapeutically recognized as a key player. Identification of the cellular sources and inducers of IL-17 is crucial in our understanding of the drivers of inflammation in AS.

Recently, mucosal associated invariant T (MAIT) cells have been implicated in autoimmune diseases. MAIT cells recognize bacteria-derived vitamins presented by the MHCI-like molecule, MR1. Their gut origin, effector phenotype, and expression of multiple AS-associated genes, such as IL7R and IL23R, makes them potential contributors to the pathogenesis of AS.

Methods. Mononuclear cells from AS patients (n=50), healthy controls (HC) (n=30) and rheumatoid arthritis (RA) (n=12) patients were isolated from blood and synovial fluid (SF). Flow cytometry was used to identify MAIT cells. Phenotype was assessed by intracellular staining for cytokines and granzyme.

Function was assessed by antigen-specific stimulation using Salmonella, or antigen non-specific activation via priming with IL-7 or IL-23. MAIT cells were reduced in frequency in the blood of AS patients compared to HC (% of T cells: 2.7±0.34 vs. 1.9±0.29, p=0.01), yet AS patients had an elevated frequency IL-17+ MAIT cells (%IL-17; 6.0±0.63 vs. 4.1±0.48, p=0.02). There was an enrichment of MAIT cells in SF, which had an exaggerated IL-17 phenotype. In all subjects, MAIT cells were found to have high expression of the IL-7R compared to other cell types. Further, IL-7R was elevated on AS patient MAIT cells compared to HC (IL-7R MFI 2030±476 vs 1516±85, p=0.0001), but not on conventional T cells. IL-17 elevation in AS MAIT cells was dependent on priming with IL-7 but not IL-23 or antigen stimulation. The AS-associated IL7R SNP, rs11742270, had no correlation with IL-7R expression or MAIT cell function in the experiments performed.

Conclusion. This study reveals a potential role for MAIT cells in the pathogenesis of AS and is the first link IL-7 to the elevated IL-17 profile in patients through the AS-associated risk gene IL7R.

09 HIGH DOSE NSAIDS AND TUMOR NECROSIS FACTOR INHIBITORS USE SYNERGIZE TOWARDS LESS RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS — A LONGITUDINAL ANALYSIS

1University of California, San Francisco, Dept. of Medicine, San Francisco; 2University of Texas Health Science Center at Houston, Dept. of Medicine, Houston; 3National Institute of Health (NIH), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), Bethesda; 4Cedars Sinai Medical Center, Dept. of Medicine, Los Angeles, USA; 5Queensland University of Technology, Brisbane, Australia

Introduction/Aim. Over the last decade, the effects of NSAIDs and Tumor Necrosis Factor inhibitors (TNFi) have resulted in controversial studies. No study has examined their relationship longitudinally addressing both NSAID and TNFi on radiographic progression in AS.

Patients and Methods. We included 527 patients meeting the modified New York criteria in a prospective cohort with at least 2 years of clinical and radiologic follow up. Progression was defined longitudinally, with ≥2 modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) unit increase in 24 months. Patients were censored when they could not progress over the next follow up period. We used a mixed-effects longitudinal logistic regression model to determine the multivariable associations between TNFi use and radiographic progression accounting for correlations within patients.

Results. Patients were followed for 3.67 (2.68, 6.00) years. NSAIDs and TNFi were used in 78.0% and 58.4% of patients respectively. Of 1,413 visits included in this analysis, 386, 29% and 23% had an NSAID index of 0, >0 ≤, and >0, respectively. Multivariable results showed an increased effect of using both TNFi and NSAIDs (p=0.034), however the adjusted odds ratio of progression was only significant for those using TNFi and NSAIDs with an index >50 (OR=1.07, 95%CI 1.05, 1.05, p=0.003).

Conclusion. There is less radiographic progression in AS patients taking higher doses of NSAIDs regularly and using TNFi via effect modification.
targeting the microbiome may be effective in AS prevention and/or treatment. A primary event in AS pathogenesis rather than secondary to disease or its treatment.

Conclusion.

is consistent with the microbial signature described in AS cases.

TI also showed clear and distinct clustering of HLA-B27+ from HLA-B27- samples (p<0.001; PERMANOVA). The T1 also showed clear and distinct clustering of HLA-B27+ from HLA-B27- samples (p=0.0063; PERMANOVA). The T1 showed clear and distinct clustering of HLA-B27+ from HLA-B27- samples (p<0.001) and Clostridiales (p<0.05) and increases in Bacteroidaceae (p<0.05) and Ruminococcaceae (p<0.05).

Fig. 1. Estimated probability of progression based on NSAID index and TNFi use.

O11

POSITIVE SACROILIAC JOINT MRI IN ASYMPTOMATIC PATIENTS WITH RECURRENT ACUTE ANTERIOR UVEITIS: A PROOF OF CONCEPT

Oliveira T.L., Mackeymowich W.P.L.; Lambert R.G.; Maccioni C.; Pinheiro M.J.; Rheumatology Division, Federal University of São Paulo, São Paulo, Brazil; 2Dept. of Medicine, University of Alberta, Edmonton; 3Dept. of Radiology and Diagnostic Imaging, University of Alberta, Edmonton, Canada; 4Ophthalmology Division, Federal University of São Paulo, São Paulo, Brazil

Background. Recurrent acute anterior uveitis (rAAU) is associated with spondyloarthritides (SpA).

However, it is not known if patients with rAAU but no back symptoms could have positive findings on sacroiliac joint (SIJ) MRI.

Aim. To assess the prevalence of definite SpA by combined TWIST/STIR MRI (global MRI), to quantify acute and chronic lesions in SIJ using MRI in patients with rAAU with and without back symptoms, and to assess which MRI lesion-based criteria optimally reflect the global MRI designation of definite SpA.

Patients and Methods. A total of 50 consecutive patients with rAAU without prior rheumatologic diagnosis were included in this cross-sectional study and were compared to 21 healthy volunteers.

MRI scans were read by two rheumatologists according to the SPARC/MORPHO protocol.

Results. rAAU patients were classified as axial SpA (Group 1, n=20), according to ASAS criteria (2009); non-specific back pain (Group 2, n=8) and asymptomatic (Group 3, n=24). The groups were similar regarding age, sex, ethnicity, age at onset of uveitis, current uveitis activity and duration of eye disease. HLA-B27 was positive in 44% of those with rAAU. Considering only group 3, nine (37.5%) patients had SIJ MRI and/or X-ray positive for axial SpA (5 MRI and x-ray, 1 MRI, 3 x-ray). MRI scans compatible with SpA in groups 1(n=12) and 3 (n=6) were similar regarding acute and chronic lesions analysed according to MORPHO. The best sensitivity/specificity criterion to define a positive global MRI assessment was bone marrow edema (BME) ≥ 3 (92%/94%).

Conclusions. This is the first study evaluating SIJ MRI in patients with rAAU without back symptoms showing positive findings for sacroiliitis, confirming a uvea-axial spine link, and BME ≥ 3 as optimal for a positive MRI.

O12

A FAMILY-BASED GENOME-WIDE ASSOCIATION STUDY REVEALS AN ASSOCIATION OF Spondyloarthritis with MAPK14


1INSERM U1173, Faculty of Health Sciences Simone Veil, University of Versailles Saint-Quentin-en-Yvelines; 2Erinville Hospital (AP-HP), Boulogne-Billancourt; 3National Genotyping Center, Evry, France; 4Rheumatology Division, Cedars-Sinai Medical Center, Los Angeles, California; 5Rheumatology and Clinical Immunogenetics, University of Texas Health Science Center at Houston, Houston, Texas, USA

Aim. More than 45 loci have been associated to ankylosing spondylitis (AS) but less is known about genetic associations in spondyloarthritis (SpA) as a whole. We conducted a family-based genome-wide association study (GWAS) to identify new non-MHC genetic factors associated with SpA.

Methods. 906 subjects from 156 French multiplex families, including 438 with SpA, were genotyped using Affymetrix 250K microarrays. Association was tested with Unphased. The best-associated non-MHC SNPs were then genotyped in two independent familial cohorts, (including 215 French and 294 North American SpA patients, respectively) in order to replicate associations.

Results. 43 non-MHC SNPs yielded an association signal with SpA in the discovery cohort (p<1x10^-10). In the extension studies, association was replicated at a nominal p value of p<0.05 for 16 SNPs in the second cohort and for 3 SNPs in the third cohort. Combined analysis identified an association close to genome-wide significance between rs761118, an intronic SNP of MAPK14, and SpA (p=3.5x10^-10).

Conclusions. We report here for the first time a family-based GWAS study on SpA and identified an associated polymorphism near MAPK14. Further analyses are needed to better understand the functional basis of this genetic association.

Table 1. Longitudinal association of NSAID and TNFi use with radiographic progression, taking into account interaction, while controlling for potential confounding.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adj. Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID use vs. no NSAID use</td>
<td>0.73 (0.57, 0.93)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NSAID use vs. no NSAID use</td>
<td>0.86 (0.65, 1.13)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NSAID use vs. no NSAID use</td>
<td>0.93 (0.80, 1.08)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NSAID use vs. no NSAID use</td>
<td>0.98 (0.86, 1.12)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>NSAID use vs. no NSAID use</td>
<td>0.99 (0.88, 1.12)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
P1  
**ASDAS-BASED REMISSION WAS LESS FREQUENT THAN BASDAIL-BASED REMISSION, AND BOTH WERE RELATED TO CRP AND SMOKING IN EARLY AXIAL SPONDYLOARTHRITIS – THE DESIR COHORT**  
Wendling D., Guillot X., Gossec L., Prati C., Saraux A., Dougadois M.  
CHRU Besançon, Pitié Hospital, Paris; CHU Brest; Cochin Hospital, Paris, France

Remission is the final goal for treat to target strategy in axial spondyloarthritis (axSpA). No clear definition is currently recognized, but ASDAS- CRP inactive state or BASDAI threshold (1) have been proposed. The frequency of remission using these definitions and factors associated with remission are unknown in early axSpA.

**Aim:** To evaluate the percentage of patients in remission in early AxSpA, comparing different definitions of remission, and to evaluate factors associated with remission inclusion in the DESIR cohort and after 24 months.

**Methods:** DESIR is a prospective observational cohort of patients with recent onset (less than 3 years) inflammatory back pain, beginning before 45 years, suggestive of axial SpA. For each of three definitions of remission (ASAS partial remission (PR), ASDAS-CRP less than 1.3 (ASDAS-R), BASDAI less than 3.6 (1)BASDAI-R), the ability to detect patients in remission according to the two other definitions was assessed through ROC curves and Areas Under the Curve (AUC). Data at baseline (M0) and M24 were analyzed, to look for factors (clinical, biological and imaging) associated with remission in univariate and multivariate analysis by logistic regression.

**Results:** 706 patients were evaluated at M0 and 577 at M24. At M0, the percentage of patients in remission was 4% (PR), 8% (ASDAS) 34 % (BASDAI), and at M24 15%, 24% and 54% respectively, in the whole population and in Amor, ESSG and ASAS classed patients, but lower in mNY patients (data not shown). BASDAI less than 3.6 detected best patients in PR and ASDAS-R, with AUC of 0.84 and 0.86 respectively. In univariate analysis at M0, lower ESR and CRP, DKK-1, low BMI, male gender, absence of psoriasis, less smoking, HLA B27 positivity, ASAS criteria fulfillment, positive sacro iliac imaging, less analgesics use and less subsequent use of anti TNF at M24 were associated with remission (ASDAS-R, BASDAI-R). No association was found with age, disease duration, disease duration, ankylosing spondylitis, ureditis, IBD, NSAID use, mSASAE. In multivariate analysis, remission was associated with lower ESR, less smoking, use of analgesics. At M24, low ESR and CRP, female gender, less smoking, less NSAID use, lower NSAID score, ASAS criteria fulfillment, lower biologics use and lower systemic steroid use were associated with remission in univariate analysis. In multivariate analysis, remission was associated with less smoking, less analgesics, ASAS clinical arm fulfillment, less NSAIDs (ASDAS-R), low CRP (ASDAS-R), low BMI/BASDAI-R (Table I).

**Conclusion:** In this population suggestive of early SpA, BASDAI less than 3.6 seems a fair assessment of remission. As expected, acute phase reactants and analgesics were associated with remission at baseline and M24, but smoking appears as a major marker of disease activity and remission in early AxSpA.

**Acknowledgements:** The DESIR cohort is supported by an unrestricted grant from PPFZER France.

**Reference**  

Table I. Results of multivariate analysis; r: regression coefficient, *p<0.05; **p<0.001; ***p<0.0001

<table>
<thead>
<tr>
<th>Remission</th>
<th>ASDAS-R</th>
<th>ASDAS-c1.3</th>
<th>r,p</th>
<th>BASDAI-R</th>
<th>BASDAI&lt;3.6</th>
<th>r,p</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0 N=706</td>
<td>CRP</td>
<td>-0.59***</td>
<td>0.59</td>
<td>ESR</td>
<td>-0.04*</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>Smoking</td>
<td>-1.5**</td>
<td>0.55</td>
<td>Smoking</td>
<td>-0.93*</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>Analgesics</td>
<td>1.55***</td>
<td>0.39</td>
<td>Analgesics</td>
<td>1.39**</td>
<td>0.39</td>
</tr>
<tr>
<td>M24 N=577</td>
<td>CRP</td>
<td>-0.6***</td>
<td>0.6</td>
<td>BMI</td>
<td>-0.14**</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>Smoking</td>
<td>-1.08*</td>
<td>0.6</td>
<td>Smoking</td>
<td>-1.16**</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>ASDAS clinical</td>
<td>1.76*</td>
<td>0.5</td>
<td>ASDAS clinical</td>
<td>1.28*</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>NSAIDs</td>
<td>-1.4**</td>
<td>0.5</td>
<td>NSAIDs</td>
<td>-1.4**</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Analgesics</td>
<td>-2.02***</td>
<td>0.0001</td>
<td>Analgesics</td>
<td>-1.74***</td>
<td>0.0001</td>
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</table>

P2  
**EVOLUTION OVER THIRTY YEARS OF THE PROFILE OF IN-PATIENTS WITH REACTIVE ARTHRITIS IN A TERTIARY RHEUMATOLOGY UNIT**  
Brinster A., Guillot X., Prati C., Wendling D.  
CHRU, Besançon, France

Reactive arthritis (ReA) are sterile arthritis occurring after extra articular bacterial infection, mainly located in gut or genito urethral mucosa.

**The aim of this study was to analyze, over 30 years, frequency as well as clinicobiological and therapeutic characteristics of ReA, comparing two periods.**

**Methods:** In this retrospective monocentric study, the charts of all the patients followed in our unit between January 1st 1984 and April 2014 with the diagnosis of ReA, according to International Classification Criteria (1), were recorded and clinic biological features, management and outcome were analyzed, and compared between two periods: from January 1984 to December 1993, and from January 2004 to December 2013.

**Results:** 62 patients fulfilling international diagnosis criteria were analyzed. We found no significant differences (Table) between the two periods in incidence of new cases, clinical presentation (rheumatologic and extra articular features), biological and microbiological data or outcome. Change in therapeutic management was obvious with occurrence of anti TNF use in the recent period.

**Conclusion:** Reactive arthritis is still a current rheumatologic problem, with an apparently stable incidence in a developed country, with a need of early and tailored rheumatologic management.

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Number of patients included</td>
<td>15</td>
<td>31</td>
</tr>
<tr>
<td>Number of patients hospitalized</td>
<td>7438</td>
<td>11 823</td>
</tr>
<tr>
<td>Men</td>
<td>13</td>
<td>28</td>
</tr>
<tr>
<td>Median age at diagnosis</td>
<td>37</td>
<td>30</td>
</tr>
<tr>
<td>HLA B27 (+) (%)</td>
<td>91</td>
<td>63</td>
</tr>
<tr>
<td>Delay between infection/articular symptoms (days) median</td>
<td>5.9</td>
<td>9</td>
</tr>
<tr>
<td>Leucocytes (giga/l)</td>
<td>9.8</td>
<td>10.6</td>
</tr>
<tr>
<td>CRP (mean) (mg/l)</td>
<td>87.4</td>
<td>90.1</td>
</tr>
<tr>
<td>Evidence of infectious agent (%)</td>
<td>53</td>
<td>61</td>
</tr>
<tr>
<td>TJC / SJC</td>
<td>2.8 / 1.8</td>
<td>3.2 / 2</td>
</tr>
<tr>
<td>Dactylitis (%)</td>
<td>13</td>
<td>29</td>
</tr>
<tr>
<td>Enthesitis (%)</td>
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<td>26</td>
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<tr>
<td>Extra articular features (%)</td>
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<td>35</td>
</tr>
<tr>
<td>Axial symptoms (%)</td>
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<td>29</td>
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<tr>
<td>DMARDS use (%)</td>
<td>36</td>
<td>62</td>
</tr>
<tr>
<td>Median delay of DMARD introduction (days)</td>
<td>210</td>
<td>50.5</td>
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<tr>
<td>Biologic agents use (%)</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td>Remission at last follow-up (%)</td>
<td>57</td>
<td>47</td>
</tr>
</tbody>
</table>

P3  
**WORK STATUS AND RELATED VARIABLES IN PATIENTS WITH ANKYLOSING SPONDYLITIS**  
Sag S., Nas K., Sag M.S., Tekeoglu I., Kamanli A.  
Sakarya University Medical Faculty, Division of Rheumatology, Dept. of Physical Medicine and Rehabilitation, Sakarya, Turkey

**Objectives:** The aim of this study was to determine the work status in patients with ankylosing spondylitis (AS) while also defining the factors related to work disability.

**Patients and Methods:** Fifty patients with AS (35 males, 15 females; mean age 41.5±7.7 years) and thirty patients with healthy control (20 males, 10 females; mean age 42.6±7.8years) were included in the study. The demographic and disease-related variables were recorded. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASM) and Bath Ankylosing Spondylitis Functional Index (BASFI) in AS patients, to determine disease activity and functional status. The Short Form Health Survey (SF-36) Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL), Hospital Anxiety and Depression Scale (HAD), Work Productivity and Activity Impairment Questionnaire: Specific Health Problem V2.0 (WP/SHP) were used to assess quality of life (Qol.), depression and anxiety, work productivity respectively.

**Results:** The mean age, age at onset of disease, education level and gender of the patients and healthy control were similar between the group (p>0.05). The diagnosis age of the patient was 7.2±6.25. In patients with AS according to control group, time lost from work was more due to health problems. Reduction
P4

HIGHER SERUM LEVEL OF LEPTIN MIGHT BE RESPONSIBLE FOR LESS STRUCTURAL DAMAGE IN THE SPINE IN FEMALE PATIENTS WITH ANKYLOSING SPONDYLITIS

Podrubny D.1, Hartl A.1, Hermann K.G.1, Ruuwadele M.2, Sieper J.1
1Charité Universitätsmedizin Berlin, Berlin; 2Klinikum Bielefeld Rosenhöhe, Bielefeld, Germany

Objective. The aim of this study was to investigate the gender-specific role of adipokines as predictors of radiographic spinal progression in patients with ankylosing spondylitis (AS).

Materials and Methods. Altogether 120 patients (82 men and 38 women) with AS from the Effects of NSAIDs on Radiographic Damage in AS (ENRADAS) trial who completed the study per protocol were included into the analysis. Serum levels of adipokines (leptin, adiponectin, lipocalin-2, omentin, visfatin, resistin, and chemerin) were measured at baseline using ELISA.

Results. The significant association with radiographic spinal progression was found for leptin only. Mean baseline leptin levels were significantly lower in patients with mSASSS worsening by ≥2 units after 2 years (p=0.02) as compared to those without progression (n=91): 10.1±6.6 vs. 15.7±13.4 ng/ml, respectively, p0.002, and in patients with syndesmophyte formation (n=25) as compared to those without syndesmophyte formation (n=95): 10.1±6.6 vs. 15.7±13.4 ng/ml, respectively, p=0.002. This difference was especially evident in males, but not in females. However, in females the serum level of leptin at baseline was in general significantly higher than in males: 24.0±17.4 vs. 10.2±6.8 ng/ml, p<0.001 that was independent of body mass index. In the logistic regression analysis, a protective value of higher leptin levels was found for baseline syndemophytes, elevated C-reactive protein (CRP), smoking, body mass index, sex, and disease-related factors. In the logistic regression analysis, a protective value of higher leptin levels was found for baseline syndemophytes, elevated C-reactive protein (CRP), smoking, body mass index, sex, and disease-related factors.

Conclusions. Higher serum levels of leptin seem to protect patients AS from radiographic spinal progression. Female patients with AS have significantly higher leptin levels that might explain lesser extent of structural damage in the spine in female AS patients in general.

P5

ARE INDIVIDUAL OR COUNTRY LEVEL SOCIO-ECONOMIC DETERMINANTS RELATED TO DISEASE ACTIVITY AND SELF-REPORTED PHYSICAL FUNCTION IN PATIENTS WITH SPONDYLOARTHRITIS? RESULTS FROM MULTI-NATIONAL CROSS-SECTIONAL STUDY ASAS-COMOSPA

Putrik P.1, Ramirez S.2, Molto A.3, Keszei A.4, Dougdos M.1, van der Heijde D.2, Landewé R.3, Boonen A.1
1MUMC, Maastricht; 2LUMC, Leiden, The Netherlands; 3Paris Descartes University, Paris, France; 4Aachen University, Aachen, Germany; 5ARC, Amsterdam, The Netherlands

Introduction/Aim. In RA, socio-economic health inequalities were observed, and unequal uptake of biologic DMARDs (bDMARDs) played an important role. It is not known whether the same pattern is present in spondyloarthritis (SpA). The objective of this study was to assess: (1) independent associations of individual and country level socio-economic determinants with disease outcomes in SpA (2) if confirmed, whether this relation is mediated by uptake of bDMARDs. Materials and Methods. Data from the cross-sectional COMORbilities study in SpA (ASAS-COMOSPA) were used. Contribution of individual socioeconomic factors (age, gender, education) and country of residence to ASDAS and BASFI was explored in regression models, adjusting for clinical confounders. Next, country of residence was replaced by gross domestic product (low vs high) adjusted for purchasing power parity (GDP-PPP). Finally, the role of bDMARDs uptake in the relationship between education or GDP and ASDAS was explored by testing indirect effects.

Results. In total 3,984 patients with SpA from 22 countries were included: 65% males, mean age 44(SD14), ASDAS 2.0(±1.1), ASDAS 2.0(±1.1), and BASFI 3.0(±2.7). Five to 78% of patients were currently treated with bDMARDs. Females had higher ASDAS (β=0.20 [95% CI 0.12-0.28]) and BASFI (β=0.47 [95% CI 0.33;0.62]). The effect of age was negligible for both outcomes. Low vs university educated individuals had higher ASDAS and BASFI (β=0.24 [0.12;0.36] and β=0.45 [0.23;0.67], respectively). Independent of the individual confounders, large country differences were observed. Low GDP was associated with higher ASDAS (β=0.34 [0.26;0.42]) and higher BASFI (β=0.19 [0.04;0.34]). Uptake of bDMARDs did not mediate relationship between education or GDP with ASDAS.

Discussion/Conclusions. Health inequalities across individual and country level socio-economic factors exist also in SpA. Females, lower educated patients and patients from low income countries have higher disease activity and to a lesser extent worse physical function.

P6

PREVALENCE OF PERIPHERAL AND EXTRA-ARTICULAR DISEASE IN ANKYLOSING SPONDYLITIS VERSUS NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: A META-ANALYSIS

De Winter J.J.1, Van Mens L.J.1, Van der Heijde D.2, Landewé R.1, Baeten D.L.1,2,3,4,5
1Dept. of Clinical Immunology and Rheumatology, Amsterdam Rheumatology and Immunology Center, Academic Medical Center/University of Amsterdam, Amsterdam; 2Dept. of Rheumatology, Leiden University Medical Center, Leiden; 3Dept. of Experimental Immunology, Academic Medical Center/University of Amsterdam, Amsterdam, The Netherlands

Background. Peripheral arthritis, enthesitis and dactylitis and extra-articular disease (uveitis, psoriasis and inflammatory bowel disease) are common in ankylosing spondylitis (AS) and non-radiographic axial spondylarthritis (nr-axSpA). So far, however, summary data on the prevalence are lacking. The objective of this meta-analysis was to assess the prevalence of peripheral extra-articular manifestations in ankylosing spondylitis (AS) and nr-axSpA.

Methods. We performed a systematic literature search to identify publications describing the prevalence of peripheral and extra-articular disease manifestations in patients with AS and nr-axSpA. We assessed the risk of bias, between-study heterogeneity and extracted data. Pooled prevalence and prevalence differences were calculated.

Results. Eight studies including 2236 AS patients and 1242 nr-axSpA patients were included. Seven out of 8 studies were longitudinal cohort studies. There was a male dominance in AS (70.4%; 95%CI 64.4-76.6%) but not in nr-axSpA (46.8%; 95% CI 41.7-51.9), which was independent from HLA-B27 prevalence. HLA-B27 prevalence was similar in AS (78.0%; 95% CI 73.9-81.9%) and nr-axSpA (77.4%; 95% CI 69.8-84.9%). The pooled prevalence of arthritis (29.7% [95% CI 22.4-37.4%] versus 27.9% [95% CI 16.0-41.6%]), enthesitis (30.4% [95% CI 3.7-65.8%] versus 34.1% [95% CI 4.7-71.0%]), dactylitis (6.0% [95% CI 4.7-7.5%] versus 6.0% [95% CI 1.9-12.0%]), psoriasis (10.2% [95% CI 7.5-13.2%] versus 10.9% [95% CI 9.1-12.7%]), uveitis (0.26% [95% CI 0.10-0.46%] versus 0.6% [95% CI 0.3-0.9%]), and inflammatory bowel disease (15.0% [95% CI 11.8-18.3%] versus 15.9% [95% CI 11.8-20.4%]).

Conclusion. Peripheral and extra-articular manifestations are equally prevalent in AS and nr-axSpA, except for uveitis, which is slightly more prevalent in AS. These data provide evidence for the largely equal nature of disease manifestations in nr-axSpA and AS.
ASSOCIATION OF THE PROFILE OF JOINT INVOLVEMENT IN THE SPONDYLOARTHRITIDES IN REGIONS OF DIFFERENT ETHNIC BACKGROUND IN BRAZIL

Ribeiro S.L.E.1, Campos A.P.B.2, Palomino P.E.3, Bortoluzzo A.B.4, Costa M.A.C.1, Ribeiro T.O.1, Sampaio-Barros P.D.9
1Hospital Universitário Gênero Vargas, Rheumatology Dept., Federal University of Amazonas, Manaus; 2Hospital Universitário Evangélico de Curitiba, Rheumatology Dept., Curitiba; 3Hospital de Clínicas de Porto Alegre, Rheumatology Dept., Federal University of Rio Grande do Sul, Porto Alegre; 4Inspier Institute of Education and Research, Sao Paulo; 5Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

Aim. To analyze the profiles of joint involvement in the Spondyloarthritides (SpA) in regions of different ethnic background in Brazil.

Methods. A common protocol of investigation was prospectively applied to 204 SpA patients distributed in the North (Manaus, n=66) and in the South (Curitiba, n=84 and Porto Alegre, n=54) of Brazil. All the patients were classified as axial or peripheral SpA according to the Assessment of SpondyloArthritis international Society (ASAS) criteria. Clinical and demographic variables and disease indexes (BASDAI, ASDAS-ESR, ASDAS-CRP, BASFI, MASES, SPARCC, LEI, ASQoL) were analyzed. According to the ethnic background, patients were considered as whites and non-whites; among the non-whites, we compared those from the South with those from the North.

Results. Comparing demographic and clinical data according to ethnicity, white patients (n=158, 77%) had higher positive HLA-B27 (p=0.001) and nail involvement (p=0.032), and performed more physical exercise (p=0.026). Non-whites were statistically associated with peripheral arthritis in the lower (p=0.035) and upper trunk (p=0.005), and rheumatoid arthritis (p=0.008). The comparison among the non-white patients from the north with those from the south showed that while patients from the north were more frequently males (p=0.010) with higher intake of NSAIDs (p=0.001) and methotrexate (p=0.035), patients from the south were statistically associated with female gender (p=0.01), arthritis in the lower limbs (p=0.033), anterior uveitis (p=0.011), higher values of BASDAI (p=0.012), ASQoL (p=0.001), ASDAS-CRP (p=0.001) and HAQ (p=0.001), and were more frequently prescribed adalimumab (p=0.001).

Conclusion. Ethnic background is associated with a distinct clinical profile in SpA patients from different Brazilian regions.

COMPARISON OF CLINICAL CHARACTERISTICS BETWEEN SMOKING AND NON-SMOKING PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A META-ANALYSIS

Barnish M.S.1,2, Dean L.E.3,4, Jones G.T.1,2, Pathan E.3,4, Macfarlane G.J.1,2
1Epidemiology Group, University of Aberdeen, Aberdeen; 2Aberdeen Centre for Arthritis and Musculoskeletal Health, University of Aberdeen, Aberdeen; 3Dept. of Rheumatology, Aberdeen Royal Infirmary, Aberdeen, UK

Introduction/Aim. Cigarette smoking has been associated with worse clinical markers of disease in axial spondyloarthritis (axSpA). The aim of the current study was to quantify these adverse effects.

Materials and Methods. We searched seven bibliographic databases, six rheumatology journals, and Google Scholar up to April 2016. Abstracts from major international conferences from 2014/2015 and reference lists of identified articles were also searched. Eligible studies of patients with axSpA were required to quantify the relationship between smoking (ever vs never, or current vs non-current) and at least one of the following: disease activity (BASDAI), global severity (BAS-G), functional ability (BASFI) and quality of life (ASQoL). The association between smoking status and these clinical measures was examined using random effects meta-analysis.

Results. From 934 publications identified, 18 papers from 14 studies were eligible. Compared to “never smokers”, “ever smoking” patients reported significantly worse BASDAI (mean difference 0.35, 95%CI 0.06-0.63), BAS-G (0.95, 0.23-1.68), BASFI (0.88, 0.63-1.12) and ASQoL (1.65, 0.59-2.72). Current smokers (compared to patients not currently smoking) had significantly worse BASDAI (1.07, 0.71-1.54), BASFI (1.31, 1.06-1.64) and ASQoL (1.99, 1.64-2.41). There was insufficient data to compare global severity (BAS-G) between current and non-current smokers.

Discussion/Conclusions. Smoking in patients with axSpA was associated with worse disease severity, functional ability and quality of life. Effects of smoking status were smaller for BASDAI than for other clinical measures. Overall, the difference between current smokers and non-current smokers was greater than between “ever smokers” and “never smokers”. Clinicians should encourage, and provide support for, smoking cessation as part of their routine management, to realise not only general health benefits but also to improve markers of disease severity.

WORK INSTABILITY IS ASSOCIATED WITH INCREASING WORK ABSENCE AND IMPAIRMENT IN THE SHORT TERM: RESULTS FROM THE SCOTLAND REGISTRY FOR ANKYLOSING SPONDYLITIS (SIRAS)

Jones G.T.1,2, Dean L.E.3,4, Harkess J.1, Macfarlane G.J.1,2
1Epidemiology Group, University of Aberdeen, Aberdeen; 2Aberdeen Centre for Arthritis and Musculoskeletal Health, University of Aberdeen, Aberdeen; 3Fife Rheumatic Diseases Unit, Whytemans Brae Hospital, Kirkcaldy, UK

Introduction. Ankylosing spondylitis (AS) may substantially impact on both performance and ability to remain in work. The AS Work Instability Scale (AS-WIS) aims to identify those at highest risk of work loss (work unstable) but has, to date, not been widely utilised. The aim of this analysis was to assess, longitudinally, work outcomes amongst AS patients identified as being work unstable.

Patients and Methods. The Scotland Registry for AS (SIRAS) is a disease registry collecting information on AS patients seen in rheumatology. Postal questionnaires collect patient-reported data at recruitment and yearly follow-ups, including the ASWIS, and Work Productivity and Activity Impairment: Specific Health Problem (WPAI-SHP). The relationship between being work unstable at initial follow-up, and work loss one year later was assessed by Poisson regression. Changes in work absence/impairment (WPAI-SHP absenteeism/presenteeism) were also assessed. Results are expressed as risk ratios with 95% confidence intervals.

Results. Information was available for 388 employed participants, of whom 39% were characterised as being work unstable (ASWIS score 11-20). After one year; 7% of this group had experienced work loss (versus 1% of work stable; RR 6.3, 95%CI 3.75-10.7) and a higher proportion reported increases in both sickness absence and work impairment (11% versus 3%; 4.1, 1.1-15.9, and 51% versus 25%; 1.6, 1.1-2.3 respectively). Of those still employed 10% had changed their job whereas 3% had left work. Although few participants experienced work loss, those who were characterised as being work unstable were at higher risk of work impairment and absence after one year. Studies with longer follow-up are required to assess the stability and work impairment of this group.
Poster Presentations

Tenth International Congress on Spondyloarthritides

P11
INCREASED SMOKING EXPOSURE IS ASSOCIATED WITH INCREASED DISEASE SEVERITY IN AXIAL SPONDYLO-ARTHRITIS: RESULTS FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER FOR ANKYLOSING SPONDYLITIS (BSRBR-AS)
Zhao S.1, Jones G.T.2, Barnish M.S.2,3, Dean L.E.2,3, Macfarlane G.J.1,2, Singru T.2, Goodson N.1
1Dept. of Rheumatology, Aintree University Hospital, Liverpool; 2Epidemiology Group, University of Aberdeen, Aberdeen; 3Aberdeen Centre for Arthritis and Musculoskeletal Health, University of Aberdeen, Aberdeen; 4Royal United Hospitals Bath NHS Foundation Trust, Bath, UK

Introduction. Several studies have shown that, in axial spondyloarthritis (axSpA), smoking is associated with worse disease. However, previous studies are limited in their ability to evaluate any potential dose effects. This study aimed to quantify the effect of smoking status, cessation, and dose, across several disease outcomes.

Methods. The BSRBR-AS recruits biologics-naïve ASAS-classification axSpA and patients. Data collection includes self-reported smoking status and various measures of disease severity. Multivariable linear models were used to examine the relationship between smoking and disease activity (BASDAI), function (BASFI), metrology (BASMI), spinal pain (VAS), and quality of life (AQoL).

Comparisons were made between ever versus never-smokers; current versus ex-smokers; and heavy versus light smokers. Results. 932 axSpA patients were analysed (71% male, mean age 50yrs) including 19% current smokers, 37% ex-smokers, and 44% never smokers. Ever smokers reported a mean BASDAI score >1 unit higher than never smokers (1.04; 95%CI: 0.72, 1.36). Similarly, current smokers reported higher BASDAI than ex-smokers (0.90; 0.43, 1.37). Worse disease was evident among ever smokers and current smokers across all five disease markers (see table). Heavy smoking (>10 cigarettes per day) was reported by 37%. However, smoking dose was associated with no statistically significant differences in any disease outcome measured (see table).

Discussion. This large study of biologics-naïve axSpA patients has demonstrated that smoking is associated with worse disease, across a number of disease metrics. Ever smokers have worse disease than never smokers, and current smokers have worse disease than ex-smokers. Every effort should be made to help axSpA patients stop smoking altogether; the data suggest that cutting down (to <10 cigarettes per day) may not be sufficient to yield improvements in disease outcome.

Table. Multivariable linear regression models demonstrating associations between markers of disease severity and smoking status. All analyses are adjusted for age, gender, BMI and HLA-B27.

<table>
<thead>
<tr>
<th>N</th>
<th>BASDAI</th>
<th>BASFI</th>
<th>BASMI</th>
<th>Spinal VAS</th>
<th>AQoL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever smoker</td>
<td>724/408</td>
<td>1.04</td>
<td>1.34</td>
<td>0.61</td>
<td>1.11</td>
</tr>
<tr>
<td>never-smoker</td>
<td>(0.72, 1.36)</td>
<td>(0.98, 1.69)</td>
<td>(0.36, 0.87)</td>
<td>(0.74, 1.49)</td>
<td>(2.01, 3.41)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>173/347</td>
<td>0.90</td>
<td>1.21</td>
<td>0.50</td>
<td>0.87</td>
</tr>
<tr>
<td>non-smoker</td>
<td>(0.43, 1.37)</td>
<td>(0.67, 1.74)</td>
<td>(0.12, 0.88)</td>
<td>(0.30, 1.45)</td>
<td>(1.42, 3.52)</td>
</tr>
<tr>
<td>Heavy smoker</td>
<td>64/108</td>
<td>0.29</td>
<td>0.55</td>
<td>0.34</td>
<td>0.84</td>
</tr>
<tr>
<td>light smoker</td>
<td>(0.46, 1.03)</td>
<td>(0.32, 1.43)</td>
<td>(0.34, 1.02)</td>
<td>(0.04, 1.73)</td>
<td>(0.49, 2.9)</td>
</tr>
</tbody>
</table>

1Among current smokers; heavy smoking defined as >10 cigarettes per day; smoking quantity data missing for 5 participants.

P13
ASSESSING PHYSICAL ACTIVITY IN AXIAL SPONDYLOARTHRITIS PATIENTS: MODIFICATION OF THE SQUASH
Maas F.1, Baron A.J.2,3, Wink F.R.1,2, Bos R.1, Kamsma Y.P.T.2, Bootma H.1, Arends S.1,2, Spoorenberg A.1,2
1Rheumatology and Clinical Immunology, University Medical Center Groningen; 2Center for Human Movement Sciences, University Medical Center Groningen; 3Rheumatology, Medical Center Leeuwarden, The Netherlands

Introduction. Improvement of physical function and physical activity are important goals in the management of axial spondyloarthritis (axSpA). Although physical function is included in the ASAS/OMERACT core domains for axSpA, no physical activity questionnaire has been developed for axSpA. The Short Questionnaire to Assess Health-enhancing physical activity (SQUASH) is a validated questionnaire that measures the intensity and frequency of physical activity in five domains (i.e. commute, work, household, recreation and sports). Our objective was to explore the opinion of axSpA patients and experts towards the content and adaptation requirements of the SQUASH in order to develop a disease-specific SQUASH.

Methods. A qualitative study design based on a stepwise approach was used. First, a semi-structured, in-depth interviews concerning the SQUASH domains in relation to the disease were performed with 9 professional axSpA experts (e.g. rheumatologists, rehabilitation specialists, physiotherapists). Second, a structured focus group concerning the SQUASH domains was performed with 8 axSpA patients (7 AS and 1 nr-axSpA) from the GLAS cohort and suggestions for possible adaptations were discussed. Data were recorded, transcribed, and analyzed using an objective thematic strategy. Finally, the SQUASH was adapted based on adaptations suggested by ≥5 experts and ≥5 patients.

Results. The SQUASH was found to be relevant and easy to complete. The experts and patients suggested 34 adaptations of which 16 were implemented. The most important adaptations were: explanation of intensity concepts (e.g. increased heart rate, sweating), changing intensity concepts, standardization of frequency across the entire questionnaire, and adding more specific options to the domains (e.g. exercise therapy, other transportation goals). The original SQUASH was modified to a more standardized disease-specific questionnaire in collaboration with both patients and experts to measure physical activity in axSpA.

The next step will be to assess the construct validity and the test-retest reliability of this axSpA-specific SQUASH.
P14
SERUM-BASED SOLUBLE MARKERS MAY DIFFERENTIATE PSORIATIC ARTHRITIS FROM OSTEOARTHRITIS
Chandran V.1, Perruccio A.V.2, Li S.3, Abji F.1, Gandhi R.1, Gladman D.D.2
1University of Toronto, Divisions of Rheumatology and Orthopaedics, Canada

Aim. It is often difficult to differentiate psoriatic arthritis (PsA) from osteoarthriti-
sis (OA) in clinical practice.

We aimed to identify soluble biomarkers that differentiate PsA from OA.

Methods. Serum samples from 201 patients with OA (mean age 65 years, 43.3% males), 77 patients with PsA satisfying CASPAR criteria (mean age 45 years, 54.5% males) and 76 healthy controls (mean age 37 years, 50% males) were ob-
tained. Soluble markers of cartilage metabolism (COMP, hyaluronan), metabolic syndrome (adiponectin, adipin, resistin, HGF, insulin, leptin) and inflammation/immune response (CRP, IL-1b, IL-8, TNF-α, MCP-1, NGF) were assayed in the samples using Luminex multiplex assay. Marker levels in serum were com-
pared across the 3 groups using the Kruskal-Wallis test. Pair-wise comparisons were made with Wilcoxon rank sum test. To identify markers that differentiate PsA from OA, multivariate logistic regression analyses, adjusted for age and sex, were constructed using markers determined to be significant at a p<0.1 in univar-
iate analyses. Discriminative ability was assessed using ROC curves. The final model was further validated in an independent set of 73 PsA and 75 OA samples.

Results. Univariate analyses revealed the following markers significantly dif-
fered across groups (p<0.001): COMP, hyaluronan; resistin, HGF, insulin, leptin; CRP, IL-6, -8, TNF-α, MCP-1, NGF. When comparing PsA to OA, the follow-
ing markers significantly differed (p<0.001): COMP, hyaluronan; resistin, HGF, insulin: CRP, IL-6, -8, TNF-α, MCP-1, NGF. Multivariate analysis demonstrated that COMP (OR 1.24, 95% CI 1.06, 1.46), resistin (OR 1.26, 95% CI 1.07, 1.48), MCP-1 (OR 1.10, 95% CI 0.07, 1.48) and NGF (OR <0.001, 95% CI <0.001, 0.25) were independently associated with PsA vs. OA. The area under the ROC curve (AUROC) for this model was 0.99. Internal cross-validation of the model was further validated in an independent set of 73 PsA and 75 OA samples.

Conclusion. A panel of 4 biomarkers (COMP, resistin, MCP-1, NGF) may dis-
tinguish PsA from OA.

P15
PLASMA CALPROTECTIN IN SPA-PATIENTS, A BIOMARKER FOR PERIPHERAL ARTHRITIS
Hansen L.M., Fiere O.T., Bakland G.1
1Medical Dept. Helgedalssykehuset Mo i Rana; 2University of Oslo, Oslo; 3University Hospital of Northern Norway, Tromso, Norway

Introduction. Spondyloarthritis (SpA) is a rheumatic disease with axial and peripheral inflammatory arthritis. Inflammatory biomarkers as SR and CRP are strongly correlated with disease activity. Calprotectin, mainly secreted by neutrophilic granulocytes is elevated in sites of active inflammation.

P-Calprotectin is elevated in RA, SLE and IBD.

Aims: To investigate Plasma-Calprotectin in SpA-patients from Rana, Norway. Is P-Calprotectin elevated in SpA compared to healthy relatives and relatives with symptoms of SpA?

Materials and Methods. SpA-patients were recruited from hospital registers, family doctors and local newspaper-advertisement. Patients fulfilling ESSG-criteria were included. First-degree relatives were asked for symptoms of syno-

vitis or inflammatory back pain by questionnaire. Symptomatic relatives were included. 273 patients with inflammatory back-pain had x-ray and MRI of spine or inflammatory back pain by questionnaire. Symptomatic relatives were included. 273 patients with inflammatory back-pain had x-ray and MRI of spine or inflammatory back pain.

Results. Calprotectin levels are not significantly different in men, women, SpA-
patients, relatives with symptoms and healthy relatives. In SpA-patients there is no difference in Calprotectin-levels in inflammatory back-pain, radiological sacroiliitis, sacroiliitis on MRI, psoriasis, IBD, uveitis, reactive arthritis and HLA B27 positivity. Calprotectin levels were correlated to inflammatory markers. Calprotectin is correlated to BMI and swollen joint count but not to BASDAI, BASFI or MHAQ.

Conclusions. Se-Calprotectin could be a valuable biomarker in SpA, especially in peripheral Spa with polyarthritis.

P16
ASDAS PERFORMANCE IN PATIENTS WITH SPONDYLO-A RTHRITIDES FROM DIFFERENT BRAZILIAN REGIONS
Campos A.P.B.1, Palomino P.E.2, Ribeiro S.L.E.1, Simioni J.3, Bortolozzo A.B.1,2, Skare T.1, Sampaio-Barros P.D.1,3
1Hospital Universitário Evangélico de Curitiba, Rheumatology Dept., Curitiba; 2Hospital de Clínicas de Porto Alegre, Rheumatology Dept., Federal University of Rio Grande do Sul, Porto Alegre; 3Hospital Universitário Getúlio Vargas, Rheumatology Dept., Federal University of Amazonas, Manaus; Instituto of Education and Research, Sao Paulo; 4Faculdade de Medicina da Universidade de São Paulo, Division of Rheumatology, São Paulo, Brazil

Aim. To analyze the capacity of Ankylosing Spondylitis Disease Activity Score (ASDAS) to measure disease activity in spondyloarthropathies (SpA) from different Brazilian regions.

Methods. A common protocol of investigation was applied to 204 SpA patients that attended at two distinct Brazilian regions: South [Curitiba; n=84 and Porto Alegre (PA); n=54] and North (Manaus; n=66).

All patients fulfilled the Assessment of Spondyloarthritis International Society criteria. Protocol included clinical and demographic data. ASDAS-CRP (C-Re-

active Protein), Bath Ankylosing Spondylitis Disease Activity index (BASDAI), Bath Ankylosing Spondylitis Disease Functional index (BASFI), Maastricht Ankylosing Spondylitis Score (MASES), Spondyloarthritis Research Consortium of Canada (SPARC), Leeds Enthesitis Index (LEI) and Ankylosing Spondylitis Quality of Life questionnaire (ASQoL). ASDAS values were correlated through Spearman test with all indexes.

Results. Epidemiological and clinical differences were observed in the stud-
ied centers. Non-whites predominate in the North (71.9% vs 20.2%/24.1%) and HLA-B27+ in the South (53.9% / 53.6% vs 34.8%). ASDAS-CRP showed good correlation with the instruments used to measure disease activity, function and enthesis: BASDAI (Curitiba with p<0.0001; PA with p<0.0001); BASFI (Curitiba with p=0.0001; PA with p=0.0001); Maastricht Ankylosing Spondylitis Score (MASES), Spondyloarthritis Research Consortium of Canada (SPARC), Leeds Enthesitis Index (LEI) and Ankylosing Spondylitis Quality of Life questionnaire (ASQoL).

Conclusions. ASDAS-CRP proved to be a good indicator of inflammatory activity and showed a good correlation with outcome measures in SpA patients from different Brazilian regions.
**P17**

**DKK-1 LEVELS ARE ELEVATED IN PATIENTS WITH ENTHESITIS RELATED ARTHRITIS WITHOUT SACROILIAC JOINT FUSION**

Fisher C.1, Bourke L.1, Radziszewska A.1, Jadon D.2, Sengupta R.1, Bray T.1, Hall-Craggs M.1, Sen D.1, Ioannou Y.1

1Arthritis Research UK Centre for Adolescent Rheumatology, University College London, London; 2Rheumatology Dept., Addenbrooke’s Hospital, Cambridge; 3Royal National Hospital for Rheumatic Diseases, Bath; 4Centre for Medical Imaging, University College London, London, UK

**Introduction.** Dkk-1 is an inhibitor of the Wnt signalling pathway and therefore plays an important role in bone remodelling. Studies in adults with ankylosing spondylitis have suggested that Dkk-1 may be an important factor in bony ankylosis but there have been no studies of Dkk-1 in a younger population with enthesitis related arthritis (ERA)-subtype of juvenile idiopathic arthritis.

**Methods.** Patients were recruited from adolescent and young adult clinics at University College London Hospital. Serum samples were stored at -80°C until needed. Dkk-1 levels were measured by ELISA (Quantikine, R&D Systems, Minneapolis, MN) as per manufacturer's instructions.

**Results.** Serum from 78 patients with ERA (median age 17 years) and 20 age and gender matched healthy controls was tested. Dkk-1 was significantly higher in patients with ERA (median=2971pg/ml, IQR 2258-3511pg/ml) compared to healthy controls (median=1806pg/ml, IQR 1307-2950pg/ml, p=0.0014) (Figure 1A). Patients who were HLA-B27 positive had higher Dkk-1 levels (median=3081pg/ml, IQR 2337-3680) than those who were HLA-B27 negative (median=2445pg/ml, IQR 1832-3365, p=0.0488) (Figure 1B). There was no correlation between Dkk-1 and CRP, ESR, patient age, treatment or disease duration.

Eleven patients with ERA had developed bony ankylosis of their sacroiliac joints; in this group Dkk-1 levels were lower (median=2114pg/ml, IQR 2103-2618pg/ml) compared to those with no evidence of bony fusion (median=3042pg/ml, IQR 2323-3670pg/ml, p=0.0355) (Figure 1C).

**Conclusions.** Dkk-1 levels are elevated in ERA compared to healthy controls but may reduce with the occurrence of bony fusion.

**Fig. 1. A.** Dkk-1 levels were significantly higher in patients with ERA compared to healthy controls. **B.** Levels were higher in patients with ERA who were HLA-B27 positive compared to negative. **C.** Patients with SIJ bony fusion had significantly lower Dkk-1 levels than those with no bony fusion.

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**P18**

**IGA ANTIBODIES AGAINST CD74 ARE ASSOCIATED WITH STRUCTURAL DAMAGE IN THE AXIAL SKELETON IN PATIENTS WITH ANKYLOSING SPONDYLITIS**

Witte T.1, Köhler M.1, Georgi J.1, Schweikhard E.2, Matthias T.1, Baerlecken N.1, Rudwaleit M.1, Sieper J.1, Podubnyy D.4

1Dept. of Immunology and Rheumatology, Medical University Hannover; 2Dept. of Rheumatology, Helios-Ostseeklinik, Damp; 3Aeskus.Diagnostics, Wendelsheim; 4Dept. of Rheumatology, Charité Universitätsmedizin Berlin, Germany

**Introduction/Aim.** To study the association between the presence of antibodies against CD74 and structural damage in the sacroiliac joints and spine in patients with ankylosing spondylitis (AS).

**Patients and Methods.** A discovery cohort was established in Damp, Germany. 117 consecutive AS patients (disease duration > 10 years). 38 blood donors served as controls. Grading of sacroiliitis was performed by the local radiologist. As a confirmation cohort, sera of 117 patients from the prospective ENRADAS cohort were obtained. Spinal radiographs (baseline and year 2) had been assessed for mSASSS by two trained reader blinded for the time-point and for all clinical data.

IgG and IGA antibodies against CD74 were measured using an ELISA of Aeskus. Diagnostics. The measurements were performed blinded to the evaluations of the radiographs.

**Results.** The sensitivity of IgG and IGA anti-CD74 antibodies for AS was 39% and 56% in the Damp cohort and 15% and 54% in ENRADAS, with a specificity of 94% (IgG) and 97% (IgA).

IgA, but not IgG, anti-CD74 antibodies significantly correlated with the presence of grade 4 sacroiliitis (47% (IgApositive) versus 25% (IgAnegative), p=0.017) in the Damp cohort and with accelerated mSASSS progression in ENRADAS (1.49x2.81 (IgApositive) versus 0.65x1.85 (IgAnegative) (p=0.046)).

Patients with and without IgA or IgG anti-CD74 did not differ with regard to age and disease duration.

**Discussion.** CD74 is a receptor of macrophage migration inhibitory factor (MIF), which is upregulated in axial spondyloarthritis and stimulates osteoblasts. IgG and IgA antibodies against CD74 may be involved in the receptor activation and mimic MIF effects.

**Conclusion.** IgA antibodies against CD74 are not only markers of AS, but seem to be associated with structural damage development in the sacroiliac joints and in the spine.

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**P19**

**THE ASSOCIATION OF EXTRA-ARTICULAR MANIFESTATIONS WITH DISEASE DURATION IN AXIAL SPA: RESULTS FROM THE (BE-) GIANT COHORT AND THE ASPECT STUDY**

Varkas G.1, Cypers H.1,2, Vasteaesegher N.3, Van Praet L.1,2, Cartron P.1,4, Raerman F.3, Devick M.1, Gyselbrecht L.1, Corley L.1, Piette Y.1, Thevissen K.1,2, Stuer A.1, Van den Bosch F.1, Elewaut D.1,4

1Dept. of Rheumatology, Ghent University Hospital; 2VIB Inflammation Research Centre, Ghent University, Ghent; 3MSD; 4Be-Giant Consortium, Belgium

**Background.** The prevalence of extra-articular manifestations (EAMs) in ankylosing spondylitis (AxSpA) is now made much earlier in the disease the prevalence of the EAMs may be different. Moreover, the introduction of anti-TNF therapy may have altered the incidence of EAMs.

**Objective.** To assess the association of EAMs with disease duration in AxSpA patients (n=245) in the post-anti-TNF era compared to a historic cohort of Belgian AxSpA patients (n=1023) from the pre-anti-TNF era.

**Methods.** The Belgian Inflammatory Arthritis and spoNdylitis cohorT (Bel-Giant) and The Ghent Inflammatory Arthritis and spoNdylitis cohort (GIANT) are post-anti-TNF observational cohorts that include consecutive patients since 2010, diagnosed with AxSpA by their treating rheumatologist. Patients who fulfill the ASAS classification criteria, are prospectively followed every 6 months. Two-hundred and forty-five patients were included, of whom almost 36% of patients fulfilled the Modified NY criteria. Follow-up consisted of patient-reported outcomes, a standardized clinical examination (joint counts, entheses, axial metrology), standard laboratory analysis and imaging. The ASPECT cohort is a Belgian cross-sectional pre-anti-TNF cross-sectional SpA database containing information on 1023 patients, of whom 82.8% fulfilled the New York modified criteria for AS, included between February 2004 and February 2005.

**Results.** In a cohort of 1268 Belgian AxSpA patients, the presence of extra-articular manifestations was significantly linked to disease duration, independent of gender, HLA-B27 status or cohort (p<0.001). In AS, but not in nr-AxSpA, the presence of EAMs was associated with disease duration.
Conclusions. The prevalence of extra-articular manifestations seems to increase with disease duration both in the pre-anti-TNF and the post-anti-TNF era, and may be linked to longer cumulative exposure to inflammation.

P20
INTERSPA: SENSITIVITY AND SPECIFICITY OF AUTOANTIBODIES AGAINST CD74 IN EARLY AXIAL SPONDYLOARTHRITIS

1 Medical-University Hannover; 2 Rheumazentrum Ruhrgebiet, Herne; 3 Hannover; 4 University-Hospital, Freiburg; 5 Blaubeuren; 6 Berlin; 7 University-Hospital, Bad Abbach; 8 Nienburg; 9 Aesku, Diagnostics, Wendelsheim; 10 Medical-University, Heidelberg; 11 Seesen; 12 Fachklinik Bad Pyrmont; 13 Medical University, Erlangen; 14 Göttinger; 15 Klinikum-Bielefeld, 16 Charité Universitätsmedizin, Berlin; 17 Hildesheim, Germany

Introduction/Aim. Antibodies against CD74 are a multicenter study, conducted to compare the sensitivity and specificity of anti-CD74 and HLA-B27 in patients with axSpA of recent onset.

Patients and Methods. Patients between 18 and 45 years and inflammatory back pain (IBP) for maximally 2 years were recruited. MRI of sacroiliac joints, HLA-B27 (genotyping) and anti-CD74 (CE certified kit of AESKU Diagnostics) were obtained in all patients. 100 blood donors served as specificity controls for HLA-B27 and anti-CD74. The MRI reading and the laboratory procedures were performed blinded.

Results. 122 of 205 recruited patients suffering from IBP can be completely evaluated so far (mean age 30 years, mean duration of IBP 13 months, 50% female). Sacroiliitis in MRI was diagnosed in 59% by the expert reader X. Baraliakos, HLA-B27 was present in 66%. The sensitivities of IgA anti-CD74, IgG anti-CD74 and HLA-B27 were 64.6%, 24.4% and 75% in the axSpA patients fulfilling the imaging arm, 65.4%, 23.1% and 80.7% in the patients fulfilling ASAS criteria, and 3%, 5% and 8% in the blood donors. The likelihood ratios were 21.5 (IgA anti-CD74), 4.9 (IgG anti-CD74) and 9.4 (HLA-B27) when considering the patients with a pathologic MRI only, and 21.8 (IgA anti-CD74), 4.6 (IgG anti-CD74) and 10.1 (HLA-B27) when considering all patients fulfilling ASAS criteria.

Conclusions. IgA anti-CD74 is a useful addition to our diagnostic tools for axSpA. Acknowledgement. This study is funded by AbbVie Deutschland GmbH & Co. KG.

P21
SCLEROSTIN AND ANTI-SCLEROSTIN ANTIBODIES SERUM LEVELS PREDICT THE ONSET AND SITE OF ARTICULAR INVOLVEMENT IN ENTEROPATHIC SPONDYLOARTHRITIS: IMPLICATIONS FOR THE CLINICAL PRACTICE

Luchetti M.M.1, Ciccia F.2, Benfareno D.3, Avellini C.4, Farinelli A.4, Rossi M.1, Capecci W.1, Ciferri M.1, Triolo G.2, Gabrielli A.3
1 Dip. Scienze Cliniche e Molecolari, Università Politecnica delle Marche, Ancona; 2 Dipartimento Biometrico di Medicina Interna e Specialistica, Università degli Studi di Palermo, Italy

Introduction. Pathogenesis and early diagnosis of enteropathic spondyloarthropathy (ES) still represents an important issue in clinical practice and novel biomarkers to address these points are needed. In this respect, we evaluated the role of sclerostin (SOST), an antagonist of the Wnt/β-catenn signaling pathway, which is activated in AS and likely contributes to bone inflammation.

Methods. SOST and anti-SOST antibodies (anti-SOST-IgG) were assayed using a commercial or a specific peptide-binding ELISA, respectively, in a cohort of 54 ES patients, 33 (61%) with axial SpA (Ax-ES), and 23 (39%) with peripheral SpA (Per-ES). Only 5 patients were HLA-B27 positive. IBD, RA, AS patients, and healthy individuals were used as controls.

Results. SOST resulted significantly lower than controls in ES cohort. However, subgroup analysis demonstrated that SOST decrease was significant, and comparable to AS, only in Ax-ES (p<0.001), but not in Per-ES. By ROC analysis a cut-off value of <165.9 pg/ml predicted axial involvement with good accuracy (sensitivity 90.32%, specificity 84.62%, likelihood ratio 5.87). Anti-SOST-IgGs resulted significantly higher in Ax-ES than in IBD (p<0.01) and, more importantly, in Per-ES patients (p<0.001).

By ROC analysis a cut-off value of anti-SOST > 20.4 UI/ml predicted axial involvement with sensitivity 90.3% and specificity 46.2%. Pearson’s analysis demonstrated a strong negative correlation between SOST and anti-SOST-IgG levels only in Ax-ES (p<0.001).

Discussion. Our study shows that SOST and anti-SOST-IgGs can be useful for the differential diagnosis in patients with ES, predicting axial inflammation with a good accuracy. Further studies are needed to establish their pathogenic role.

Conclusion. Decreased SOST and increased anti-SOST-IgG serum levels are novel biomarkers that may be helpful in the early diagnosis of axial spondyloarthritis in IBD patients with articular symptoms.
ones were determined after a reaction with 5,5′-dithiobis-(2-nitrobenzoic) acid. Half of the difference between native and total thiols ensured the dynamic disulfide changes. After the detection of dynamic disulfide, native, and total thiol levels, disulfide/native thiol and disulfide/total thiol ratios were calculated.

Results. In our patient group 32 patients (45%) have axial involvement, 36 (51%) polyarthritis and 13 (18%) distal inter-phalangeal joint arthritis. The mean serum CRP levels (mg/dL), DASS28 and BASDAI scores were 1.2±1.9, 2.8±1.2 and 3.2±2.3 respectively in our PaA patients. Serum native thiol (267.7±89.7 vs 300.6±62.7umol/L) and total thiol levels (304.9±54.8 vs 327.4±40.7umol/L) were found to be significantly decreased in the PaA patients in comparison with the control group (p=0.029 and 0.044).

Although serum disulfide levels (8.5±4.8 vs 7.7±4.7 umol/L), disulfide/native and disulfide/total thiol ratios increased in the PaA group, this increase did not reach statistical significance. In PaA patients native thiol levels were negatively correlated with age and patient reported pain (VAS).

Conclusions. Serum thiol levels decreased significantly in PaA and this reduction was independent from the type of involvement. Our results suggested that the reduction in thiols may play a role in the development of disease and substitution of thiol deficiency (correction of thiol-disulfide imbalance) may be beneficial.

P23

RHEUMATOLOGICAL MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASE PATIENTS: A CROSS-SECTIONAL STUDY


Background. Extraintestinal manifestations (EIM) occur rather frequently in inflammatory bowel disease (IBD), e.g. ulcerative colitis (UC) and Crohn’s disease (CD). Rheumatic manifestations are the most frequent EIM of IBD with prevalence between 17% and 39% and include peripheral arthritis, axial involvement and enthesopathy.

Objectives. To determine the prevalence of rheumatologic manifestations in a sample of Portuguese patients with IBD.

Methods. All adult IBD patients who exhibited a controlled disease were systematically evaluated on a prospective basis from a University Hospital of Portugal. The protocol with IBD department was implemented on June 2013. Patients were evaluated consecutively by a rheumatologist and we describe all patients included until December 2015. IBD duration, treatment and concomitant rheumatic symptoms were analyzed. Standard pelvic X-rays (Xr) for sacroiliac joints evaluation and/or magnetic resonance (MRI) were performed only when clinically indicated (inflammatory back pain (IBP) – and/or positive sacroiliac joints maneuvers). Descriptive statistics, t-test and qui2 tests were used to compare differences between the UC and CD patients for continuous and dichotomous data, respectively.

Results. Total of 119 patients were included, with a mean age of 43.3 (±12.6) years-old, the majority females (n=66, 55.5%). Eighty (67.2%) had CD and 39 (31.8%) had UC. Mean duration of IBD was 11(±8) years. Forty-five (37.8%) were under biological therapy due to IBD (36 infliximab, 8 adalimumab and 1 goli mumab). Other therapies in use were azathioprine, sulphasalazine and mesalazine. Twenty-five (21%) IBD patients mentioned peripheral (joint pain and enthesopathy) symptoms and 33 (28%) IBD. Fifteen of these 33 patients had radiological (Xr or MRI) evidence of sacroilitis. Seventeen (16%) patients who denied axial complaints had radiographic changes suggestive of sacroilitis.

Other EIM observed were 3 cases of uveitis, 7 cases of psoriasis and 1 case of AA amyloidosis. Other diagnoses beyond spondyloarthritis were established: 4 cases of diffuse idiopathic skeletal hyperostosis, 1 case of acute parvovirus B19 infection and 1 case of fibromyalgia.

We found statistically significant differences in the prevalence of IBD between gender (higher in males, p=0.03) and age at diagnosis (higher when diagnosis of IBD occurs at earlier ages, p=0.03).

No statistically significant difference and was detected between the frequency of the rheumatologic manifestations and the IBD clinical subtypes (p=0.94) and age (p=0.16).

Conclusions. Musculoskeletal manifestations are frequently present in patients with IBD. However, a substantial group of patients is not evaluated by the rheumatologist. Gastroenterologists play a key role in early referral of these patients, once to avoid serious complications. Nowadays, their early and adequate treatment is mandatory.

P24

THE PREVALENCE OF AXIAL SpondyloArthritis WITH MRI VALIDATION IN PATIENTS PRESENTING WITH ACUTE ANTERIOR UVeITIS

Sykes M.1, Hamilton L.1, Jones C.2, Gaffney K.1

1Rheumatology; Ophthalmology, Norfolk & Norwich University Hospitals NHS Foundation Trust, Norwich, UK

Introduction. Estimates for the prevalence of axial spondyloarthritis (axSpA) in patients presenting with acute anterior uveitis (AAU) range from 11-28%. However, to date no studies have classified patients according to the MRI-based Assessment of Spondyloarthritis International Society (ASAS) criteria.

Methods. Consecutive patients presenting to a university teaching hospital between February 2014 and March 2015 with AAU were invited to participate. Those who reported chronic back pain commencing before age 45 were evaluated clinically and underwent blood tests and MRI scans.

Results. Of 366 patients with AAU, 57 had a pre-existing diagnosis of axSpA; 76 others fulfilled the study eligibility criteria and 73 (95%) completed the study. Sixteen patients (22%) were diagnosed with axSpA according to the ASAS definition of a positive MRI (12 sacroiliac, 4 spinal). Including those with a previous diagnosis, the minimum prevalence of axSpA in patients presenting with AAU was 19.9%; of these 22% were previously undiagnosed. The median age of ‘new’ axSpA patients was 54 and half were female.

Nine patients (56%) were HLA-B27 positive; 31.3% had a raised CRP; 37.5% were current smokers; 6.3% had psoriasis, 18.8% inflammatory bowel disease. The mean BASDAI was 3.16, spinal pain VAS 4.31, BASMI 1.63 and BAFS 2.74. The median back pain duration was 20.5 years with median 3 AAU episodes per patient. At the first episode of uveitis, the median back pain duration was 15.5 years.

Conclusions. This is the first study to use MRI to classify patients with AAU and chronic back pain. At least one-fifth of patients presenting to secondary care with AAU have an underlying diagnosis of axSpA. There was a significant hidden burden of disease in that 22% of axSpA patients were previously undiagnosed despite having a long duration of symptoms. Patients presenting with AAU should be screened for chronic back pain and referred to a rheumatologist; this represents an opportunity to shorten the diagnostic delay.

P25

A PROSPECTIVE EVALUATION OF THE DUBLIN UVEITIS EVALUATION TOOL (DUET) IN UK CLINICAL PRACTICE

Sykes M., Hamilton L., Gaffney K.
Norfolk & Norwich University Hospitals NHS Foundation Trust, Rheumatology, Norwich, UK

Introduction. Targeted screening of patients with acute anterior uveitis (AAU), the commonest extra-articular manifestation of axial spondyloarthritis (axSpA), may allow earlier treatment of axial disease.

The Dublin Uveitis Evaluation Tool (DUET) was developed to direct referral of appropriate AAU patients to rheumatology. The validation exercise reported 96% sensitivity and 97% specificity for axSpA, however limited radiological data were reported. We used MRI to evaluate the performance of the DUET algorithm in a UK population and classified patients according to the imaging arm of the ASAS criteria.

Methods. Over a 13 month period consecutive adult patients presenting to the ophthalmology department of a university teaching hospital with AAU and a self-reported history of chronic back pain starting before the age of 45 years were invited to participate. Fifty-seven patients with an existing diagnosis of axSpA were excluded and 76 eligible patients identified. All eligible patients were evaluated clinically and underwent MRI of SI joints and thoracolumbar spine.

Results. Seventy-three patients completed the study; mean age 48 years, 31.5% HLA-B27 positive, 62% female. Sixteen (22%) had positive MRI as defined by ASAS. Of the 27 patients classified for referral by the DUET algorithm only 9 (33%) had a positive MRI. A further 7 patients with a final diagnosis of axSpA (positive MRI, HLA-B27 negative, no psoriasis) would not have been referred according to the algorithm. The sensitivity and specificity of the DUET algorithm in our patient population was calculated at 56% and 68% respectively.

Conclusions. The DUET algorithm performed less well in our prospective patient cohort than in the original validation group. By using HLA-B27 positivity and/or psoriasis as the criteria for referring a patient for further investigation, there is a potential to miss over 40% of patients with radiological disease.
Regional registry as a tool for improvement of management of ankylosing spondylitis: evaluation of psychological state


1Kazan State Medical University, Dept. of Hospital Therapy; 2Republican Clinical Hospital, Kazan, Russia

According to conception “T2T” patient with ankylosing spondylitis (AS) takes an active part in treatment that determines importance of his psychological state.

Aim. To evaluate interconnection between psychological state of the patient with AS and disease course.

Materials and Methods. Within the regional registry which is part of epidemiological study of AS in Russia, 40 patients (32 males, 8 females, age 21-56 years, average 40.3±10.0) were examined.

Average BASDAI on day 1 was 5.54 ± 1.8, BASFI – 5.34 ± 2.48. Functional status was evaluated by means of BASMI, psychological state – EQ-5D questionnaire.

Results. 42.5% patients had anxiety and depression: moderate – 15 (88.2%), severe – 2 (11.8%).

With the disease duration of < 5 years propensity for depression and anxiety was noted by 54.5% patients, 5 to 10 years – 16.7%, >10 years – 52.9%. In patients with mild disease activity anxious and depressive states were not observed, with moderate activity they were revealed in 42.8%, with severe activity – in 42.8%, with very severe activity – in 50%. Among patients without limitation of motion and activity depression was revealed in 18.2%, with moderate limitation –33.3%, with severe limitation –81.8%.

According to BASMI 1 out of 2 patients without limitation of motion had anxiety and depression, 31.5% – with moderate limitation and 52.6% with severe limitation. The direct correlation was revealed between EQ-5D score and BASFI (r=0.996), between EQ-5D and BASDAI (r=0.855), concurrently such correlation was absent between BASMI and EQ-5D. Among patients without anxious and depressive states 60.8% patients take NSAIDs regularly while among the patients who noted propensity for anxiety and depression only 41.7% take NSAIDs regularly.

Conclusions. Patients with short and long AS duration, severe disease activity and functional limitation are more prone to anxiety and depression. Such patients are less compliant with therapy.

These data should be considered when the programs of AS patients’ management are developed.

Fecal calprotectin analysis will significantly improve the sensitivity of disease detection in blood and stools, making it a marker of neutrophil and inflammatory activity.

Reference

Prevalence of osteoporosis in an ankylosing spondylitis cohort


1Rheumatology Dept., St James’s Hospital, Dublin; 2Rheumatology Dept, St Vincent’s Hospital, Dublin; 3Rheumatology Dept., Galway University Hospital, Galway; 4Rheumatology Dept., Midlands Regional Hospital Tullamore, Offaly; 5Rheumatology Dept., University Hospital Waterford, Waterford; 6Rheumatology Dept., Blackrock Clinic, Dublin; 7Rheumatology Dept., Sligo General Hospital, Sligo; 8Rheumatology Dept., Kerry General Hospital, Kerry; 9School of Medicine, University College Dublin, Dublin; 10Rheumatology Dept., Tallaght Hospital, Dublin, Ireland

Introduction. The prevalence of osteoporosis is higher in ankylosing spondylitis (AS) patients than controls. The true prevalence is unknown and there is no data for an Irish AS cohort. The Ankylosing Spondylitis Registry of Ireland (ASRI) was established in 2013 to provide epidemiological data on the AS population in Ireland.

Aim. To determine the prevalence of low bone mineral density (BMD) in an Irish AS cohort.

Materials and Methods. A standardised assessment was performed on each patient. Disease severity was assessed by Bath AS Disease Activity Index (BASDAI); Bath AS Functional Index (BASFI) and Health Assessment Questionnaire (HAQ). Presence of dual-energy x-ray absorptiometry (DXA) testing and result was recorded. Bone mineral density (BMD) was categorised according to the World Health Organisation criteria, into normal BMD, osteopenia or osteoporosis.

Statistical analysis was performed using SPSS.

Results. To date, 416 patients are enrolled in ASRI: 78.1% males, mean age 47.95 (SD 12.4), mean disease duration 20.9 years (SD 12.2), average delay to diagnosis of 8.8 years (SD 8.3). Mean BASDAI is 3.8 (SD 2.5), BASFI 3.7 (SD 2.7) and HAQ 0.53 (SD 0.51). DXAs have been performed in 24.75% (n=103) of the cohort, of which 39.8% (n=41) have osteopenia and 10.7% (n=11) have osteoporosis. Low BMD is significantly correlated with men and advancing age.

There is no association with disease activity. The self-reported prevalence of osteoporosis is 6.4% (n=27; 19 males).

Conclusion. Half of this cohort has low BMD, with no association with disease severity. The majority of affected patients are unaware.

Fecal calprotectin as a new diagnostic tool in diagnosing spondyloarthopathies


1Dept Rheumatology, OLV Hospital, Aalst; 2Dept. Clinical laboratory OLV Hospital, Aalst, Belgium

Introduction. Spondyloarthopathies (SpA) are characterized by clinical and radiographic features on which the ASAS classification criteria are based. The use of the ASAS criteria in the diagnosis of SpA has a sensitivity of 79.5% and a specificity of 83.3%. Calprotectin is a protein derived from neutrophils that can be detected in blood and stools, making it a marker of neutrophil and inflammatory activity.

The aim of this non-interventional prospective study is to investigate the putative role of fecal calprotectin in the diagnostic process of SpA.

Patients and Methods. The dosage of fecal calprotectin (Quantum Blue Calprotectin) was performed among patients consulting the department of rheumatology of the OLV Hospital Aalst and with clinical suspicion of SpA. Patients were asked to bring the intake of NSAIDs 2 weeks before collection of the sample. The calprotectin values of > 30 µg/g were considered positive. Patients with inflammatory bowel disease were excluded.

Results. Seventy-nine patients were included in the study. The majority of the patients was female (73.4% vs 26.6% male). The mean age ± SEM was 42 ± 12 years. HLA-B27 positivity was found in 17.7% of patients. Of the patients, 39.2% was diagnosed with SpA based on ASAS criteria. The dosage of fecal calprotectin was significantly elevated in patients with SpA compared to patients without SpA (152 ± 113 µg/g vs 96 ± 92 µg/g; p<0.030). The value of fecal calprotectin was also significantly elevated in SpA patients without sacroiliitis on MRI-imaging (p=0.020), and in patients without arthritis (p=0.040).

Conclusion. Fecal calprotectin analysis will significantly improve the sensitivity of the diagnostic process of SpA, especially in patients without sacroiliitis on MRI-imaging or patients without arthritis.

Serum amyloid A levels in psoriatic arthritis patients – a marker of disease activity?

Martins-Rocha T., Bernardes M., Rosa-Gonçalves D., Aguiar F., Bernardo A., Costa L.

Rheumatology Dept., Centro Hospitalar São João, Porto, Portugal

Introduction. Serum amyloid A (SAA) has a role in the pathophysiology of inflammatory arthritis and related joint destruction, but its clinical use in monitoring disease activity is yet to be determined in Psoriatic Arthritis (PsA) patients. Aim. Investigate the association between SAA levels and disease activity and function parameters in a group of PsA patients.

Methods. Observational cross-sectional study including consecutive patients with PsA (CASPAR criteria) under biologic therapy followed in our Rheumatology department. SAA levels were measured and demographic and clinical data were collected by consulting the national database (Reuma.pt).

Disease activity and functional scores were calculated, including DAS28 3V/4V (ESR and CRP), CDAI, SDAI, HAQ, BASDAI, BASFI, BASMI, MASES and SPARC indices. Correlations between variables were studied using Spearman correlation analysis.

Results. 40 patients were included, 21 (53%) were females, with a mean age of 49.2 ± 10.2 years and median disease duration of 9 years [1-28]. All patients were treated with biologic therapy. Median SAA levels were of 7mg/L [8-116], SAA levels correlated more strongly with CRP (r=0.55; p<0.001) than with ESR (r=0.35; p=0.027). SAA had a significant correlation with ASDAS CRP (r=0.53; p<0.001) and DAS28 3V/4V (CRP) (r=0.40 and r=0.44, respectively; p<0.05) and weaker correlations with DAS28 3V/4V (ESR) (r=0.32 and r=0.36; p<0.05), ASDAS ESR (r=0.34; p=0.03) and BASMI (r=0.33; p=0.04).
No significant correlations were found for other disease parameters. Comparing to SAA correlations, ESR had lesser strength associations with DAS28 4V (CRP) and ASDAS CRP (r=0.38 and r=0.39, p<0.05) and was more strongly correlated with BASMI and BASFI (r=0.51 and 0.42, p<0.05). CRP had more strongly associations with DAS 28 3V/4V (ESR) and ASDAS (ESR) (r=0.46, r=0.45 and r=0.40, p<0.05).

Conclusions. SAA levels had significant correlation with CRP and to a lesser extent with ESR and some functional and disease activity scores. Dosing SAA may represent a valuable indicator for disease activity and damage assessment in PsA patients.

P30
LOW BONE MINERAL DENSITY AND ITS ASSOCIATED CLINICAL FEATURES IN SPONDYLOARTHRITIS
Martins-Rocha T., Aguiar F.,Bernardes M.,Bernardo A.,Costa L. Rheumatology Dept., Centro Hospitalar São João, Porto, Portugal

Introduction. Spondyloarthritis (SpA) patients have an increased risk of osteoporosis and vertebral fragility fractures (FF). We aim to determine the prevalence of low bone mineral density (BMD) and its associations with clinical and disease parameters in a cohort of SpA.

Methods. Observational retrospective study with consecutive SpA patients followed at our Rheumatology Department. Clinical data were collected from the national database. BMD (g/cm²) measurements of the lumbar spine (L) and femoral neck (FN) were collected from the most recent dual-energy X-ray absorptiometry (DXA). Low BMD was defined as a Z-score ≤ -2 (pre-menopausal women and men aged <50 years) and as T-score ≤ -1 for the others. Patients were classified as having or not secondary causes of low BMD (SC vs non-SC). Correlations between variables were studied using Spearman correlation analysis.

Results. 126 SpA patients, 65 (50%) were female with a mean age 47.75 ± 11.86 years and median disease duration of 14 years (0-46); 77 (67%) had Ankylosing Spondylitis, 33 (26%) Psoriatic Arthritis, 11 (8.7%) IBD-SpA and 5 (4%) Undifferentiated SpA. 98 (78%) were under biologic therapy, 41 (33%) had low BMD, 26 (22%) low L-BMD, 24 (20%) low FN-BMD and 13 (10%) had previous vertebral FF. Non-SC patients (n=77) had significantly lower proportion of females (40%, p=0.01) and higher proportion of axial involvement (92% vs 80%, p<0.05). In this group, FN-BMD had significant positive correlations with Body Mass Index (r=0.38, p<0.05). L-BMD had negative association with ESR (r=-0.34, p=0.005) and positive correlation with disease duration (r=0.43, p<0.001). Lower proportion of low L-BMD in the Biologic group (9% vs 4%, p=0.02) was observed. In SC group, FN-BMD was negatively associated with disease duration and CRP (r=-0.40 and r=-0.38, p<0.05).

Conclusions. BMD had a negative association with ESR and CRP which might reflect the role of systemic inflammation in lowering BMD. L-BMD correlated with disease duration, which might be influenced by spinal osteoporosification.

P31
SPONDYLOARTHRITIS PREVALENCE IN EUROPE, A EU-LAR ENDORSED SURVEY


Men & Women

<table>
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<tr>
<th>Country</th>
<th>Men (0.12-0.47)</th>
<th>Women (0.16-0.45)</th>
<th>Total (0.19-0.44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>0.29</td>
<td>0.31</td>
<td>0.30</td>
</tr>
<tr>
<td>Lithuania</td>
<td>0.38</td>
<td>0.39</td>
<td>0.39</td>
</tr>
<tr>
<td>Turkey</td>
<td>0.17</td>
<td>0.57</td>
<td>0.37</td>
</tr>
<tr>
<td>Serbia</td>
<td>0.38</td>
<td>0.32</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Conclusions. Age- and sex-standardized SpA prevalence estimates in France, Turkey and Serbia were in line, but were as twice as high in Lithuania, confirming a north-south decreasing gradient using homogenous sampling and case ascertainment method. Standardized SpA prevalence estimates in men and women were similar in France and Serbia, but not in Turkey and Lithuania. This study adds to previous observation on similarity of RA and SpA prevalence estimates.

References

HLA-B27/B82m DROSOPHILA A NEW MODEL TO STUDY HLA-B27 IMPLICATION IN SPONDYLOARTHRITIS
Jah N.1,2, Grandem B.,1,2,3, Runcheval-Arnold A.4, Guenal I.2, Gaumer S.1, André C.1,2, Breban M.4,5, Chiozio G.1,2
1INSERM U1173 Inflammation and infection, France, Faculty of Health Sciences Simone Veil, Montigny-le-Bretonneux; 2University of Versailles Saint-Quentin-en-Yvelines, Inflamex Laboratoire d’Excellence, Paris; 3Laboratory Genetics and Cellular Biology, Faculty of Health Sciences Simone Veil, Montigny-le-Bretonneux; 4Service de Rhumatologie, Ambroise Paré Hospital, University of Versailles Saint-Quentin-en-Yvelines, Boulogne, France

Aim. Mechanisms underlying the striking association of spondyloarthritis (SpA) with the MHC class I molecule HLA-B27 remain poorly understood. Using genetic models such as Drosophila might be helpful for deciphering the whole cellular cascade, including both specific interactors and downstream elements and allows easier gene function study. For these reasons, we hypothesized that Drosophila could be a relevant model to study HLA-B27 at the cellular and molecular level. To understand HLA-B/B82m intracellular trafficking, localization and consequence of its expression, we developed HLA-B27/B5, HLA-B0702 (control) and Human Beta-2-microglobulin (hB2m) transgenic Drosophila.

Methods. Gateway Technology was used for developing transgenic HLA-B/human B2m Drosophila.

Results. Transgenic HLA-B27/B82m Drosophila was expressed in Vg domain. We observed positive staining with HC10 (class I heavy chain) and ME1 (control) and human Beta-2-microglobulin (hB2m) transgenic Drosophila. hB2m was inserted in long arm of chromosome 3 and HLA-B2705 and HLA-B0702 were inserted in the short arm of same chromosome position. At first, vestigial (Vg) driver was used to produce lines allowing tissue-specific GAL4 expression and the responder lines carry the coding sequence for the gene HLA-B0702 and hB2m or HLA-B2705 and hB2m under the control of UAS sites. Results. Transgenic HLA-B2705/hB2m Drosophila was expressed in Vg domain. We observed positive staining with HC10 (class I heavy chain) and ME1
(anti-HLA B/C) antibodies, suggesting a proper conformation of HLA-B27 with hB2m in Vg-domain. In contrast, transgenic HLA-B/0702/hB2m had positive staining only for HC10 antibodies. On the other hand, in transgenic HLA-B/hB2m, we observed positive staining with W6/32 antibody which recognizes suitable HLA-A, HLA-B and HLA-C conformation. However, we showed that HLA-B2705/hB2m only seems to reach plasma membrane and be expressed at cell surface. Furthermore, we observed specific and different physiological consequences of HLA-B7 and B27 expression in Drosophila. 

Conclusion. Taken together, our data suggest that transgenic HLA-B-H/hB2m were expressed in Vg-domain and on plasma membrane for HLA-B2705/hB2m but not for HLA-B0702/hB2m. This is the first time that difference in localization between HLA-B2705 subtype associated with SpA and not associated HLA-B0702 is reported. These results suggest that transgenic Drosophila might be a pertinent model to decipher molecular mechanisms involved in HLA-B27 trafficking and to better understand potential different compartment of HLA-B subtypes.

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HLA-B27-DRIVEN INFLAMMATION IN THE GUT CONTROLS THE CENTRAL AND PERIPHERAL MONOCYTE COMPARTMENTS AND THEIR OSTEOCLASTIC POTENTIAL

Ansolone C., Utriaiien L., Milling S., Goodyear C.G., Institute of Infection, Immunity and Inflammation, College of Medicine, Veterinary Medicine and Life Sciences, University of Glasgow, Glasgow, UK

Introduction/Aim. Human HLA-B27 transgenic (B27) rats spontaneously develop chronic inflammation that resembles human spondyloarthropathies, including bone loss and gut inflammation. Bone loss in B27 rats has been linked with increased TNF-α-dependent osteoclastogenesis, and we have linked colitis to altered dendritic cell differentiation and function. We therefore aimed to further characterise the myeloid compartment, intestinal pathology and bone loss in B27 rats.

Materials and Methods. Rat monocytes from the bone marrow (BM) and blood of 14-16 week old B27 and control (HLA-B7 transgenic and wild type (WT)) rats were characterised using flow cytometry. B27 and WT animals were given oral antibiotics for 4 weeks and then gut pathology was assessed by H&E staining. The effect of antibiotics on monocytes and pre-osteoclasts (OCs) in the BM and blood was evaluated by flow cytometry and the capacity of BM cells to generate OCs in the presence of TNF-α was assessed in vitro. Plasma CCL2 levels were measured by ELISA.

Results. We demonstrated that B27 rats have altered monocytes, with more “inflammatory” CCR2+CD43low monocytes both in the central and peripheral compartments. Antibiotic treatment of B27 rats reduced ileitis and decreased the number of circulating CCR2+CD43low monocytes, by normalising CCL2 plasma levels. Furthermore, BM monocyte populations in antibiotic-treated B27 rats were also normalised. Finally, antibiotic treatment reversed the TNF-α-driven enhancement of B27 osteoclastogenesis.

Discussion. We have demonstrated that oral antibiotics in B27 rats not only reduce intestinal inflammation, but also impact systemic inflammation by decreasing the levels of plasma CCL2 and circulating CCR2+CD43low monocytes. This reduced inflammation in B27 rats in turn affects BM osteoclast precursors and reduces their potential to differentiate into mature osteoclasts.

Conclusion. We consider a link between intestinal and systemic inflammation in spondyloarthropathies, and also propose a mechanism connecting these with B27-associated bone loss.

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MODULATOR ROLE OF INDUCTIBLE COSTIMULATOR (ICOS) IN SPONDYLOARTHRITIS ANIMAL MODEL

Araujo L.M.1,2, Jouhault Q.1,2, Cherquiou B.1,2, Jobart-Malfait A.1,2, Anegon I.1, Chiochicia G.1,2, Breban M.1,2,1, INSERM U1173, University of Versailles Saint-Quentin-en-Yvelines; 1Univer- sité Paris Diderot, Sorbonne Paris Cité, Laboratoire d’Excellence; 1Service de Rhumatologie, Ambroise Paré Hospital; 1INSERM UMR 643-CHU de Nantes, France

Background/Aim. HLA-B27/hB2m transgenic rats (B27 rats), a model of spondyloarthritides (SpA) develop spontaneous colitis and arthritis. Recently, we demonstrated that altered DCs function promotes a biased expansion of pro-inflammatory Th17 cells and modification of regulatory T cells function. Interestingly, in vitro blockade of ICOS-ICOSL interaction reverses IL-10/IL-17 imbalanced production by T cells. These data led us to investigate in vivo the consequence of ICOS/ICOSL interaction blockade in experimental SpA using a genetic approach producing B27 rats with icos homozygous deletion (B27-ICOS-/- rats).

Material and Methods. ICOS-/- rats were produced using TALEN technology, and backcrossed onto the B27 transgenic background (P344). B27+/+ and B27-ICOS-/- rats were weekly weighted, examined and scored for clinical symptoms (colitis, arthritis, alopecia and orchitis). Inflammatory pattern was determined by histological analysis and ex-vivo production of pro-inflammatory cytokines.

Results. As expected, chronic diarrhea was the most common manifestation, starting at 9 weeks of age in all B27+/+ rats. Arthritis and alopecia developed only in some B27+/+ rats. The clinical score progressively worsened in B27+/+ rats. In contrast, the B27-ICOS-/- rats did not develop any symptom of disease until age of 16 weeks and attenuated symptoms were observed until 24 weeks. Decreased production of pro-inflammatory cytokines and increased IL-10 production by T cells were observed in B27-ICOS-/- rats.

Conclusions. Those results, still preliminary, suggest a protective effect of ICOS deletion on onset and severity of SpA in B27 rats. The protective effect could be associated to both, a decrease of pro-inflammatory T cells and increased proportion of IL-10-producing T cells. These data corroborate our previous in vitro observation demonstrating a key role for ICOS signaling in the generation and maintenance of imbalanced production of IL-10 and IL-17 by T cells in B27-rat model of SpA.

P35

REGULATION OF INFLAMMATION BY IL-27 IN A RAT MODEL OF SPONDYLOARTHRITIS

Jouhault Q.1,2, Feri I.1,2, Breban M.1,2,1, Araujo L.M.1,2, Chiochicia G.1,2,1, INSERM U1173, University of Versailles Saint-Quentin-en-Yvelines; 1Paris-Diderot University, Sorbonne Paris Cité, Laboratoire d’Excellence; 1Service de Rhumatologie, Ambroise Paré Hospital, Boulogne, France

Background/Aim. Spondyloarthritides (SpA) is a chronic inflammatory rheumatic disorder with osteo-articular and extra-articular manifestations. HLA-B27/human β2-microglobulin transgenic rats spontaneously develop a phenotype closely resembling human SpA. Disease development in these rats is correlated with accumulation of IL-17+ helper T cells (Th17), IL-17/IL-10 imbalance in regulatory T cells (Tregs) associated with ICOS overexpression and abnormal function of dendritic cells (DCs).

Transcriptomic study of B27 DCs revealed a decreased expression of IL-27, an anti-inflammatory cytokine able to decrease IL-17 and increase IL-10 production by T cells. We investigated if addition of exogenous IL-27 could be able to reverse the proinflammatory phenotype observed in B27 rats.

Material and Methods. Sorted T cell subsets and sorted CD103+ DCs from B27 rats were cocultured in the presence of recombinant IL-27. Effectors T cells and Tregs were cultured 3 days with coated anti-CD5. naive T cells were cultured 6 days with coated anti-CD5 in Treg or Th17 polarizing conditions. Cytokine production was evaluated by intracellular staining after PMA/ionomycin stimulation and by ELISA in the supernatants.

Results. The addition of exogenous IL-27 inhibited IL-17- and ICOS-expression and increased IL-10 production on several CD4+ T cells subsets, as effector T cells or Tregs. In vitro blockade of IL-27 with a blocking antibody demonstrated that this cytokine was not implicated in the modulatory effect of IL-27.

Moreover, using B27-ICOS-/- rats we observed no impact of ICOS expression on the inhibitory effect of IL-27, because IL-27 still significantly decreased IL-17 production in T cells from B27-ICOS-/- rats.

Conclusions. Our results reveal that IL-27 is able to reverse the pro-inflammatory phenotype observed in T cells from B27 rats. The effect of IL-27 on IL-17 production is IL-10 and ICOS independent. Given that IL-17 is considered a pro-inflammatory cytokine, these data prompt us to consider the potential therapeutic tool for SpA.
P36 WANT SIGNALING MODULATOR EXPRESSION BY FLS IN INFLAMMATORY JOINT DISEASES
Resende G.G.1, Machado C.R.L.1, Macedo R.B.V.1, Rocha M.A.1, Nascimento V.C.1, Bueno Filho J.S.S.1, Kakihana A.M.1, Andrade M.V.M.1
1Faculty of Medicine, Federal University of Minas Gerais, Belo Horizonte; 2Dept. of Exact Sciences, Federal University of Lavras, Lavras, Brazil

Introduction. Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS) are examples of inflammatory joint diseases (IJD) with different joint remodeling patterns. The fibroblast like synoviocytes (FLS) are involved in the transition from a acute and reparable phase to a chronic and persistent stage in these diseases. The distinction of joint phenotypes involves inflammatory cytokines such as TNF-α, IL17 and IL22 directly or through key signaling pathways such as Wnt.

Objectives. To evaluate the expression of two canonical Wnt inhibitors (sFRP3 and Dkk1) by FLS of patients with different IJD, in response to IL17, IL22 or TNF-α.

Methods. FLS were cultivated from the synovial fluid of patients with IJD. The levels of Dkk1 and sFRP3 were measured by ELISA in the culture supernatants after different inflammatory stimulus and directly in the synovial fluid.

Results. sFRP3 and Dkk1 are constitutively expressed by FLS. IL22 and sFRP3 were positively correlated (r0.76; p0.01) in synovial fluid and higher levels of sFRP3 were observed in AS patients compared to PsA and RA patients (p<0.01). The stimulation with IL22 to FLS was able to increase its production of sFRP3, but not of DKK1, with greater effects seen at doses of 1 and 10 ng/ml and time intervals between stimulus and collecting of 24 and 48 hours (p<0.01). TNF-α and IL17 did not alter the basal expression of sFRP3 neither of Dkk1.

Conclusions. These results show, for the first time, the ability of IL22 to increase the expression of sFRP3 in FLS by FLS in both in vitro and ex vivo models. This finding links IL22 to local inhibition of Wnt signaling, with consequent blockade of these signaling pathways in AS patients.

P37 WINDOW OF OPPORTUNITY: CIRCULATING OSTEOBLAST PRECURSORS WERE DECREASED AFTER INFILXIMAB THERAPY IN PATIENTS WITH ANKYLOSING SPONDYLITIS
Kwon S.1, Park W.1, Son M.1, Lim M.1, Jung K.1, Park S.2
1Rheumatism Center, Inha University Hospital, Incheon; 2Dept. Occupation and Environmental Medicine, Inha University Hospital, Incheon, Republic of Korea

Introduction. It was known TNF-alpha blocker therapy had little or no effect on structural remodeling in patients with ankylosing spondylitis (AS). Aim. We studied the differentiation and activity of osteoblast by cell culture of osteoblast precursors in peripheral blood of candidates for infliximab therapy with AS and controls.

Materials and Methods. Male sixteen individuals with AS were enrolled, met for modified New York criteria and were candidates for infliximab therapy. Sex and age matched nineteen controls were also recruited. Peripheral blood mononuclear cells were collected and cultured in growth medium. Once cell multi-layering has been observed, cells were transferred to differentiation medium and cultured for 3 weeks. They were then fixed and stained with alizarin S stain to detect any calcified nodules. The optical density (OD) of alizarin S was measured for quantitative analysis.

We evaluated 1) the numbers of circulating osteoblast precursors in peripheral blood, 2) the OD of alizarin red A staining of circulating osteoblast precursors, 3) total procollagen type 1 N-terminal propeptide (P1NP) as osteoprogenitor marker.

Results. The serum level of P1NP (osteoprogenitor marker) was significantly higher in patients with AS than in the controls (p<0.008), but that of osteocalcin (mature osteoblast marker) was not. (p>0.09) The number of osteoblast precursor cells and optic density of alizarin S were decreased after infliximab therapy (p<0.028 for optic density of alizarin S). The serum level of P1NP was decreased after infliximab therapy (p=0.002), but that of osteocalcin was increased (p=0.007).

Conclusions. These results support the hypothesis, ‘window of opportunity’ that acute inflammation resolved completely but mature lesion could not alter the new bone formation.

P38 CONDITIONAL DISRUPTION OF THE CIRCADIAN MOLECULAR CLOCK IN MESENCHYMAL CELLS CAUSES ACHILLES TENDON OSSIFICATION AND SMALL JOINT ARTHROPATHY
Errunza J.1, Brigham and Women’s Hospital, Division of Rheumatology, Immunology and Allergy, and Harvard Medical School, Boston, MA, USA

Introduction. Morning stiffness is a prominent clinical feature in spondylarthritides suggesting that circadian rhythms play a role in spondylarthritides pathogenesis. However, the function of intrinsic circadian molecular clocks in cells of the musculoskeletal system is poorly understood. Previous studies have shown that mice with germline deletion of the transcription factor Brain and muscle Arnt-like 1 (Bmal1), a core regulator of the circadian molecular clock, develop tendon mineralization and joint ankylosis. The goal of this study was to identify cell lineages and candidate signaling pathways driving musculoskeletal pathology in Bmal1-deficient mice.

Methods. Mice with a floxed Bmal1 allele (Bmal1fl) were crossed with Ptx1cre mice to delete Bmal1 in mesenchymal cells of the embryonic limb bud. Pheno-type analysis included histopathology and microcomputed tomography. Gene expression in the Achilles tendon was analyzed by real-time quantitative PCR. Musculoskeletal lesions were also characterized after deleting Bmal1 in osteochondroprogenitor cells (Bmal1Dermo-cre) and in tendon/tendon progenitor cells (Bmal1Lscx-cre).

Results. Bmal1 germline mutant mice and Bmal1Ptx1cre mice developed similar peripheral joint abnormalities, including Achilles tendon ossification and a not previously described osteoproliferative arthropathy in the small joints of the forepaws. Both phenotypes were fully penetrant by 8 weeks of age. There were no inflammatory infiltrates. Canonical target genes of the Hedgehog (Hh) but not the bone morphogenetic protein (BMP) signaling pathway were up-regulated in Achilles tendons of Bmal1Ptx1cre mice. Bmal1 deletion in Scx+ cells, but not in Dermo1+ osteochondroprogenitor cells, induced Achilles tendon ossification to the same degree as Ptx1cre mediated deletion and partially reproduced the forepaw phenotype.

Conclusion. Genetic disruption of the circadian molecular clock in mesenchymal cells in mice results in pathological new bone formation in tendons and joints. This phenotype maps to Bmal1 deficiency in a largely Scx+ mesenchymal cell population and appears to involve unrestrained Hh signals.
ASSOCIATION BETWEEN IMPROVEMENT IN ENTHESOPATHY AND QUALITY OF LIFE: RESULTS FROM ANTI-TNF-NAIVE PATIENTS WITH PSORIATIC ARTHRITIS IN TWO PHASE 3 USTEKINUMAB TRIALS

McInnes I.B.; Puig L.; Gottleib A.B.; Ritchlin C.; You Y.; Song M.; Kaifra S.; Tang K.L.; Morgan G.J.; Rahman P.; Kavanaugh A.

1Rheum, University of Glasgow, Glasgow, UK; 2Rheum, Universitat Autonoma de Barcelona, Barcelona, Spain; 3Der, Tufts Medical Center, Boston, USA; 4Rheum, University of Rochester, Rochester, NY; 5Stats, Janssen Research & Development, LLC, Spring House; 6Rheum, Janssen Scientific Affairs, LLC, Horsham, USA; 7Rheum, Memorial Hospital, St. John’s, Canada; 8Rheum, UCSD, La Jolla, USA

Aim. Assess changes in enthesisopathy and function/health-related QoL (HRQoL) in anti-TNF-naive patients with PsA receiving ustekinumab (UST).

Methods. Adult patients in 2 PK3 trials (n=747 anti-TNF naive) with active PsA (≥5 SJC & CRP ≥0.3mg/dL) despite DMARD & or NSAIDs were randomized to UST45mg, 90mg or PBO at wk0/4, & q12wks. Stable concomitant MTX was permitted but not mandated. At wk16, patients with ≥5 improvement in TJC & SCC entered blinded early escape (EE)EE(PBO →UST45mg; UST45mg →90mg; 90mg →90mg). Presence or absence of enthesopathy, HAQ-DI&SF-36 were assessed at baseline(BL) & wk24. In this post-hoc analysis, enthesopathy of the Achilles tendon & plantar fascia was assessed as present or absent. Patients categorized thereafter as: improved (enthesisopathy at BL, but not at wk24), worsened (enthesisopathy at wk24, but not at BL) & unchanged. Patients with enthesisopathy assessment missing at either time point were included in unchanged category; those with enthesisopathy data missing at both time points were excluded. EE patients were excluded from this analysis. Improvements in HRQoL (SF-36 PCS&MCS & physical function (HAQ-DI) were assessed by enthesisopathy response category.

Results. 591 anti-TNF-naive patients from both trials were included; 45% of patients were female, mean age 47.7 years, mean PsA duration 6.7yrs, & 74% had ≥3% BSA affected at BL. Proportion of patients with enthesopathy at BL was similar in combined UST (46.5%) & PBO (49.4%) groups. At wk24, proportions of patients with enthesopathy were 22.8% & 35.9% for combined UST&PBO groups, respectively. Across all patients, those with improvement in enthesisopathy had greater improvement in functioning & HRQoL, vs those who did not (p<0.05). When the analysis was restricted to those who achieved ACR20, patients with improvement in enthesisopathy showed a trend of greater improvement in functioning & HRQoL vs those who had worsened.

Conclusion. There is an association between improvement in enthesopathy of the Achilles tendon & plantar fascia & improvement in physical function & HRQoL in anti-TNF-naive patients with PsA in 2 UST trials. Some, not all, improvement may be explained by improvements in peripheral arthritis.

P40

ABILITY OF GENERAL PRACTITIONERS TO DISTINGUISH BETWEEN INFLAMMATORY AND NON-INFLAMMATORY SYMPTOMS IN PATIENTS AT RISK FOR SPONDYLOARTHRITIS: THE APPSPA STUDY

Karrenman C.M.1, Haze J.M.W.1, Weel A.E.A.M.1, 2
1Rheumatology, Erasmus University Hospital, Rotterdam; 2Rheumatology, Maassstad Hospital, Rotterdam, The Netherlands

Background. To optimize the effect of early arthritis clinics, adequate referrals are required to shorten the doctors’ delay. Therefore, general practitioners (GPs) should be aware of symptoms distinguishing between inflammatory and non-inflammatory diseases. The objective of this study was to investigate the awareness and recognition of SpA symptoms among GPs.

Methods. The AppSpA study was set up, a cross-sectional study focusing on awareness and knowledge of SpA in GPs. For the present study a single survey was developed and sent out to GPs in various regions of the Netherlands. The survey contained questions about inflammatory joint and back pain as well as SpA specific questions.

Results. 183 of the 950 GPs completed the survey, leading to a participation rate of 19.3%. Of the participating GPs the mean age was 47.2 years (SD 10.3) and 47.5% were male. Almost all GPs (94.5%) indicated to be familiar with the term SpA, but 55.5% associated it only with axial manifestations. Up to one third of the GPs associated the term SpA with psoriatic arthritis (23.7%) and Inflammatory Bowel Disease (33.5%).

With regard to the recognition of signs of inflammatory pain, especially morning stiffness and pain relief by NSAIDs were recognized (Table I), whereas pain improvement with exercise was recognized in less than 25% of cases. When we focus on the peripheral manifestations of SpA; out of six signs for inflammatory peripheral disease, only 43.2% of GPs recognized at least three of these symptoms. For the eight axial signs, 60.6% recognized at least four symptoms.

If GPs thought about inflammatory symptoms, the majority asked for the presence of arthritis (61.8%), enthesitis (83.6%) and inflammatory bowel disease (72.1%). GPs less often asked about non-inflammatory symptoms such as uveitis (61.8%), enthesis (19.1%) and dactylitis (19.1%).

Conclusions. Overall, recognition of inflammatory disease by GPs is suboptimal. The recognition of these signs and symptoms of SpA in primary care needs improvement in order to facilitate the necessary referrals to rheumatologists.

Disclosure of Interest. This survey is part of initiative to develop a communication platform which was financially supported by AbbVie.

Table I. Proportion of GPs who identified correct signs of inflammatory joint and back pain (n=183).

<table>
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<th>Signs of inflammatory disease</th>
<th>Peripheral</th>
<th>Axial</th>
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<tbody>
<tr>
<td>Insidious onset of complaints, n (%)</td>
<td>53 (29.0)</td>
<td>90 (49.2)</td>
</tr>
<tr>
<td>Symptom duration&gt;3 months, n (%)</td>
<td>57 (31.2)</td>
<td>93 (50.8)</td>
</tr>
<tr>
<td>Pain improved with exercise, n (%)</td>
<td>25 (13.7)</td>
<td>38 (21.3)</td>
</tr>
<tr>
<td>Pain not relieved by rest, n (%)</td>
<td>30 (16.4)</td>
<td>40 (21.9)</td>
</tr>
<tr>
<td>Pain relieved by NSAIDs, n (%)</td>
<td>160 (87.4)</td>
<td>150 (82.0)</td>
</tr>
<tr>
<td>Morning Stiffness&gt;30min, n (%)</td>
<td>141 (77.1)</td>
<td>138 (75.4)</td>
</tr>
<tr>
<td>Nocturnal Pain, n (%)</td>
<td>Not Applicable</td>
<td>143 (78.1)</td>
</tr>
<tr>
<td>Alternating Buttock Pain, n (%)</td>
<td>Not Applicable</td>
<td>37 (20.2)</td>
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</table>
THE PREVALENCE OF AXIAL AND PERIPHERAL SPONDYLOARTHRITIS IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW & META-ANALYSIS

Karreman M.C.1,2, Luime J.J.1, Hazes J.M.W.1, Weel A.E.A.M.1,2
1Rheumatology, Erasmus University Hospital, Rotterdam; 2Rheumatology, Maasstad Hospital, Rotterdam, The Netherlands

Background. Inflammatory Bowel Disease (IBD) is a chronic disease, comprising both Crohn’s Disease (CD) and ulcerative colitis (UC). Various extra-intestinal manifestations can occur, among which spondyloarthritis (SpA). SpA can manifest with both axial and peripheral manifestations, but prevalence estimates of these manifestations differ widely.

Aim. To provide pooled estimates of the prevalence of axial and peripheral manifestations of SpA in patients with IBD and to identify factors that might influence the prevalence estimates.

Methods. We systematically searched various databases from inception to May 2014. All articles addressing the prevalence of axial and/or peripheral manifestations of SpA in adult IBD patients were included. Risk of bias was assessed using a quality assessment tool including items on selection bias, non-response bias, sample size and misclassification of SpA diagnosis.

Results. Out of 4846 studies, 60 studies were included. Sample size varied from 9 to 4454. Methodological quality of the included studies was moderate. With regard to axial manifestations, the pooled prevalence of sacroilitis was 0.11 (95% CI 0.08–0.14), whereas the pooled prevalence for ankylosing spondylitis was 0.03 (95% CI 0.03–0.04). For peripheral arthritis the pooled prevalence was 0.14 (95% CI 0.12–0.16). Few estimates were available for the prevalence of enthesitis (range from 0.01 to 0.54) and dactylitis (range from 0 to 0.04). For both axial and peripheral manifestations, the prevalence was higher in patients with CD than in patients with UC.

Heterogeneity between studies was large, which might be explained by methodological quality as well as difference in geographic area, clinical setting and the use of criteria for case ascertainment as shown in figure 1 for the prevalence of SI and AS.

Conclusions. SpA is a common extra-intestinal manifestation in IBD. Peripheral arthritis is slightly more common with a pooled prevalence of 0.14 than axial manifestations as sacroilitis (0.11) and ankylosing spondylitis (0.03). For both axial and peripheral manifestations, the prevalence is higher in patients with CD than in patients with UC.

LACK OF INFORMATION FOR PATIENTS AT RISK FOR SPONDYLOARTHRITIS: THE APPSPA STUDY

Karreman M.C.1,2, Hazes J.M.W.1, Weel A.E.A.M.1,2
1Rheumatology, Erasmus University Hospital, Rotterdam; 2Rheumatology, Maasstad Hospital, Rotterdam, The Netherlands

Background. Patients with psoriasis (PSO) and inflammatory bowel disease (IBD) are at risk for developing spondyloarthritis (SpA). Patients’ delay might be reduced if patients themselves are aware of their risk to develop SpA.

Aim. To assess whether patients with PSO or IBD are aware of the risk of developing SpA and if so how they became aware.

Methods. A cross-sectional study was set up including PSO and IBD patients between 18 and 55 years of age. Patients were invited to participate either by their GP or by the patient organizations for PSO and IBD. Patients willing to participate completed a set of questionnaires regarding their disease, level of awareness and presence of musculoskeletal complaints.

Results. 552 PSO patients completed the questionnaires, of which 43.1% indicated to be aware of the possibility of developing a rheumatic condition already before the study-invitation. Of these 238 patients, 34% indicated to have gained this knowledge by themselves, 13.5% was informed by their GP and 24.4% by their medical specialist. Of the IBD patients, 344 completed the questionnaires, of which 41.9% was aware of the possibility of developing SpA and if so how they became aware.

For both PSO and IBD, patients who were recruited via the patient organizations were significantly more aware than patients recruited via the GPs.

Conclusions. Less than half of the patients with psoriasis or IBD are aware of the possibility of developing a rheumatic condition. If patients are aware, the majority gained this knowledge by themselves and 60% were not informed by a medical professional. More awareness could be achieved if medical professionals like the GP or the medical specialist would have more knowledge about symptoms of SpA and are trained in informing their patients about the increased risk of developing SpA.
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VALIDATION OF THE CONTEST QUESTIONNAIRE TO SCREEN FOR PSORIATIC ARTHRITIS IN PRIMARY CARE PSORIASIS PATIENTS

Karreman M.C.1, Weel A.E.A.M.1,2, van der Ven M.1, Vis M.1, Tchetverikov L.1, Wakkee M.1, Nijsten T.E.C.3, Hazes J.M.W.4,5, Luime J.J.1
1Erasmus University, Rheumatology, Rotterdam; 2Maasstad Hospital, Rheumatology, Dordrecht; 3Erasmus University, Dermatology, Rotterdam, The Netherlands

Background. Various screening tools have been developed and validated over the years in order to enhance early recognition of psoriatic arthritis (PsA) among psoriasis patients, but their performance remains subsatisfactory. In 2014 the CONTEST-group developed a new screening tool consisting of the most discriminating questions from 3 existing tools (PEST/PASE/TOPAS).

Aim. To externally validate the CONTEST questionnaire in primary care psoriasis patients.

Methods. Data from the SENSOR study was used, a cross-sectional study in adult primary care psoriasis patients with musculoskeletal complaints. Patients completed the PEST and PASE screening-questionnaires before clinical evaluation. Since we did not include the TOPAS, items from this questionnaire included in the CONTEST were replaced by similar questions. We calculated sensitivity, specificity and area under the curve (AUC) for the CONTEST, the CONTEST-w (weighted version) and the CONTEST-j (including the PEST mamink). Results from our dataset were compared with data from the development cohort and with the performance of the PEST.

Results. For this analysis 473 psoriasis patients were available. Sensitivity was considerably lower in our dataset (0.30-0.51) than in the development cohort (0.66). specificity was higher in our dataset (0.75-0.87) compared with the development cohort (0.35-0.48). AUCs were around 0.7 for all three versions, comparable with the AUCs found in the development of CONTEST. Comparing these results with the performance of the PEST in our population, it shows that the sensitivity is lower for the CONTEST (0.30-0.51) than for the PEST (0.68), while the specificity is slightly higher (0.75-0.87 vs. 0.71).

Conclusions. External validation of the CONTEST questionnaire in primary care psoriasis patients with musculoskeletal symptoms resulted in lower sensitivity and higher specificity compared to the development cohort, while AUCs were comparable. The performance of the CONTEST questionnaires does not seem to exceed the performance of the PEST in primary care.

Disclosure of Interest. This study was financially funded by an investigator-initiated grant from Pfizer bv.

Table 1. Level of Awareness in Patients with Psoriasis or IBD

<table>
<thead>
<tr>
<th>Psoriasis (n=552)</th>
<th>IBD (n=344)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Awareness</td>
<td>43.1</td>
</tr>
<tr>
<td>% Informed by GP</td>
<td>13.5</td>
</tr>
<tr>
<td>% Informed by medical specialist</td>
<td>24.4</td>
</tr>
<tr>
<td>% Via surroundings</td>
<td>18.5</td>
</tr>
<tr>
<td>% Looked it up themselves</td>
<td>34.0</td>
</tr>
<tr>
<td>% Patient organization</td>
<td>8.4</td>
</tr>
<tr>
<td>% Other</td>
<td>1.3</td>
</tr>
</tbody>
</table>

*Only selecting patients with a positive PEST and/or PASE questionnaire.

P46

PERFORMANCE OF ASAS-, BERLIN-, AND CALIN CRITERIA OF INFLAMMATORY BACK PAIN TO DETECT AXIAL SPONDYLOARTHRIITIS

Herrmann J., Leitgeb Ch., Husic R., Dejaco Ch., Graninger W.
Dept. of Internal Medicine, Medical University Graz, Austria

Introduction/Aim. ASAS-, Berlin-, and Calin-criteria of inflammatory back pain (IBP) are available to screen patients for axial spondyloarthritis (axSpA). We compared the performance of these criteria in the diagnosis of axSpA.

Materials and Methods. Patients with undiagnosed chronic back pain attending the Rheumatology outpatient clinic were prospectively enrolled in the study. After signing the patient consent form, each parameter of the ASAS-, Berlin-, and Calin-criteria of IBP were assessed by a rheumatologist. Each patient underwent a clinical investigation, laboratory tests including HLA-B27 and radiographs of the sacroiliac joints and the spine as well as MRI of the sacroiliac joints and clinically affected areas of the vertebral column in order to establish or rule out a diagnosis of axSpA.

Results. A total of 101 patients were enrolled, 34 patients (25 male, mean age 35.9±12.4 years, median symptom duration 3.6 years, 73.5% HLA-B27 positive) were diagnosed with axSpA and 67 patients suffered from non-inflammatory conditions. 15(44.1%), 25(73.5%) and 21(35.3%) patients in the axSpA group and 2(31.3%), 40(59.7%) and 7(31.3%) in the non-axSpA patients fulfilled ASAS-, Calin- and Berlin-criteria of IBP, respectively. The Calin-criteria showed the highest sensitivity (0.74, 95%CI 0.56-0.87) and the ASAS- and Berlin-criteria the highest specificity (0.69, 95%CI 0.56-0.79) for the presence of axSpA. The Berlin-criteria revealed the highest possible likelihood ratio to predict axSpA (LR+ 2.0) and significantly differentiated between patients with and without axSpA (p<0.01).

Discussion. Three sets of criteria of IBP are available but to our knowledge only in the validation study for the ASAS-criteria of IBP these criteria were compared in the same cohort. Although our study confirms the high sensitivity of the Calin-criteria, the ASAS-criteria were equally specific for the presence of axSpA as the Berlin-criteria of IBP.

Conclusion. The Calin-criteria of IBP may be used to screen for axSpA in primary care whereas the ASAS- and Berlin-criteria might be preferred in the diagnostic workup of patients with chronic back pain.

P47

GENDER DIFFERENCES IN ANKYLOSING SPONDYLITIS PATIENTS TREATED WITH ANTI-TNF IN DAILY PRACTICE WITH TEN YEAR FOLLOW UP

Rusman T.1,2, ten Wolde S.3, Euser S.1,2, van der Ploeg T.1,2, van Hall O.2,3, van der Horst-Bruinisse I.E.1,4
1VU University, Health Sciences, Amsterdam; 2Kennemer Gasthuis, Dept. of Rheumatology, Haarlem; Regional Laboratory of Public Health, Kennemerland Haarlem; 3Sparna Medical Centre Alkmaar; 4VU University Medical Centre, Dept. of Rheumatology Amsterdam; 5Linnaeusinstiut Sparne Gasthuis, Haarlem, The Netherlands

Introduction/Aim. Anti-TNF treatment is available for Ankylosing Spondylitis (AS) for many years now, but the data on long term follow up in daily practice are limited. To determine treatment survival and adverse events of anti-TNF treatment in AS patients in a large peripheral hospital in daily practice. Also, gender differences in drug survival and side effects were studied.

Materials and Methods. Retrospective data were collected from AS patients treated with etanercept, infliximab and adalimumab in the period of January 2004 until January 2014 in the Kennemer Gasthuis. Statistical analyses were performed with Kaplan Meijer survival curves to describe the drug survival and occurrence of adverse events in time.

Results. In total 122 ankylosing spondylitis patients were included with 159 treatment episodes (defined as time on drug) over a 10-year time period. The mean treatment duration was 51 months (range 1-127 months). Females showed a significantly shorter treatment period compared to males (33.6 vs. 44.9 months). Overall, 21% of the patients stopped the TNF alpha inhibitor after a mean period of 15 months, mainly due to inefficacy (53.7%). Only 6 patients stopped because of infections (mild) and no patients had malignancies. Female patients switched more often compared to male patients (26.9% vs. 16.3%) (Figure 1). Females had a significantly higher risk (26%) at developing infections compared to males (19%).

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Conclusion. Over a mean treatment period of 4.3 years (51 months), nearly 80% of the patients treated with anti-TNF treatment continued using these drugs. Females showed a significant shorter treatment period compared to males (33.4 vs. 44.9 months). The most important stop reason was inefficacy. Women developed significantly more often infections during anti-TNF treatment than men.

P48

QUALITY OF LIFE IN IBD PATIENTS IS LOWER WHEN HAVING MUSCULOSKELETAL COMPLAINTS: RESULTS OF THE CROSS-SECTIONAL APPSPA SURVEY

Kareman M.C.1,2, Hazes J.M.W.1, Weel A.E.A.M.1,2 1Rheumatology, Erasmus University Hospital, Rotterdam; 2Rheumatology, Maasstad Hospital, Rotterdam, The Netherlands

Background. Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the gastrointestinal tract, comprising both ulcerative colitis (UC) and Crohn’s disease (CD). In addition to the bowel symptoms, patients often suffer from musculoskeletal complaints (MSC). Until now it has not been fully investigated what the additional impact of these MSC is on the health-related quality of life (HRQoL) in patients with IBD.

Aim. To describe the HRQoL in IBD patients with and without MSC compared to the Dutch reference population.

Methods. A cross-sectional survey was set up including unselected IBD patients between 18 and 55 years of age. Patients were invited to participate either by their GP or by the patient organization. Patients willing to participate completed a set of questionnaires regarding their disease, presence of musculoskeletal complaints and quality of life (SF-36 (general), IBDQ (disease-specific)).

Results. 345 patients (of the 658 invited) completed the questionnaires, with a mean age of 42.3 (SD9.3) and 74.5% being female. IBD type was equally distributed with 46% suffering from CD and 45% suffering from UC. Of the patients treated with anti-TNF treatment continued using these drugs. Females showed a significant shorter treatment period compared to males (33.4 vs. 44.9 months). The most important stop reason was inefficacy. Women developed significantly more often infections during anti-TNF treatment than men.

Conclusion. Over a mean treatment period of 4.3 years (51 months), nearly 80% of the patients treated with anti-TNF treatment continued using these drugs. Females showed a significant shorter treatment period compared to males (33.4 vs. 44.9 months). The most important stop reason was inefficacy. Women developed significantly more often infections during anti-TNF treatment than men.

P49

PERFORMANCE OF THE ASAS CLASSIFICATION CRITERIA FOR AXIAL AND PERIPHERAL SPONDYLOARTHRITIS – A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

Sepriano A.1,2, Rubino R.1, Ramiro S.1, Landewé R.1, van der Heijde D.1 1LUMC, Leiden, The Netherlands; 2CEDOC, NMS, Lisbon, Portugal; 3ARC, Amsterdam, The Netherlands

Introduction/Aim. The Assessment of SpondyloArthritis International Society (ASAS) has developed and validated classification criteria for axial spondyloarthritis (axSpA) and peripheral SpA (pSpA). Following their release, the ASAS criteria have been ‘challenged’ in different cohorts. Our aim was to summarize the evidence on the performance of the ASAS classification criteria for axSpA (also imaging and clinical arm separately), pSpA and the entire set, when tested against the Rheumatologist’s diagnosis (‘reference standard’).

Methods. A systematic literature review was performed to identify eligible studies. Raw data was obtained from the authors of the selected publications. A meta-analysis was performed to obtain pooled estimates for sensitivity and specificity. With a series of sensitivity analyses we assessed the possible effects of: i) target population (original validation study inclusion criteria vs different inclusion criteria); ii) setting (hospital vs community); and iii) disease duration (< 2 years vs ≥ 2 years).

Results. Of the 1,647 retrieved articles, 8 fulfilled the inclusion criteria (N=5,042 patients). The entire set of the ASAS SpA criteria yielded high pooled sensitivity (73%) and specificity (88%) (2 studies). Similarly, good results were found for the axSpA criteria (6 studies; sensitivity: 82%; specificity: 88%). Splitting the axSpA criteria in ‘imaging arm only’ and ‘clinical arm only’ resulted in much lower sensitivity (30% and 23% respectively) but retaining very high specificity (97% and 94% respectively).

As for pSpA, the pSpA have shown a similarly high pooled specificity (87%) but lower sensitivity (63%) (3 studies). Sensitivity analyses yielded consistently...
good results for the axSpA criteria (sensitivity: range) 78%-86%; specificity (range): 86%-93%). For pSpA there were few studies therefore hampering sensitivity analyses.

Conclusions. Accumulated evidence confirms the good performance of the various ASAS SpA criteria. The clinical and imaging arm have high specificity but lack sensitivity if applied separately, indicating that the full set of axSpA criteria is the preferred set.

P50

CLINICAL DISEASE ACTIVITY MEASURES ARE ASSOCIATED WITH RADIOGRAPHIC SPINAL PROGRESSION IN EARLY AXIAL SPONDYLOARTHRITIS

Poddbuny D.1, Protopopov M.1, Haibel H.1, Braun J.2, Rudwaleit M.2, Sieper J.1
1Charité Universitätsmedizin Berlin, Berlin; 2Rheumazentrum Ruhrgebiet, Herne; Klinikum Bielefeld Rosenhöfe, Bielefeld, Germany

Introduction/Aim. It has been shown in the past that elevated C-reactive protein (CRP) and the composite Ankylosing Spondylitis Disease Activity Score (ASDAS) are associated with radiographic spinal progression in axial spondyloarthritis (axSpA). It is not clear, however, whether patient-reported measures of disease activity might also play a predictive role. The aim of the study was to investigate the association between patient-reported measures of disease activity and radiographic spinal progression over two years in early axSpA.

Materials and Methods. Altogether 178 patients with definite axSpA (100 with ankylosing spondylitis and 78 with non-radiographic axSpA) from the German Spondyloarthritis Inception Cohort (GESPIEC) were included in the current study. Spinal radiographs were scored according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) and for the presence of syndesmophytes. Clinical and lab data were collected at baseline and every 6 months thereafter. Time-averaged values (over 2 years) of the patient global assessment of disease activity (PG), BASDAI and its components, CRP and CRP-based ASDAS were calculated.

Results. In the logistic regression analysis there was a significant association between time-averaged patient global and syndesmophyte formation: the adjusted OR was 1.30 (95%CI 1.01-1.69). The BASDAI demonstrated no significant association with radiographic spinal progression, but duration (OR=1.36, 95%CI 1.01-1.85) and severity of morning stiffness (OR=1.25, 95%CI 1.01-1.57) were both significantly associated with syndesmophytes formation after two years. Similar trends although not always significant were observed for the mSASSS worsening by 2 points and more after two years. CRP and ASDAS did show an already known association with radiographic spinal progression in early axial SpA.

Conclusions. Higher patient global, duration and severity of morning stiffness are clinical parameters, which are associated with increased risk for syndesmophyte formation in patients with early axial spondyloarthritis.

P51

FUNCTIONAL RELEVANCE OF STRUCTURAL DAMAGE DEVELOPMENT IN THE SPINE IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS

Poddbuny D.1, Haibel H.1, Braun J.2, Rudwaleit M.2, Sieper J.1
1Charité Universitätsmedizin Berlin, Berlin; 2Rheumazentrum Ruhrgebiet, Herne; Klinikum Bielefeld Rosenhöfe, Bielefeld, Germany

Introduction/Aim. It has been shown in the past that radiographic spinal progression is an important determinant of the functional outcome in patients with advanced axial spondyloarthritis (SpA). The objective of the current study was to investigate functional relevance of structural damage development in the spine in patients with early (up to 10 years symptom duration) axial SpA.

Materials and Methods. Altogether 210 patients with early axial SpA from the German Spondyloarthritis Inception Cohort (GESPIEC) were included. Clinical data reflecting disease activity (BASDAI), functional status (BASFI), and spinal mobility (BASMI) were collected at baseline and every 6 months thereafter. Structural damage in the spine was assessed on spinal radiographs at baseline and after two years according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS).

Results. The association between the mSASSS and BASFI status scores at baseline was rather weak: the BASDAI-adjusted parameter estimate (b) in the linear regression analysis was 0.04 (95%CI 0.02-0.07). At the same time, BASDAI itself was strongly associated with BASFI at baseline: b=0.87 (95% CI 0.78-0.96). For the mSASSS change score after 2 years, the parameter estimate b was 0.04 (95%CI 0.00-0.08), meaning that radiographic progression in 25 mSASSS points over 2 years would be responsible for a 1-point difference in BASFI (adjusted for the BASDAI change and mSASSS at baseline). In contrast, BASDAI change score demonstrated a strong association with the BASFI change score: b=0.11 (95% CI 0.01-0.21). Similar results were obtained also for the association between mSASSS and BASMI: b=0.09 (95% CI 0.07-0.12) for the status scores and b=0.01 (95% CI 0.08-0.09) for the change scores.

Conclusions. The functional relevance of the structural damage development in the spine in the majority of patients with early axial SpA seems to be low, while disease activity has a major impact on the function of the spine and should be, therefore, considered as the primary treatment target in these patients.
Poster Presentations

Tenth International Congress on Spondyloarthritides

P53

IMMUNE RESPONSE TO HEPATITIS B VIRUS VACCINATION IN PATIENTS WITH SPONDYLOARTHRITIS TREATED WITH ANTI-TNF THERAPY VS HEMODIALYZED PATIENTS

Valls-Pascual E., Ybáñez García D., Martínez Ferrer À., Vicens Bernabéu E., Vergara Dangond C., Aguilar Zamora M., Alegre Sancho J.J.
Rheumatology, Hospital Universitari Doctor Peset, Valencia, Spain

Introduction. Hepatitis B virus (HBV) vaccination is recommended in patients with inflammatory arthropathies on biologic treatment. Up to the present moment the immune response to HBV vaccination in patients with SpA treated with anti-TNF has not yet been assessed.

Objectives. Main objective: to evaluate the effect of anti-TNF therapy on immune response to HBV vaccination in SpA patients.

Secondary Objectives. To identify potential effect modifiers on immune response to HBV vaccination; comparison with a group of hemodialyzed patients (HD).

Methods. Study type: This is an observational cohort study both prospective and retrospective.

Patients: SpA group: Patients with SpA treated with anti-TNF. HD group: Patients on HD who had received HBV vaccination following HD schedule.

Statistical Analysis. Proportions for categorical variables and average ± SD (or median if appropriate) for continuous variables were calculated. Categorical variables were compared by chi-square test (applying continuity correction if necessary). T-test (or Kruskal-Wallis if appropriate) was used to compare averages.

Results. 30 patients in the SpA group and 19 patients in the HD group were included. 17 patients (89.5%) in the SpA group showed immune response to HBV vaccination whereas only 14 patients (46.7%) in the HD group did. Immune response to vaccination was independent of any of the variables analyzed in the SpA group. When immune response was compared between the two different doses of vaccination (including all patients both from the SpA and the HD groups), a significant statistical difference was observed (p=0.034). The proportion of ‘responders’ was higher if the dose received was 40 mg/ml.

Conclusions. In our study, immune response to HBV vaccination in patients with SpA treated with anti-TNF was lower than in hemodialyzed patients and general population. The proportion of response was larger in patients who received the higher dose of vaccination. This study is limited by the small sample size.

P54

IN PATIENTS WITH SPONDYLOARTHRITIS ANTI-TNF THERAPY IS NOT ASSOCIATED WITH AN INCREASE IN NEOPLASIAS: RESULTS OF GISEA REGISTER

Atzeni F.1,2, Carletto A.1, Fisi R.1, Sebastiani M.1, Panetta V.1, Salafi F.1, Iannone F.1, Gresem E.1, Govoni M.1, Marchesoni A.1, Marchesoni A.1, Gorla R.1, Ramonda R.1,2, Sarzi-Puttini P.1,2, Ferrariaci Gi1, Lapadula G.2
1Rheumatology Unit, L. Sacco, University Hospital, Milan; 2Rheumatology Unit, University of Verona, Verona; 3Rheumatology Unit, Vittorio-Emmanuele University Hospital, Catania, Catania; 4Rheumatology Unit, Azienda Ospedaliero-Universitaria di Modena, Modena; 5L’altrestatistica, Bioistatistics Office, Rome; 6Rheumatology Unit, Polytechnic University of Marche, C. Urbani Hospital, Jesi; 7Rheumatology Unit, University of Bari, Bari; 8Rheumatology Unit, Institute of Rheumatology, Catholic University of the Sacred Heart, Rome; 9Rheumatology Unit, University of Ferrara, Ferrara; 10Rheumatology Unit, Orthopedic Institute G. Pini, Milan; 11Rheumatology and Immunology, Spedali Civili di Brescia, Brescia; 12Rheumatology Unit, University of Padova, Padova; 13Rheumatology Unit, L. Sacco University Hospital, Milan, Italy

The aim was to evaluate the risk of malignancies in SpA patients on TNFi from GISEA registry and to assess predictors.

Methods. GISEA registry was designed to prospectively collect real-world clinical data on patients with RA and SpA treated with biological drugs. Baseline information included demographics, disease duration, HAQ score, BASFI and BASMI scores, steroid use, smoking history and comorbidity were recorded.

Results. In total, 3321 SpA patients (1731 Males (52.2%); mean age 47±13 years; median disease duration 3 [interquartile range (IQR) 0, 8] years) treated with TNFi were included in this analysis: 1065 (32%) treated with infliximab (INF), 1052 (32%) with adalimumab (ADA), and 1204 (36%) with etanercept (ETN). 2105 patients (63.4%) had comorbidities median number 1 [interquartile range (IQR) 0, 2]. In combination with the biological drug, 919 (27.7%) of the patients received steroids and 2451 (79.9%) at least one DMARD. The median (IQR) follow-up time in the TNFi was 3 months (12 years).

50 patients had experienced at least one of the 56 neoplasias during the 12 years of treatment with TNFi, 28% of the patients in the first 12 months. The overall incidence was 6.3/1000 patient-years of follow-up (95% CI 4.7–8.2); 7.3/1000 patient-years (95% CI 4.1–11.8) among those treated with ADA; 6.1/1000 patient-years (95% CI 3.8–9.4) among those treated with ETN; and 5.8/1000 patient-years (95% CI 3.5–9.1) among those treated with INF. Univariate analysis showed that the age at the start of anti-TNF treatment (p=0.001), and number of comorbidities (p=0.01) and value of HAQ score (p=0.002) were associated with high risk of malignances. Multivariate models confirmed that male sex (hazard ratio [HR] 4.5; 95%CI: 1.3–16.0; p=0.020) and age at the start of TNFi (HR 1.10; 95%CI: 1.01–1.11; p=0.020), value of HAQ score (HR 2.8; 95%CI: 1.5–5.3; p=0.002), were statistically significant predictors of malignances. Ten out of fifty patients that experienced neoplasia had a previous cancer (HR 11.2 95%CI 4.4–28.4, p=0.001).

Conclusions. TNFi therapy is not associated with a significant overall risk of malignances in SpA patients, although to have a previous cancer is a predictor factor for a new neoplasia.

P55

BODY MASS INDEX IS RELATED WITH THE PRESENCE OF SYNDENSMOPHYTE IN AXIAL SPONDYLOARTHRITIS: DATA FROM KOREAN COLLEGE OF RHEUMATOLOGY BIOLOGICS (KOBIO) REGISTRY COHORT

Division of Rheumatology, Dept. of Internal Medicine, Arthritis & Autoimmunity Research Center, Catholic University of Daegu School of Medicine, Daegu, Republic of Korea

Objective. We cross-sectionally investigated whether body mass index (BMI) is associated with parameters of disease activity and clinical manifestations in axial spondyloarthritis (axSpA).

Methods. Demographic, clinical, and radiological features and disease activity indexes from 789 axSpA patients (619 males and 170 females) were obtained from the Korean College of Rheumatology Biologics (KOBIO) registry cohort. BMI (kg/m²) was classified into normal (BMI <23.0), overweight (23.0 ≤BMI <25.0), and obese (BMI ≥25.0). Disease activity indexes included ESR, CRP, ASDAS, BASDAI, and BASFI.

Results. The mean BMI in patients with axSpA was 23.8±1.3. 50.2% of all patients were overweight or obese. Overweight/obese female patients showed higher ESR, CRP, ASDAS-ESR, and ASDAS-CRP than normal patients (p=0.045, p=0.011, p=0.035, and p=0.029, respectively). Patients with ASDAS score ≥2.1 showed higher BMI than patients with ASDAS score <2.1 (p=0.019). A greater increase in BMI was noted in patients with syndesmophyte than in those without syndesmophyte (p=0.001). Multivariate regression analysis showed that increased BMI was closely related with presence of syndesmophyte (β=0.932, p=0.002). In addition, syndesmophyte was found to be influenced by BMI (OR=1.087, 95% CI 1.033 - 1.145, p=0.007).

Conclusion. Our results imply that increased BMI was related with presence of syndesmophyte and in part associated with disease activity in axSpA.

P56

UNMET NEEDS IN PSORIATIC ARTHRITIS: ONE THIRD OF THE PATIENTS WITH QUESCIENT DISEASE ACCORDING TO THE RHEUMATOLOGIST'S OPINION DO NOT ACHIEVE MINIMAL DISEASE ACTIVITY

van Mens L.1,2, van Kuijik A.1, Baeten D.1
1AMC; 2Reade, Amsterdam Rheumatology and Immunology Center, Amsterdam, The Netherlands

Introduction. Several new drugs including ustekinumab, apremilast, and secukinumab, became available for the treatment of psoriatic arthritis(PsA). Achieving a lowest possible disease activity in all domains is associated with better long-term outcomes, and new therapeutic modalities may potentially benefit patients with partial but not full disease control with the current treatment options. Defining an acceptable disease state in routine clinical practice is becoming increasingly important to identify who could potentially benefit from treatment adjustment.

Aim. Assess how many patients with quiescent disease according to the treating rheumatologist have an acceptable disease state defined as minimal disease activity (MDA).

Methods. This cross-sectional study was performed in 2 rheumatology centers and included 250 PsA patients. Key inclusion criteria were fulfillment of the
P57

SUBCLINICAL Atherosclerosis in Ankylosing Spondylitis – Does It Really Exist and Which Are the Effects of Treatments? a Systematic Review

Prati C.1,2, Demougeot C.2, Guillot X.1,2, Verhoeven F.1,2, Wendling D.1
1Rheumatology Dept., University Hospital, Besançon; 2FDE EA4267, FHU INCREASE, Bourgogne Franche-Comté University, Besançon, France

Objectives. Accelerated atherosclerosis and increased cardiovascular morbidity and mortality have been associated with ankylosing spondylitis (AS). Non-invasive methods have been developed to evaluate vascular dysfunction which is correlated with future development of atherosclerosis. The objectives were to determine the presence or not of a subclinical vascular dysfunction in AS and if treatments could have an effect on it.

Methods. Studies evaluating subclinical atherosclerosis and vascular function in AS were identified using Pubmed. (Ovid, EMBASE). Search terms included “ankylosing spondylitis” AND (endothelial OR vascular OR intima media thickness (IMT) OR Flow mediated dilatation (FMD) OR pulse wave velocity (PWV) OR atherosclerosis). This identified 353 results after limiting to French and English. The final selection identified 29 publications.

Results. 1529 AS patients were included: 8 studies about endothelial function, 198 AS patients and 130 healthy control (HC); 20 studies about carotid IMT, 900 AS and 644 HC; 10 studies about arterial rigidity, 431 AS and 285 HC. In cross-sectional studies, 4/6 indicated endothelial dysfunction in AS versus HC, 9/18 indicated increased cIMT and 3/5 increased arterial rigidity. About ED, 3 open label studies noted positive effect of TNF-α blockers and spironolactone on FMD, and rosuvastatin improved FMD in a placebo controlled study. TNF-α blockers do not seem to improve either cIMT or arterial rigidity. Exercise alone improved arterial rigidity in 15 patients after 12 weeks.

Conclusion. Whereas early and accelerated atherosclerosis is present in AS, presence of subclinical atherosclerotic lesions is controversial in the literature, especially concerning cIMT and arterial stiffness. This is reinforced by the lack of TNF-α blockers efficacy. Conversely it seems that exercise is present and reversed in patients with both TNF-α blockers and statins and spironolactone. These results are consistent to treat AS patients with early effective treatment to prevent the risk of CV morbidity and mortality.

P58

VALIDATION OF THE ASAS HEALTH INDEX: RESULTS OF A MULTICENTER INTERNATIONAL STUDY IN 23 COUNTRIES

Kiltz U.1, van der Heijde D.1, Boonen A.2, Braun J.3, on behalf of working group 4ASAS International validation
1Rheumazentrum Ruhrgebiet, Herne, Germany; 2Leiden University Medical Center, Dept. of Rheumatology, Leiden; 3Aarhus University Medical Center, Division of Rheumatology, Aarhus, The Netherlands

Aim. To test in 23 countries construct validity, reliability and responsiveness of the ASAS HI and its 17 translations.

Methods. A convenient sample of SpA patients fulfilling the ASAS classification criteria for either axial (axSpA) or peripheral SpA (pSpA) were included into the study. Data were collected by the local rheumatologist.

Results. 1548 patients were included: 64.9% male, mean (SD) age 42.0 (13.4) years, mean (SD) BASDAI 4.1 (2.5). There were 1299 patients with axSpA (375 nr-axSpA and 924 AS patients) and 256 patients with pSpA. The total score of the ASAS HI was 6.7±4.3 (mean ± SD). Floor or ceiling effects were limited (0.8 and 6.9%, respectively). Convergent validity ranged as hypothesized with Spearman correlations from low (age: r=0.10) to good (BASDAI: r=0.70). ASAS HI scores showed a high internal consistency with a Cronbach’s-α of 0.95. The ASAS HI discriminated well between patients with different stages of disease activity and function irrespective of the tool applied (ASDAS, BASDAI and BASFI) (Table 1). The groups with greater disease activity and more impaired functioning had higher mean ASAS HI scores (indicating impaired functioning) than those with lower disease activity. Reliability (tested in 578 patients) was good (ICC: 0.87 (95%CI 0.84 to 0.89), p<0.01) and comparable in all disease subtypes. Sensitivity to change (tested in 246 patients) showed a moderate SRM of -0.44 for NSAIDs (n=75 patients) 0.69 for DMARDs (n=41) and -0.85 for TNFi (n=127). The smallest detectable change in this cohort was 3.0.

Conclusions: The ASAS HI is a valid, reliable and responsive measure of disease severity in patients with SpA. It should be used in clinical trials to evaluate the impact of SpA and its treatment on overall functioning and health.

Table 1. Discriminant ability of the ASAS HI stratified by disease activity.

<table>
<thead>
<tr>
<th></th>
<th>Inactive (n=245)</th>
<th>Moderate (n=280)</th>
<th>High (n=503)</th>
<th>Very high (n=589)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS HI</td>
<td>2.9 ± 3.1</td>
<td>5.1 ± 3.5</td>
<td>7.3 ± 3.6</td>
<td>10.4 ± 3.5</td>
</tr>
<tr>
<td>BASFI</td>
<td>0.9 ± 1.4</td>
<td>2.1 ± 1.9</td>
<td>3.7 ± 2.5</td>
<td>5.9 ± 2.5</td>
</tr>
<tr>
<td>BASDAI</td>
<td>1.2 ± 0.9</td>
<td>2.7 ± 1.3</td>
<td>4.7 ± 1.7</td>
<td>7.0 ± 1.6</td>
</tr>
</tbody>
</table>

All values given as mean±SD.

P59

STUDY OF PREVALENCE AND PREDICTORS OF MINIMAL DISEASE ACTIVITY (MDA) STATE IN A SPANISH POPULATION WITH PSORIATIC ARTHRITIS - MAAPs STUDY

Quero R.1, Abad M.A.2, Sellas A.2, Rodríguez F.J.3, Bermúdez A.2, Romero M.2, Riesco M.1, Cobeta J.C.2, Medina F.2, Aragón A.2, Gómez S.2, Montero M.2, Cáceres A.1
1HU Central de Asturias, Oviedo; 2H. Virgen del Puerto, Plasencia; 3H. Vall d’Hebron, Barcelona; 4H. Santa Luzia, Cartagena; 5H. Virgen de la Arrixaca, Murcia; 6H. Complejo Hospitalario Jaén; 7H. Juan Ramón Jiménez, Huelva; 8H. Royo Villanueva, Zaragoza; 9H. Puerta del Mar; 10H. Getafe, Madrid; 11Medical Dept., Pfizer, Madrid, Spain

Background. Minimal disease activity (MDA) has become the optimal target in the treatment of PsA, waiting for a standardized definition of remission. Knowing the proportion of PsA patients in the MDA state could provide information on the quality of management of these patients.

Objective. To determine the prevalence of MDA in patients with PsA in Spain as well as its potential predictors.

Methods. This was a non-interventional, cross-sectional, multicenter study, which aimed to evaluate the prevalence of MDA in a Spanish population with PsA. The study was carried out at 25 rheumatology outpatient clinics between May/2014 and Feb/2015. A total of 238 adult patients diagnosed with PsA (CASPAR criteria) with at least one year disease duration and treated with biological and non-biological DMARDs were included. Finally, 227 were considered evaluable.

Clinical, demographic, treatment data, physical function (HAQ) and quality of life (PsAID) were obtained. The patient acceptable symptoms state (PAS) has been defined as a PsAID value < 4. All patients gave informed consent. An Ethics committee board approved the final version of this study.

Results. Overall, 133 out of 227 (58.6%) subjects achieved MDA. MDA patients had significantly lower impact of the disease (PsAID: 3.3±2.0 vs non-MDA Patients: 7.1±3.5, p<0.001). All domains of the disease were significantly better in MDA patients. In multivariate logistic regression analysis, male gender (OR 2.74, p=0.001), sedentary lifestyle (OR 3.13, p=0.002), familial history of PsA (OR 0.38, p=0.036), CRP level (OR 0.92, p=0.010) and use of corticoids (OR 0.33, p=0.007) were predictors of MDA.

Conclusions. In this study, nearly 60% of patients reached the MDA state, similar to what has been published in other countries. The MDA is a good therapeutic target in PsA, as patients who reach this state have better functional status, a better quality of life, and are more actively working.
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CORRELATION OF THREE ENthesises INDICES WITH DISEASE ACTIVITY AND FUNCTION IN BRAZILIAN PATIENTS WITH SPONDYLOARTHRITIDES


1Hospital of Clínicas of Porto Alegre, Rheumatology Dept.; 2Hospital Universitário Evangélico de Curitiba, Rheumatology Dept.; 3Universidade Federal do Amazonas, Faculdade de Medicina; 4Universidade Federal do Rio Grande do Sul, Medical Students; 5Hospital of Clínicas of Porto Alegre, Biostatistic Dept.; 6Universidade de São Paulo, Faculdade de Medicina, Brazil

Introduction. Although enthesitis are associated with higher disease activity, more disability and poorer quality of life in spondyloarthritides (SpA), there is currently no consensus for the best score to assess enthesitis in SpA.

Aim. To compare the correlation of MASES, SPARCC and LEI with measures of disease activity and function in a heterogeneous population of Brazilian patients.

Material and Methods. A cross-sectional study was conducted in three Brazilian hospitals; patients fulfilling ASAS criteria for peripheral and/or axial SpA were recruited and measures of disease activity and function were collected and correlated to MASES, SPARCC and LEI.

Results. 204 patients were included, 29.9% (N=61) fulfilled criteria for pure axial SpA and 28.9% (N=59) for pure peripheral SpA; 41.2% (N=84) fulfilled both axial and peripheral criteria. In axial SpA, MASES performed better than LEI (p=0.018) and equal to SPARCC (p=0.212) regarding correlation with disease activity (BASDAI) and function (BASFI). In peripheral SpA, MASES was slightly better than SPARCC when the correlation with HAQ was studied (p=0.046) and in PsA there was no statistical difference among the three indices.

Conclusion. In the Brazilian population, where patients have a broad spectrum of clinical manifestations, MASES is an appropriate tool to evaluate enthesitis since it has satisfactory correlation with measures of disease activity and function in both axial and peripheral patterns of SpA.

P61

PREVALENCE OF MINIMAL DISEASE ACTIVITY IN “REAL LIFE”: CROSS SECTIONAL STUDY IN BRAZILIAN PATIENTS WITH PSORIATIC ARTHRITIS AND A LITERATURE REVIEW


Hospital de Clínicas de Porto Alegre, Rheumatology Dept.; Hospital Evangélico de Curitiba, Rheumatology Dept.; Universidade Federal do Amazonas, Faculdade de Medicina; Hospital de Clínicas de Porto Alegre, Biostatistic Dept.; Universidade Federal do Rio Grande do Sul, Medicine student; Universidade de São Paulo, São Paulo, Brazil

Introduction. Although minimal disease activity (MDA) has been frequently used as target in psoriatic arthritis (PsA) clinical trials, there are few studies evaluating its performance in “real life”.

Aim. To analyze the prevalence of MDA among patients with PsA followed in public university hospitals in Brazil and conduct a literature review about the use of MDA in “real life”.

Material and Methods. PsA patients were recruited in three Brazilian hospitals for a cross-sectional study; the prevalence of patients fulfilling criteria for MDA, DAS28-ESR remission and DAS28-ESR low disease activity was calculated and the correlation between DAS28-ESR and MDA was analyzed using Kappa coefficient. A literature review was performed in PUBMED/MEDLINE and ACR, EULAR, GRAPPA Annual Meeting conferences abstracts; works reporting the use of MDA in real life were included.

Results. In the cross-sectional study, 58 PsA patients were included: 48.7% (N=28) were women, mean disease duration was 12.7 years (±8.3) and 22% (N=13) were currently on biological therapy. The overall prevalence of patients fulfilling MDA status, DAS28 remission and DAS28 low disease activity was 22.8%, 22.4%, and 20.7%, respectively. There was a poor correlation between DAS28 remission and MDA (Kappa’s coefficient 0.347). The literature review found 16 references, which included 2896 patients, with a mean disease duration 9.1 years (±2.8); 51.8% (N=1503) subjects were currently on biological therapy. These work reported a prevalence of MDA ranging from 15.6%.

Conclusion. The prevalence of MDA found in these Brazilian sample is in accordance with data from other real life studies.
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DOES CHANGE IN DISEASE ACTIVITY OVER ONE YEAR RESULT IN CHANGE IN HEALTH-RELATED QUALITY OF LIFE IN AXIAL SPONDYLOARTHRITIS PATIENTS?

van Lunteren M.¹, Ez-Zaitouni Z.¹, Bakker P.², Dagfinrud H.², Landewé R.², van Oosterhout M.⁴, Ramonda R.³, van Gaalen F.¹, van der Heijde D.¹
¹Rheumatology, LUMC, Leiden, The Netherlands; ²Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; ³Rheumatology, AMC, Amsterdam; ⁴Rheumatology, GHZ, Gouda, The Netherlands; ⁵Rheumatology, University of Padova, Padova, Italy

Aim. To assess the association between the change in ASDAS (CRP based) and Health Related Quality of Life (HRQoL) between baseline and one year in patients with early Spondyloarthritis (axSpA).

Methods. The SPACE study includes patients with chronic back pain (≥3 months, ≤2 years, onset ≤45 years) from five European centers. The 36-item Short-Form (SF-36) was completed by patients to assess HRQoL at baseline and one year. Physical (PCS) and Mental Component Summary (MCS) scores were calculated (adjusted for country, gender, age) ranging from 0 (worst) to 100 (best), and were compared to the general population mean (50) and standard deviation (SD). Linear regression models adjusted for age were made with change of ASDAS between baseline and one year (ΔASDAS) as a determinant and change of PCS (ΔPCS) or MCS (ΔMCS) as an outcome.

Results. Eighty-six patients fulfilled the ASAS axSpA criteria (50 clinical arm, 36 imaging arm). Patients had a mean of 27.0 (SD 15.8), mean MCS of 49.3 (SD 13.0), and mean ASDAS of 2.4 (SD 1.0) at baseline. At one year mean PCS increased to 36.0 (SD 13.9), MCS remained stable at 49.7 (SD 12.1), mean ASDAS decreased to 2.0 (SD 0.8). As MCS was not different from the general population, only the effect of ΔASDAS as a determinant and change of PCS (ΔPCS) or MCS (ΔMCS) as an outcome was investigated.

Fulfilment of imaging or clinical arm and gender had a two-way interaction. Fulfilled imaging or clinical arm and gender were tested for interaction. Results. Eighty-six patients fulfilled the ASAS axSpA criteria (50 clinical arm, 36 imaging arm).

Patients had a mean of 27.0 (SD 15.8), mean MCS of 49.3 (SD 13.0), and mean ASDAS of 2.4 (SD 1.0) at baseline. At one year mean PCS increased to 36.0 (SD 13.9), MCS remained stable at 49.7 (SD 12.1), mean ASDAS decreased to 2.0 (SD 0.8). As MCS was not different from the general population, only the effect of ASDAS on PCS was determined. In the univariable model (Table I), a decrease of one unit of ASDAS resulted in an increase of 9.7 (SE 1.5) in PCS (adjusted for country, gender, age) ranging from 0 (worst) to 100 (best), and were compared to the general population mean (50) and standard deviation (SD). Linear regression models adjusted for age were made with change of ASDAS between baseline and one year (ΔASDAS) as a determinant and change of PCS (ΔPCS) or MCS (ΔMCS) as an outcome.

Table I. Association between the change in ASDAS and the change in Physical Component Summary (PCS) at baseline and one year in axial Spondyloarthritis patients in the SPACE cohort (n=86).

<table>
<thead>
<tr>
<th>PCS</th>
<th>n</th>
<th>Coefficient</th>
<th>Standard error</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariable model</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔASDAS</td>
<td>86</td>
<td>-0.7</td>
<td>1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model for gender and ASAS classification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men fulfilling the clinical arm</td>
<td>ΔASDAS</td>
<td>18</td>
<td>-11.8</td>
<td>4.0</td>
</tr>
<tr>
<td>Men fulfilling the imaging arm</td>
<td>ΔASDAS</td>
<td>24</td>
<td>-15.8</td>
<td>2.7</td>
</tr>
<tr>
<td>Women fulfilling the clinical arm</td>
<td>ΔASDAS</td>
<td>32</td>
<td>-6.9</td>
<td>2.1</td>
</tr>
<tr>
<td>Women fulfilling the imaging arm</td>
<td>ΔASDAS</td>
<td>12</td>
<td>4.8</td>
<td>0.615</td>
</tr>
</tbody>
</table>

Fulfilment of clinical or imaging arm and gender had a two-way interaction (p=0.10, R²=38.6%). The effect of ΔASDAS on ΔPCS was most pronounced in patients in the SPACE cohort (n=86).

Six dimensions of the IPQ-R were associated with ASDAS. Stronger illness identity (β=-0.63, p=0.003), stronger beliefs in severe consequences (β=-0.32, p=0.001), less illness coherence (β=0.24, p=0.003), more negative emotions towards their complaints (β=0.22, p=0.003), stronger beliefs of psychological attributions as a cause only in men (β=0.22, p=0.034), and the belief of immunity as a cause (β=0.17, p=0.01) were statistically significantly associated with a higher ASDAS.

Conclusions. Negative illness perceptions are associated with disease activity in early axSpA patients.

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THE ASSOCIATION BETWEEN DISEASE ACTIVITY AND ILLNESS PERCEPTIONS IN EARLY AXIAL SPONDYLOARTHRITIS PATIENTS IN THE SPACE COHORT

van Lunteren M.¹, Scharloo M.², Kaptein A.¹, Ez-Zaitouni Z.¹, Bakker P.², Fongen C.³, Landewé R.¹, van Oosterhout M.¹, Lorenzin M.⁴, van Gaalen F.¹, van der Heijde D.¹
¹Rheumatology, LUMC, Leiden, The Netherlands; ²Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; ³Rheumatology, AMC, Amsterdam; ⁴Rheumatology, GHZ, Gouda, The Netherlands; ⁵Rheumatology, University of Padova, Padova, Italy

Aim. To describe illness perceptions and to explore the association between illness perceptions and disease activity in patients with early Spondyloarthritis (axSpA) at baseline.

Material. The SPACE cohort includes patients (chronic back pain ≥3 months, ≤2 years, onset ≤45 years) from five European centers. Patients completed the Revised Illness Perception Questionnaire (IPQ-R). The illness identity dimension asked patients if they have experienced a certain symptom (15) and if they believed these symptoms are related to axSpA. Other illness perception dimensions and causal attributions used 5-point Likert scales to score all items ranging from 1 (strongly disagree) to 5 (strongly agree). Disease activity was assessed by ASDAS (CRP based). Univariable linear regression models were built for each IPQ-R dimension as dependent and ASDAS as independent variable adjusted for age and gender. Results were stratified when gender was an effect modifier (p=0.10).

Results. Patients fulfilling axSpA ASAS classification (n=119) were included. The mean age was 29.7 (SD 7.9) years, 50.4% were male. The mean disease duration was 13.0 (SD 7.3) months and the mean ASDAS 2.4 (SD 3.0). Patients reported on average 4.2 (SD 2.3) symptoms to be related to axSpA. Other illness perception dimensions and causal attributions were related to ASDAS. Univariable linear regression models were built for each IPQ-R dimension as dependent and ASDAS as independent variable adjusted for age and gender. Results were stratified when gender was an effect modifier (p=0.10).

Conclusions. Six dimensions of the IPQ-R were associated with ASDAS. Stronger illness identity (β=-0.63, p=0.003), stronger beliefs in severe consequences (β=-0.32, p=0.001), less illness coherence (β=0.24, p=0.003), more negative emotions towards their complaints (β=0.22, p=0.003), stronger beliefs of psychological attributions as a cause only in men (β=0.22, p=0.034), and the belief of immunity as a cause (β=0.17, p=0.01) were statistically significantly associated with a higher ASDAS.

Conclusions. Negative illness perceptions are associated with disease activity in early axSpA patients.
IS DISEASE ACTIVITY ASSOCIATED WITH WORK PRODUCTIVITY LOSS, PRESENTEEISM, AND ABSENTEEISM IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHROPATHY? RESULTS FROM THE SPACE COHORT

van Lunteren M.1, Bakker P.1, Ez-Zaitouni Z.1, van der Vijjer J.1, Fongen C.3, Landewé R.3, van Oosterhout M.4, Ramonda R.5, van Gaalen F.5, van der Heijde D.1
1Rheumatology, LUMC, Leiden, The Netherlands; 2Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; 3Rheumatology, AMC, Amsterdam; 4Rheumatology, GHZ, Gouda, The Netherlands; 5Rheumatology, University of Padova, Padova, Italy

Aim. To investigate if the impact of disease activity, assessed by ASDAS (CRP based), on work productivity is similar in different subgroups at baseline in early axial Spondyloarthritides (axSpA) patients.

Methods. The SPACE-cohort includes patients (chronic back pain ≥3 months, ≥2 years, onset <45 years) from five European centres. Patients fulfilling ASAS axSpA criteria were included in this analysis. Work Productivity and Activity Impairment questionnaire (WPAI) was completed by patients at baseline to assess Work Productivity Loss (WPL), total work impairment due to disease), presenteeism (decreased work functionality due to disease), and absenteeism (absence at work due to disease) in the past week. Higher scores indicate greater impairment (range 0-100). Gender, age, medication use, profession, HLA-B27+, and duration of back pain were tested for effect modification (cut-off of p<0.20) in linear regression models.

Results. Eighty-seven axSpA patients working at baseline were included (53 patients fulfilled clinical arm, 34 imaging arm of the ASAS axSpA criteria). Patients were on average 30.8 years old (SD 7.6), 52.9% were male, and mean duration of back pain was 13 months (SD 7.1). Model-wise, WPL, presenteeism, and absenteeism were 34.3% (SD 28.5), 31.4% (SD 25.3), and 8.2% (SD 20.1) respectively. Patients had a mean ASDAS of 2.3 (SD 0.9). In unvariable model (Table 1), one point increase in ASDAS resulted in an increase of 19.3%, 16.9%, and 8.7% in WPL, presenteeism, and absenteeism, respectively. Gender and duration of back pain were effect modifiers and results were stratified for these variables. The associations remained statistically significant in almost all stratified models.

Table I. Association between ASDAS and Work Productivity Loss, presenteeism, and absenteeism at baseline among axial Spondyloarthritides patients who performed paid work in the SPondyloArthritis Caught Early (SPACE)-cohort (n=87).

<table>
<thead>
<tr>
<th>Variable (model(n=87))</th>
<th>Coefficient</th>
<th>p-value</th>
<th>Coefficient</th>
<th>p-value</th>
<th>Coefficient</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASDAS</td>
<td>18.3 (2.6)</td>
<td>&lt;0.001</td>
<td>18.9 (2.3)</td>
<td>&lt;0.001</td>
<td>8.7 (2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model for gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men (n=40)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASDAS</td>
<td>14.3 (5.5)</td>
<td>&lt;0.001</td>
<td>12.1 (2.8)</td>
<td>&lt;0.001</td>
<td>4.4 (2.5)</td>
<td>0.096</td>
</tr>
<tr>
<td>Women (n=47)</td>
<td>22.0 (5.7)</td>
<td>&lt;0.001</td>
<td>19.3 (3.3)</td>
<td>&lt;0.001</td>
<td>12.6 (3.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model for duration of back complaints</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 months (n=34)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASDAS</td>
<td>13.5 (4.3)</td>
<td>0.000</td>
<td>12.5 (3.9)</td>
<td>0.000</td>
<td>5.0 (0.9)</td>
<td>0.207</td>
</tr>
<tr>
<td>≥1 months (n=53)</td>
<td>21.4 (2.9)</td>
<td>0.000</td>
<td>18.3 (2.6)</td>
<td>0.000</td>
<td>11.0 (2.3)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions. The same level of disease activity seems to have more adverse impact on work productivity in women than in men, and irrespective of that, in patients with relatively long disease duration. Additionally, gender and disease duration are relevant contextual factors in explaining WPL in early axSpA patients.

ILLNESS PERCEPTIONS AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND OTHER FORMS OF CHRONIC BACK PAIN IN THE SPACE COHORT

van Lunteren M.1, Bakker P.1, Scharloo M.2, Kaptijn A.1, Ez-Zaitouni Z.2, Fongen C.3, Landewé R.3, van Oosterhout M.4, Lorenzen M.5, van Gaalen F.5, van der Heijde D.1
1Rheumatology and 2Psychology Depts., LUMC, Leiden, The Netherlands; 3Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; 4Rheumatology, AMC, Amsterdam; 5Rheumatology, GHZ, Gouda, The Netherlands; 6Rheumatology, University of Padova, Padova, Italy

Aim. To explore the association between illness perceptions and Health-Related Quality of Life (HRQoL) in patients with short symptom duration of axial Spondyloarthritides (axSpA) and other forms of chronic back pain (CBP) at baseline.

Methods. The SPACE study includes patients with CBP (≥3months, ≥2years, onset <45years) from five European centers. Revised Illness Perception Questionnaire (IPQ-R) was completed at baseline.

In illness identity dimension, patients reported if they had experienced and believed that a certain symptom is CBP-related. Other dimensions used 5-point Likert scales (1=strongly disagree; 5=strongly agree). HRQoL was assessed by 36-item Short-Form (SF-36). Physical (PCS) and Mental Component Summary (MCS) scores were calculated ranging from 0 (worst) to 100 (best). Univariable regression models were built for each IPQ-R subscale as independent and PCS or MCS as dependent variable.

Models were adjusted for age and gender and stratified in case of effect modification by gender (p<0.10).

Results. 315 patients were included (123 fulfilled axSpA ASAS criteria; 192 did not). Mean PCS was 28.0(SD 16.3) for axSpA and 24.9 (SD 14.4) for CBP patients. As MCS was only slightly decreased compared to the general population, analyses focused on PCS. Attribution of multiple symptoms to CBP related. Other dimensions used 5-point Likert scales (1=strongly disagree; 5=strongly agree). HRQoL was assessed by 36-item Short-Form (SF-36). Physical (PCS) and Mental Component Summary (MCS) scores were calculated ranging from 0 (worst) to 100 (best). Univariable regression models were built for each IPQ-R subscale as independent and PCS or MCS as dependent variable.

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Results. 315 patients were included (123 fulfilled axSpA ASAS criteria; 192 did not). Mean PCS was 28.0(SD 16.3) for axSpA and 24.9 (SD 14.4) for CBP patients. As MCS was only slightly decreased compared to the general population, analyses focused on PCS. Attribution of multiple symptoms to CBP related. Other dimensions used 5-point Likert scales (1=strongly disagree; 5=strongly agree). HRQoL was assessed by 36-item Short-Form (SF-36). Physical (PCS) and Mental Component Summary (MCS) scores were calculated ranging from 0 (worst) to 100 (best). Univariable regression models were built for each IPQ-R subscale as independent and PCS or MCS as dependent variable.

Conclusions. Negative illness perceptions are associated with lower PCS of HRQoL in patients with axSpA and other forms of CBP. This association was more pronounced in men than in women.
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**COMORBIDITIES ARE ASSOCIATED WITH WORSE CLINICAL OUTCOMES AND QUALITY OF LIFE IN PATIENTS WITH SPONDYLOARTHITIS – RESULTS FROM MULTI-NATIONAL ASAS-COMOSPA STUDY**

Nikiphrour E.1, Ramiro S.2, Landewé R.1, Moltó A.1, Doutogos M.1, Van den Bosch F.1, van der Heijde D.2
1UCL, London, UK; 2LUMC, Leiden; 3Arc, Amsterdam, The Netherlands; 4Paris Descartes University, Paris, France; 5Ghent University Hospital, Ghent, Belgium

**Introduction/Aim.** Comorbidities add to the burden of disease and its complexity. We aimed at investigating the impact of comorbidities on several disease outcomes in SpA.

**Patients and Methods.** Multi-national, cross-sectional study. Data on comorbidities collected using the Rheumatic Disease Comorbidity Index (RDCI). Univariable and multivariable linear regression analyses conducted to determine for associations between the RDCI and: (1) disease activity; (2) functional ability; (3) Quality of Life.

**Results.** Of 3370/3984 (85%) patients fulfilling the ASAS criteria, 66% were male; mean age 43 (SD 14), median disease duration 5 years (SD 5) and mean RDCI 0.7 (SD 1.1). At least one comorbid condition was found in 51% patients; 9% had ≥3 comorbidities. An increase in RDCI was associated with higher BASFI, BASDAI, ASDAS and patient global score and lower EQ5D (all p<0.001) (Table). For example, an RDCI score of 2 compared to 0 had approximately 0.7 point higher on the BASFI and one point higher on the BASDAI. The EQ5D dropped by 0.03 point with every unit increase in the RDCI.

**Table.** Relationship between comorbidities and disease outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>RDCI (β [95%CI])</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASFI</td>
<td>0.36 [0.30-0.43]</td>
</tr>
<tr>
<td>BASDAI</td>
<td>0.53 [0.45-0.61]</td>
</tr>
<tr>
<td>ASDAS</td>
<td>0.17 [0.13-0.20]</td>
</tr>
<tr>
<td>Patient’s global assessment of disease activity^</td>
<td>0.45 [0.36-0.53]</td>
</tr>
<tr>
<td>EQ5D**</td>
<td>-0.03 [-0.04-0.02]</td>
</tr>
</tbody>
</table>

^All models adjusted for age/gender
Model also adjusted for disease duration; level of education; BMI; smoking status; ASDAS and the presence of axial vs peripheral disease
Model also adjusted for level of education; BMI; smoking status; history of enthesitis
Model also adjusted for level of education; BMI; smoking status

**Conclusions.** A rising comorbidity burden is independently associated with worse disease activity, functional outcomes and quality of life in SpA. Promptly identifying and considering comorbidities in treatment decisions is therefore important for optimising disease and patient outcomes.

**P68**

**LONG-TERM (UP TO 156 WEEKS) SAFETY PROFILE OF ORAL APRIMELAST IN PATIENTS WITH PSORIATIC ARTHRITIS: POOLED ANALYSIS OF PALACE 1-3**

Mease P.J.1, Gladman D.D.1, Gomez-Reino J.J.1, Hall S.1, Kavanaugh A.1, Lespes-sailles E.1, Schet G.2, Shah K.1, Teng L.1, Wollenhaupt K.1
1Swedish Medical Center/University of Washington School of Medicine, Seattle, WA, USA; 2Trento Western Research Institute, Trento, ON, Canada; 3Hospital Clínic Universitario, Santiago, Spain; 4Monash University, Melbourne, Australia; 5UCSD School of Medicine, La Jolla, CA, USA; 6University of Orléans, Orléans, France; 7University of Erlangen-Nuremberg, Erlangen, Germany; 8Celgene Corporation, Summit, NJ, USA; 9Schön Klinik Hamburg Elbick, Hamburg, Germany

**Introduction/Aim.** PALACE 1-3 (NCT01172938, NCT01212757, NCT01212770) compared the efficacy and safety of apremilast (APR) with placebo in patients with active psoriatic arthritis despite prior conventional DMARDs and/or biologics. We assessed long-term APR safety for up to 3 years.

**Materials and Methods.** Patients were randomized (1:1:1) to placebo, APR 30 mg BID (APR30), or APR 20 mg BID (APR20). Placebo patients were re-randomized (APR30, APR20) at Week 16 (early escape) or Week 24. Double-blind APR treatment continued to Week 52; patients could continue APR during an open-label treatment phase.

**Results.** 1,493 patients were randomized; 1,441 patients had 0–≤52 weeks exposure to APR, 1,028 had >52–≤104 weeks exposure, and 865 had >104–≤156 weeks exposure at the 3-year data cut. During Weeks 0–≤52, adverse events (AEs) occurring in ≥5% of APR-exposed patients were diarrhea, nausea, headache, URTI, and nasopharyngitis. Diarrhea and nausea usually occurred/resolved without intervention early in treatment (<2 weeks/≤4 weeks). During Weeks >52–≤104 and >104–≤156, gastrointestinal AE frequency decreased; other common AEs (≥5%) decreased in frequency or remained stable. Most AEs were mild/moderate. The rate of serious AEs remained consistent across all 3 exposure periods. Discontinuation rates decreased every year, reaching 1.6% during Weeks >104–≤156. Major cardiac events, malignant neoplasms, opportunistic infections, and marked laboratory abnormalities remained infrequent throughout treatment.

**Conclusions.** APR demonstrated a favorable safety profile up to 156 weeks, marked by stable or decreasing AE incidence and lack of immunosuppression accumulation or need for laboratory monitoring.

**Acknowledgment.** Adewale O. Adejoko contributed as an original author.

**P69**

**TREATMENT WITH GOLIMUMAB OR INFlixIMAB REDUCES HEALTHCARE RESOURCE UTILIZATION (HCRU) AND INCREASES WORK PRODUCTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS (AS) IN THE QUO-VADIS STUDY**

Sarzi-Puttini P.1, Van Den Bosch F.2, Claudepierre P.2, Sijain S.3, Vastesaeger N.3, Govoni M.4, Kachroo S.4
1UDC Reumatologia, Ospedale Sacco Poli Universitiari, Milano, Italy; 2Ghent University Hospital, Ghent, Belgium; 3Université Paris Est Créteil, Créteil, France; 4Merck & Co., Inc., Kenilworth, NJ, USA; 5Msd Belgium, Brussels, Belgium; 6Msd Italy, Rome, Italy

**Introduction.** We evaluated the effect of the anti-tumor necrosis factor (TNF) agents, golimumab (GLM) and infliximab (IFX), on HCRU and work productivity in patients with AS in the QUO-VADIS study.

**Materials and Methods.** Bionaire AS patients (modified New York criteria) newly treated with GLM or IFX (originator) were followed for ~6 months in a prospective, observational study. Concomitant medications, hospitalizations, and outpatient visits were quantified over 3 months before data collection (HCRU assessment). The work productivity and activity impairment (WPAI) adapted to spondyloarthritis (WPAI-SpA) quantified work and activity impairment, presenteeism, and absenteeism in the 7 days before data collection.

**Results.** 963 patients (mean age, 42.7 years) received GLM (78%) or IFX (22%). Concomitant medication for AS treatment was reported by 84.3% of patients. Mean inpatient hospitalizations decreased from 7.3 days (131 patients) at BL to 4.1 days (50 patients) at 6 months; mean outpatient care decreased from 2.4 visits (379 patients) at BL to 2.1 visits (183 patients) at 6 months. The percent of patients receiving acute emergency care decreased from 1.6% (BL) to 0.3% (6 months). Mean number of outpatient care visits decreased from 2.4 (BL) to 2.1 (6 months). The mean (SD) number of work days missed due to AS was reduced from 6.3 (3.1) at BL to 2.7 (12.3) at 6 months. WPAI-SpA results are shown in the figure.

**Conclusions.** In the QUO-VADIS study, HCRU and impairment in work and activity were reduced in AS patients newly treated with GLM or IFX for 6 months in a routine clinical care setting.
RESULTS. The SPACE-cohort includes chronic back pain (CBP) patients (≥3 months, ≤2 years, onset <45 years) from various rheumatology centers. Baseline and one-year data were used. Patients underwent full diagnostic work-up: sacroiliac imaging, laboratory testing, and assessment of all other SpA-features. Positive SpA-features were accumulated according to “once a feature always a feature” meaning patients were not able to “lose” features over time. Total SpA-features was calculated excluding sacroiliac imaging and HLA-B27 status. Diagnosis of patients was provided by rheumatologists and ASAS-criteria for axSpA were used for classification.

RESULTS. A total of 270 CBP patients with baseline and one-year follow-up were included: 36.7% were male, mean age was 31.2 (SD 8.0) years, mean number of SpA-features at baseline, and one-year follow-up were 2.8 (SD 1.5) and 3.5 (SD 1.6). After one year 49.3% of patients gained ≥1 features. Common features were IBP (baseline: 77.0%, follow-up: 88.2%), good response to NSAIDs (baseline: 48.5%, follow-up: 70.6%), elevated CRP/ESR (baseline: 29.5%, follow-up: 43.3%), and positive family history for SpA (baseline: 48.9%, follow-up: 52.6%). Sixteen patients had no diagnosis at baseline or follow-up. Rheumatologists diagnosed 150/254 (59.1%) and 66/254 (26.0%) patients with axSpA and no axSpA at both time points, respectively. In 15.0% (38/254) of patients the diagnosis changed; 16 patients with no axSpA diagnosis at baseline were diagnosed with axSpA at follow-up of which 11/16 (68.8%) had acquired ≥1 features. In 22 patients with axSpA at baseline rheumatologists reconsidered their diagnosis at follow-up. In the 150 patients diagnosed with axSpA, 108/150 (72%) of patients already fulfilled the ASAS-criteria at baseline and 79 (52.7%) patients gained ≥1 features, which led to new axSpA classification for 9 patients at follow-up.

CONCLUSION. In patients with CBP of short duration almost half developed at least one new SpA-feature within one year, however the impact on diagnosis and classification was limited.

Figure. Number of acquired SpA-features (after medical history taking, physical examination and measurement of acute phase reactants; excluding sacroiliac imaging and HLA-B27 status) at one-year follow-up (FU) in patients with and without axSpA diagnosis.

Diagnosis

<table>
<thead>
<tr>
<th>Number of features gained after one year</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>&gt;3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>AxSpA baseline and FU</td>
<td>71</td>
<td>50</td>
<td>18</td>
<td>9</td>
<td>2</td>
<td>150</td>
</tr>
<tr>
<td>AxSpA only at FU</td>
<td>5</td>
<td>9</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>16</td>
</tr>
<tr>
<td>AxSpA only at baseline</td>
<td>11</td>
<td>8</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>22</td>
</tr>
<tr>
<td>No AxSpA baseline and FU</td>
<td>40</td>
<td>23</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>66</td>
</tr>
<tr>
<td>Total</td>
<td>127</td>
<td>90</td>
<td>41</td>
<td>11</td>
<td>2</td>
<td>254</td>
</tr>
</tbody>
</table>

Fig. 1. Number of acquired SpA-features (after medical history taking, physical examination and measurement of acute phase reactants; excluding sacroiliac imaging and HLA-B27 status) at one-year follow-up (FU) in patients with and without axSpA diagnosis.
DOES THE PRESENCE OF MULTIPLE SPA-FEATURES IN PATIENTS WITH CHRONIC BACK PAIN ALWAYS LEAD TO DIAGNOSIS OF AXISP ANDLIOARTHRITIS? 


1LUMC, Rheumatology, Leiden, The Netherlands; 2Diakonhjemmet Hospital, Oslo, Norway; 3AMC, Rheumatology, Amsterdam; 4GHZ, Rheumatology, Gouda, The Netherlands; 5University of Padova, Rheumatology, Padova, Italy

Aim. To investigate whether all patients with short duration chronic back pain (CBP) and ≥4 SpA-features, 3 SpA-features with negative X-SI 20/132 (15.2%) and 9/78 (11.5%) did not automatically lead to a clinical axSpA diagnosis but positive imaging was

Results. A total of 522 patients were analysed in this study: before sacroiliac imaging and HLA-B27 testing 164/522 (31.4%) patients had no or 1 SpA-feature, 148/522 (28.4%) patients had 2 SpA-features, 85/522 (16.3%) patients had 3 SpA-features, and 125/522 (23.9%) patients had ≥4 SpA-features respectively. Inflammatory back pain, good response to NSAIDs, and positive family history for SpA were most common in all subgroups (0 or 1 feature: 26.8%, 8.5%, and 16.5% of patients; 2 features: 72.3%, 34.5%, 39.9%; 3 features: 87.1%, 60.0%, 54.1%; ≥4 features: 94.4%, 85.2%, 68.0% respectively). Of the patients with 2 and 3 SpA-features with positive X-SI 20/132 (15.2%) and 9/78 (11.5%) did not have axSpA diagnosis despite being HLA-B27+. (Figure 1). All patients with ≥4 SpA-features and X-SI+ (n=28) were diagnosed with axSpA. In contrast to what would be expected by following the modified Berlin algorithm for patients ≥4 HLA-B27+, were not diagnosed with axSpA by their rheumatologist.

Conclusions. In this cohort of patients with CBP having numerous SpA-features did not automatically lead to a clinical axSpA diagnosis but positive imaging was the main driving factor to diagnosis of axSpA.

P73 PERFORMANCE OF MODIFIED MINIMAL DISEASE ACTIVITY (MDA) CRITERIA IN PATIENTS WITH PERIPHERAL SPONDYLOARTHRITIS: POST-HOC ANALYSIS OF ABILITY-2


1Rheumatology, University of Leeds; 2Leeds Teaching Hospitals NHS Trust, Leeds; 3NIHR/Wellcome CRF, Imperial college Healthcare NHS trust, London; 4Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath, UK; 5Rheumatology, Swedish Medical Center and University of Washington, Seattle, USA; 6Rheumatology, Leiden University Medical Center, Leiden, The Netherlands; 7Statistics, University of Illinois at Chicago, Chicago; 8AbbVie Inc., North Chicago, USA

Aim. This post-hoc analysis evaluated the performance of a modified MDA (mMDA) criteria (excluding psoriasis) in pSpA patients (pts) from the ABILIT-2 study.

Methods. The validity of mMDA was examined in pSpA pts from ABILIT-2, a 12-week trial comparing adalimumab (ADA) with placebo (PBO) followed by a 144-week extension. The mMDA was defined as achieving at least 4 or 5 out of following 6 criteria: (1) TJC 78 points; (2) SJC 66 points; (3) pain and tender joint count; (4) PAS20 ≤10 mm; (5) HA-Qol ≥5 points; and (6) 66/68 tender points ≥1.

Results. Of 163 pts (82 ADA/81 PBO) who completed wk-12, significantly greater proportion of pts receiving ADA achieved mMDA compared with PBO (p<0.001): 4/6 LEI: 40.2 vs 13.6%; 5/6 LEI: 28.0% vs 4.9%; 4/6 SPARCC: 35.4% vs 12.3%; 5/6 SPARCC: 26.8% vs 4.9%. Proportion of mMDA responders at yrs 1 and 2 was numerically higher in pts initially randomized to ADA. In pts fulfilling 4/6 criteria (LEI/SPARCC), 20-30% did not meet TJC and SJC criterion. However, 5/6 criteria (LEI/SPARCC) were more stringent with 5% and 13% not meeting the TJC and SJC criterion, respectively.

Conclusions. All 4 versions of mMDA discriminated between ADA and PBO treatment groups; both enthesitis indices performed similarly. The 5/6 mMDA versions closely representing the MDA concept could be an appropriate treatment target in pSpA pts.

P74 CLINICAL RISK FACTORS FOR THE PRESENCE AND DEVELOPMENT OF VERTEBRAL FRACTURES IN PATIENTS WITH ANKYLOSING SPONDYLITIS


1Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen; 2Rheumatology, Medical Center Leeuwarden, Leeuwarden; 3Laboratory Medicine, University Medical Center Groningen, Groningen, The Netherlands

Introduction. Vertebral fractures are the hallmark of bone fragility and frequently present in patients with ankylosing spondylitis (AS). Our objective was to investigate the prevalence and incidence of radiographic vertebral fractures and the association with patient characteristics, clinical assessments, and medication use in a large prospective cohort of patients with AS.

Methods. Consecutive AS patients from the Groningen Leeuwarden AS (GLAS) cohort with baseline and 2-year lateral radiographs of the thoracic and lumbar spine were included. Radiographs were scored for vertebral fractures (≥20% reduction in vertebral height) by two readers according to the method of Genant et al. Differences in baseline characteristics were explored between patients with and without radiographic vertebral fractures.

Results. 292 AS patients were included: 70% male, mean age 43±13 years, median symptom duration 16 (IQR: 8-25) years. Radiographic vertebral fractures were present in 59 (20%) patients at baseline. During 2 years, 15 (6%) patients developed new vertebral fractures and 7 (2%) showed an increase in severity of existing fractures. Most fractures were mild and located in the mid-thoracic and thoracolumbar region of the spine. The presence of vertebral fractures was significantly associated with older age, higher BMI, longer smoking duration, larger occupant-to-wall distance, more spinal radiographic damage, and lower hip BMD.

The development of new or progressive vertebral fractures was also associated with older age and low BMD. Patients using NSAIDs at baseline showed less prevalent and incident vertebral fractures.
Conclusions. In this large AS cohort in clinical practice, radiographic vertebral fractures were frequently present in AS, especially in older patients with more advanced disease, low hip BMD, and a less healthy lifestyle. Interestingly, NSAID use was associated with a reduced vertebral fractures risk.

**P75**

**FLARE IN AXIAL SPONDYLOARTHRITIS – RESULTS OF CLINICAL REAL PRACTICE**

Ezhes Sh.1, Dubinina T.V.1, Lapshina S.A.2, Rebrov A.P.3, Raskina T.A.4, Malyshenko O.S.5, Bugrova O.V.5, Yakubova U.A.5, Nagornova K.A.5, Otteva E.N.6

1VA. Nasonov Research Institute of Rheumatology; 2Kazan State Medical University, Ministry of Health of Russia; 3V. I. Razumovsky Saratov State Medical University, Ministry of Health of Russia; 4Kemerovo State Medical Academy, Ministry of Health of Russia; 5Orenburg State Medical Academy, Ministry of Health of Russia; 6Professor S.I. Sergeev Territorial Clinical Hospital One, Khabarovsk, Russia

**Background.** In February 2016 in Ann of Rheum Dis were published preliminary definitions of flare in axSpA, developed by ASAS members (ASAS Flare). The aim of the study was testing of preliminary definitions of ASAS flare in real practice.

**Materials and Methods.** Present study included two steps. The first step was an analyzing of axSpA databases in 6 Russian centers with data collection from patients (pts) with worsening of axSpA status according BASDAI and ASDAS-CRP, number of swollen joint, and MASES. The second step of the study was the collection the rheumatologists’ opinion about each ptm, using a special questionnaire with 12 preliminary ASAS flare definitions, included additional definition of night pain worsening (Δ pain ≥ 2.0 with final level ≥4.0; Δ pain ≥ 3.0; if initial pain ≥4.0: Δ pain ≥ 2.0, if not – Δ pain ≥ 3.0, number of swollen joints Δ ≥ 1.0, and MASES Δ ≥ 1.0. Physicians have to answer what points were taken in to account first when decision about flare was made. Dose positive decision about flare lead to changes of pts’ treatment. If «yes», then what parameter had maximal influence in treatment decision?

**Results.** Data from 661 pts with axSpA fulfilling ASAS criteria for axSpA (2009) were analyzed totally. 86 patients had flare due their physician’s decision (65 of them had anyklokyly spondylitis fulfilling mNew-York criteria, 21 – nr-axSpA, fulfilled ASAS criteria foraSpA), mean age was 34.7±9.8 years (range 19-54 years), 61.6% male. Mean disease duration was 9.2±1.2 month (min – 4, max – 363 month), mean observation period when worsening of axSpA symptoms developed was 7.3±5.7 month.

Rates of different flare definitions are present in the table 1.

**Table 1. Occurrence of different axial spondyloarthritis’ flare definitions (n=86 patients).**

<table>
<thead>
<tr>
<th>Activity measurement tool</th>
<th>Definition of flare</th>
<th>Occurrence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain (0-10)</strong></td>
<td>Δ pain ≥ 2.0 and final level ≥ 4.0</td>
<td>50.0</td>
</tr>
<tr>
<td></td>
<td>Δ pain ≥ 3.0</td>
<td>31.4</td>
</tr>
<tr>
<td></td>
<td>If initial level of pain ≥ 4.0: Δ pain ≥ 2.0, if not: Δ pain ≥ 3.0</td>
<td>47.7</td>
</tr>
<tr>
<td><strong>BASDAI</strong></td>
<td>Δ BASDAI ≥ 2.0</td>
<td>17.4</td>
</tr>
<tr>
<td></td>
<td>Δ BASDAI ≥ 2 and final level ≥ 4.0</td>
<td>36.0</td>
</tr>
<tr>
<td></td>
<td>Δ BASDAI ≥ 3.0</td>
<td>20.2</td>
</tr>
<tr>
<td></td>
<td>Δ BASDAI ≥ 3.0 and final level ≥ 4.0</td>
<td>36.0</td>
</tr>
<tr>
<td></td>
<td>If initial BASDAI ≥ 4.0: Δ pain ≥ 2.0, if not: Δ pain ≥ 3.0</td>
<td>34.9</td>
</tr>
<tr>
<td><strong>ASDAS-CRP</strong></td>
<td>Δ ASDAS ≥ 0.6</td>
<td>40.7</td>
</tr>
<tr>
<td></td>
<td>Δ ASDAS ≥ 0.9</td>
<td>29.1</td>
</tr>
<tr>
<td></td>
<td>Δ ASDAS ≥ 1.1</td>
<td>33.7</td>
</tr>
<tr>
<td></td>
<td>Δ ASDAS ≥ 0.6 and final level ASDAS ≥ 1.3</td>
<td>72.1</td>
</tr>
<tr>
<td><strong>Night pain</strong></td>
<td>Δ pain ≥ 2.0 and final level ≥ 4.0</td>
<td>44.2</td>
</tr>
<tr>
<td></td>
<td>Δ pain ≥ 3.0</td>
<td>29.1</td>
</tr>
<tr>
<td></td>
<td>If initial pain ≥ 4.0: Δ pain ≥ 2.0, if not: Δ pain ≥ 3.0</td>
<td>39.5</td>
</tr>
<tr>
<td><strong>Number of swollen joints</strong></td>
<td>Δ ≥ 1.0</td>
<td>37.2</td>
</tr>
<tr>
<td><strong>MASES</strong></td>
<td>Δ pain ≥ 1.0</td>
<td>39.5</td>
</tr>
</tbody>
</table>

The most important definitions ASAS flare according the opinion of physicians are Δ BASDAI ≥ 0.6 in case of final ASDAS ≥1.3 (it stated 53.5%); Δ BASDAI ≥ 3.0 in case of the final level of ≥4.0 (31.4%); if the observed value of ≥4.0 Δ BASDAI ≥2.0- points; or: Δ BASDAI ≥3.0 (30.2%) and if the observed level of pain, including night ≥4.0: Δ pain ≥ 2.0, or: Δ pain ≥ 3.0 (23.3%). In 69.8% of cases changes in disease activity has led to changes in therapy. Therapy increase was usually dependently changed from changes ASDAS ≥ 0.6 in case that final ASDAS ≥ 1.3 (it indicated 44.2%). In 20.9% of cases, a change in treatment strategies affect changes in number of swollen joints and MASES (when Δ ≥ 2 or more), and 7.0% in the presence of active spondylitis on MRI.

**Conclusions.** In real practice the majority of physicians concluded that pts with axSpA has flare when ASDAS or BASDAI worsened on 0.6 and 3.0 points respectively, if final level was ≥1.3 in ASDAS and ≥4.0 in BASDAI. In 69.8% of cases changes in activity led to changes in therapy.

**P76**

**LONG-TERM (156-WEEK) EFFICACY AND SAFETY PROFILE OF ORAL APREMILAST FOR PSORIATIC ARTHRITIS: RESULTS FROM THE PALACE 1 PHASE III, RANDOMIZED, CONTROLLED TRIAL AND OPEN-LABEL EXTENSION**


1UCSD School of Medicine, La Jolla, CA, USA; 2Toronto Western Research Institute, Toronto, Canada; 3Hospital Clinico Universitario de Santiago, Spain; 4Monash University, Melbourne, Australia; 5University of Orleans, Orleans, France; 6Swedish Medical Center/University of Washington School of Medicine, Seattle, WA, USA; 7University of Erlangen-Nuremberg, Erlangen, Germany; 8Celgene Corporation, Summit, NJ, USA; 9Sohn Klinikumba Lille, Hamburg, Germany

**Introduction/Aim.** Three-year PALACE 1 treatment data for apremilast (APR) in patients with active psoriatic arthritis, despite prior conventional DMARDs/biologics, recently became available.

**Patients and Methods.** Patients were randomized (1:1:1) to placebo, APR 30 mg BID (APR30), or APR 20 mg BID (APR20) stratified by baseline DMARD use. The placebo-controlled phase continued to Week 24; placebo patients were re-randomized to APR30 or APR20 at Week 16 or Week 24. Double-blind APR treatment continued to Week 52; patients could continue APR4 additional years. Week 156 data are reported.

**Results.** 504 patients were randomized (placebo: n=168; APR30: n=168; APR20: n=168). Week 16 ACR20 response rates with APR30 were significantly greater vs. placebo (p=0.0001); observed ACR20 response rates were maintained at Weeks 52 (53.2%) and 104 (65.3%). In all, 92% (260/284) of APR30 patients starting year 3 of treatment completed Week 156. At Week 156, APR30 patients demonstrated sustained improvements: ACR20 response rate (65%); HAQ-DI mean change (=0.37, from 1.3 at baseline); HAQ-DI MCID ≥0.30 (–81.2%/–73.2%); FACIT-F mean improvement of 5.5, reaching a mean FACIT-F score of 34.8; and PASI-75/PASI-50 responses (35.8%/56.7%).

**Conclusions.** Over 156 weeks, APR demonstrated sustained, clinically meaningful improvements in psoriatic arthritis signs/symptoms, including physical function and associated psoriasis. APR was generally well-tolerated with an acceptable safety profile.

**Acknowledgment.** Adewale O. Adelho contributed as an original author.

**P77**

**EFFICACY AND SAFETY OF APREMILAST AND SWITCH FROM ETANERCEPT IN PATIENTS WITH MODERATE TO SEVERE PSORIASIS: 52-WEEK RESULTS FROM THE LIBERATE STUDY**

Reich K.1, Soung J.2, Gooderham M.3, Zhang Z.4, Nograles K.4, Day R.M.4, Ferris L.1, Goodfield M.5

1SCIderm Research Institute and Dermatologikum Hamburg, Hamburg, Germany; 2University of California, Dermatology, Santa Ana, CA, USA; 3Skin Centre for Dermatology and Probiotic Medical Research, Peterborough, ON, Canada; 4Celgene Corporation, Summit, NJ, USA; 5University of Pittsburgh, Pittsburgh, PA, USA; 6Leeds General Infirmary, Leeds, UK

**Introduction/Aim.** The phase 3b LIBERATE (Evaluation in a Placebo-Controlled Trial of Oral Apremilast and Etanercept in Plaque Psoriasis) study (NCT01690299) evaluated efficacy and safety of apremilast (EVT) or etanercept (ETN) vs. placebo (PBO) in biologic-naive patients with moderate to severe plaque psoriasis.

**Patients and Methods.** 250 patients were randomized (1:1:1) to PBO, APR 30 mg BID (APR30), or ETN 50 mg QW (ETN50) through Week 16; thereafter, pa-
Farinelli A.

cantly disease activities and QoL in patients with ES.

tween gastroenterologist and rheumatologist. In our study we demonstrated that the optimal
Discussion.

to achieve an optimal therapeutic management and defined clinical

BASDAI and QoL improved significantly already at 6 months (ASDAS-CRP resulted significantly worse than IBD according to IBDQ (p<0.0001). Peripheral arthritis was present in 31/60 (52%) whereas axial involvement. Data were analyzed by paired and unpaired t tests.

chosen basing on gastrointestinal and joint disease activity and the type of articular involvement were assessed at Wks16 and 52.

At Wk16, mean percent improvement from baseline in NAPSI score and achieve-

mellaneous symptom and in 60 (24%) an active ES was diagnosed according to ASAS criteria. Peripheral arthritis was present in 31/60 (48%) patients. At baseline, the QoL in ES patients resulted significantly worse than IBD according to BBDQ (p<0.001). PGA (p<0.001) and SF-36 subscales and summary scores (p<0.0001 for both). After integrated evaluation, in ES cohort articular and gastrointestinal disease activity and QoL improved significantly already at 6 months (ASDAS-ESR p<0.0001; BASDAI p<0.0001; CDAI p=0.004; BASFI p=0.01; IBDQ p<0.0001; SF-36 PCS and MCS p<0.01). In ES patients treated with a TNF-inhibitor the improve-

ment was maintained at 12 months for all the PROs.

Discussion. ES represents a challenge for the evaluation and management of both gut and joint inflammation. In our study we demonstrated that the optimal management of both the manifestations encompasses a strong cooperation be-
tween gastroenterologist and rheumatologist.

Conclusion. Only an integrated clinical evaluation is able to improve signifi-
cantly disease activities and QoL in patients with ES.

P78

MULTIDISCIPLINARY MANAGEMENT IMPROVES DISEASE ACTIVITY AND QUALITY OF LIFE IN PATIENTS AFFECTED BY ENTEROPATHIC SPONDYLOARTHRITIS: A PROSPECTIVE OBSERVATIONAL STUDY

Benfarenco D.1, Ciccia F.2, Bolognini L.1, Ciferri M.1, Rossini M.1, Capei W.1, Farinelli A.2, Fava G.2, Mosca P.1, Luchetti M.M.1, Triolo G.1, Gabrielli A.1

1Clinica Medica, Università Politecnica delle Marche, Ancona; 2Dipartimento Bi-omedico di Medicina Interna e Specialistica, Università degli Studi di Palermo; 2Gastroenterologia, Azienda “Umberto I-G.M. Lancisi-G.Salesi”, Ancona, Italy

Introduction. In enteropathic spondylarthritides (ES) the coexistence of gut and articular inflammation advocates an integrated approach of the patients in clini-
cal practice, to achieve an optimal therapeutic management and defined clinical outcomes.

Methods. From January 2014 to January 2016, 225 patients affected by IIBD were enrolled in a prospective study and evaluated at baseline, 6 and 12 months for gastrointestinal and arthicular activity and patient-reported outcomes on qual-

ity of life (QoL). Upon multidisciplinary evaluation, the therapeutic strategy was chosen basing on gastrointestinal and joint disease activity and the type of articular involvement. Data were analyzed by paired and unpaired t tests.

Results. 102/250 patients (40.8% of screened individuals) complained articu-
lar symptoms and in 60 (24%) an active ES was diagnosed according to ASAS criteria. Peripheral arthritis was present in 31/60 (48%) patients. At baseline, the QoL in ES patients resulted significantly worse than IBD according to BBDQ (p<0.001). PGA (p<0.0001) and SF-36 subscales and summary scores (p<0.0001 for both). After integrated evaluation, in ES cohort articular and gastrointestinal disease activity and QoL improved significantly already at 6 months (ASDAS-ESR p<0.0001; BASDAI p<0.0001; CDAI p=0.004; BASFI p=0.01; IBIDQ p<0.0001; SF-36 PCS and MCS p<0.01). In ES patients treated with a TNF-inhibitor the improve-

ment was maintained at 12 months for all the PROs.

Discussion. ES represents a challenge for the evaluation and management of both gut and joint inflammation. In our study we demonstrated that the optimal management of both the manifestations encompasses a strong cooperation be-
tween gastroenterologist and rheumatologist.

Conclusion. Only an integrated clinical evaluation is able to improve signifi-
cantly disease activities and QoL in patients with ES.

P79

BURDEN OF DISEASE IN AXIAL SPONDYLOARTHRITIS AND THE POTENTIAL INFLUENCE OF COEXISTING NEUROPATHIC PAIN COMPONENT

Gok K., Cengiz G., Erol K., Ozogncmen S.

Div. Rheumatology, Dept. PMR, Erciyes University, Fac. Med., Kayseri, Turkey

Background. The potential influence of pain characteristics including the neu-
ropathic pain (NeP) component on disease burden in axial SpA have not been assessed yet. The aim of this study was first to assess frequency of NeP compo-
nent in patients with axSpA (including non-radiographic axSpA and anklyosing spondylitis/AS); and secondly to assess the potential influence of NeP on burden of disease.

Materials and Methods. Adult patients who met ASAS classification criteria for axSpA were consecutively recruited. Patients with a previous diagnosis or under treatment for NeP, or having confounding disorders were excluded. Pa-

tients were examined and evaluated for specific and generic outcome measures. Patients were evaluated using PainDetect questionnaire, applied by the same blinded physician and patients with a score ≥13 were considered as “probable or likely NeP”.

Clinical variables and outcome measures were compared in patients with and without NeP.

Results. One hundred and eighty five patients (97 male, 88 female) with axSpA (57 nr-axSpA, 128 AS) were included (mean age 36.3±10.2). NeP component was present in 33.5% of patients with axSpA according to PainDetect (35.7% in nr-axSpA vs 32.3% in AS, p=0.650). Pain characteristics like burning, electric shock, tingling, pins and needles, itching, numbness and painful cold as well as pain course were quite similar between patients with nr-axSpA and AS. Patients with and without NeP component had similar age, gender, symptom duration, however patients with NeP had significantly higher scores in VAS-pain, patient and physician global, fatigue, BASDAI, ASDASCRP and poorer QoL, anxiety scores and physical functions compared to patients without NeP component.

Conclusion. This is the first study showing that nearly one third of patients with axSpA may have NeP component regardless of having nr-axSpA or AS. NeP component may contribute worsened QoL, and poorer patient reported outcome data and should be kept in mind in the assessment of patients.

P80

A COMPARISON OF DEPRESSION AND ANXIETY LEVELS IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS WITH THOSE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Barisan E.1, Solmaz D.2, Akar S.2

1Namik Kemal University School of Medicine, Dept. of Internal Medicine, Divi-
sion of Rheumatology, Tekirdag; 2Izmir Katip Celebi University School of Medi-
cine, Dept. of Internal Medicine, Division of Rheumatology, Izmir, Turkey

Introduction. The concept of axial spondyloarthropathy (SpA) recently recom-
mentioned by the ASAS includes patients comprising the early and late stages of the disease. This concept also includes patients not meeting the criteria for an-
kylosing spondylitis (AS) but classified as non-radiographic SpA on the basis of chronic lumbar pain and other characteristics of SpA. Although this group is more heterogeneous and distinct from AS in terms of some characteristics, it still has a similar burden in terms of disease activity. Psychiatric symptoms can often be seen in patients during the course of AS.

Depressive symptoms are seen at levels of 27.4-55.5% and anxiety symptoms at levels of 19.5-60.9%. Few studies have investigated this situation in the non-
radiographic SpA group.

Aim. To assess depression and anxiety levels in AS and non-radiographic SpA groups and to review potentially associated factors.

Method. One hundred fifty-five (114 AS, 41 non-radiographic SpA) patients with axial SpA according to the ASAS definition were included in the study. The BASDAI was used to assess activity, a VAS for spinal pain, the BASFI for functional capacity and the ASQOL for quality of life. The State-Trait Anxiety inventory (STAI), Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were used to determine psychiatric symptoms.

Results. The AS patient group (mean age 39±10.8, male 73.4%) was older than

the non-radiographic SpA group (mean age 35±10.1, male 54.8%), and had a

greater preponderance of males. No difference was determined between the two groups in terms of BASDAI, VAS spinal pain or BASFI scores. Psychiatric measurements were also similar between the AS and non-radiographic SpA groups.

The STAI, BDI and BAI exhibited good correlated with BASDAI, BASFI, ASQOL and VAS spinal pain (Table).
Discussion: Despite the presence of some clinical differences between the AS group and the non-radiographic SpA group, regarded as the early stage of the disease, the two group exhibit similar features in terms of psychiatric symptoms and disease activity. Psychiatric symptoms are closely associated with disease activity, functional capacity and quality of life.

Table. Correlations between psychiatric symptoms and disease, functional capacity and quality of life scales.

<table>
<thead>
<tr>
<th>BASDAI</th>
<th>BASFI</th>
<th>VAS spinal pain</th>
<th>ASQOL</th>
</tr>
</thead>
<tbody>
<tr>
<td>STAI –I (state anxiety)</td>
<td>R</td>
<td>0.432</td>
<td>0.343</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>STAI-II (trait anxiety)</td>
<td>R</td>
<td>0.375</td>
<td>0.342</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beck anxiety</td>
<td>r</td>
<td>0.430</td>
<td>0.375</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beck depression</td>
<td>r</td>
<td>0.427</td>
<td>0.432</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P81

COMPARISON OF CLINICAL FEATURES IN PATIENTS WITH PSORIATIC AND NON-PSORIATIC SPONDYLITIS

Orcogocen S., Cengiz G., Erol K., Gok K., Dogan A.Z., Cevik R., Nas K. 1

Div. Rheumatology, Dept. PMR, Erciyes University, Fac. Med. Kayseri; 2Dicle University, Diyarbakir; 3Div. Rheumatology and Immunology, Sakarya University, Sakarya, Turkey

Aim. Axial spondyloarthritis (axSpA) comprises patients with axial psoriatic arthritis (axPsA) as well as other non-axial psoriatic forms of SpA. The aim of this study was to compare clinical features in patients with axPsA and non-axial axSpA.

Methods. Patients with PsA (meeting the CASP AR criteria for PsA) with predominantly axial involvement (presence of IBP and/or sacroiliitis on imaging), had poorer anthropometric values and differ from non-psoriatic axSpA in terms of clinical parameters in this matched cohorts (Table).

Results. Patients with axPsA were quite similar to the patients with non-psoriatic axSpA (32.2% non-radiographic axSpA) regarding age, gender, smoking, treatments and symptom duration (8.4 vs 10.4 years, respectively). However axPsA had poorer anthropometric values and differ from non-psoriatic axSpA in terms of clinical parameters in this matched cohorts (Table).

P82

PERFORMANCE OF DISEASE ACTIVITY MEASURES IN JUVENILE SPONDYLOARTHRITIS IN A PLACEBO CONTROLLED TRIAL WITH INFliximAB

Ramiro S.1, Casasola-Vargas J.C.1, van der Heijde D.1, Landewé R.2, Burgos-Vargas R.2

1LUMC, Leiden, The Netherlands; 2Hospital General de Mexico, Mexico; 3ARC, Amsterdam, The Netherlands

Introduction/Aim. Several outcome measures in trials with juvenile-onset spondyloarthritis (Jo-SpA) have been borrowed from trials in juvenile idiopathic arthritis and from adult spondyloarthritis, but a proper psychometric analysis has never been conducted in patients with Jo-SpA. Our aim was to assess discriminatory aspects of several disease activity outcome measures and response criteria for Jo-SpA.

Methods. Data from a previously reported 12-week RCT comparing infliximab (IFX) and placebo (PBO) in patients with Jo-SpA were analyzed. The trial’s primary endpoint was the number of active joints (both swollen and tender). Several other disease activity measures and response criteria were also tested. Statistics to determine how well disease activity measures could discriminate between IFX and PBO included ‘standardized mean difference’ (SMD) and ‘Guyatt’s effect size.’ For categorical response criteria, the chi-square test (χ2) was used. Higher numbers indicate better discriminatory capacity.

Results. Patients were randomised to IFX (n=12) and PBO (n=14). Of the continuous measures, the ASDAS showed the best and very good discrimination between IFX and PBO (SMD:1.98; Guyatt: 4.28). The physician’s global (SMD:1.56; Guyatt: 2.34), CRP (SMD:1.90; Guyatt: 1.93), JADAS (SMD:1.46; Guyatt: 2.22) and ISAP/ADA (SMD:1.73; Guyatt: 1.98) also discriminated well. The BASDAI (SMD:0.90; Guyatt: 1.41) (or its separate items), BASFI and spinal mobility measures performed worse. Of the response criteria ASAS40 (χ2:10.05) and ACR Pedi 90 (χ2:10.12) discriminated best between IFX and PBO. ASDAS response criteria and ACR Pedi 30-70 also performed well.

Conclusions. Of all continuous measures tested in adult axial SpA the ASDAS discriminates best between active treatment and PBO in patients with Jo-SpA. But the child specific SpADA also performs well. Of all response criteria tested the child-specific ACR Pedi 30 to 90, as well as the adult ASAS40 and ASDAS response criteria work well. One of these measures should be used as primary endpoint in trials with Jo-SpA.
A.
The Anxiety Score was 6.73±4.37 years. According to multivariate logistic regression, the Depression Score was 3.48±1.27 years. HDO Depression Score was 6.46±4.09 years and HDO Anxiety Score was 3.86±2.04 years. Fatigue Severity Score assessed in patients with PsA.

Background. Psoriatic arthritis (PsA) is associated with higher risk of metabolic syndrome (MetS) and cardiovascular disease. However, its role is not well established regarding the relationship between adiposity and disease activity. Aim. To evaluate the link between body composition (BC) measurements, food intake and disease activity in patients with PsA.

Patients and Methods. A total of 97 patients with PsA (CASPAR, 2006) were included in this cross-sectional study. All of them were evaluated concerning food intake, body composition (whole-body DXA – GE Lunar), biochemical markers (fasting glucose and insulin, HOMA-IR, hemoglobin A1c, cholesterol, creative protein) and skin (PASI, BSA) and joint (DAS28-ERP, DAS28-ESR, BASDAI) disease activity. p<0.05 was set as significant. Results were then compared using t-student test, Kolmogorov-Smirnov, chi-square and Fisher, Pearson correlation, ANOVA and multiple regressions. Results. There was higher prevalence of obesity and excess of body fat, particularly android fat pattern, but with no changes of lean or bone mass. Joint disease activity was positively correlated with total body fat (r=0.4; p<0.001), Fat Mass Index (BMI) (r=0.33; p<0.001), Body Mass Index (BMI) (r=0.20; p=0.049) and waist circumference (WC) (r=0.27; p=0.009). Moreover, it was negatively correlated with appendicular skeletal muscle mass (r=-0.38; p<0.001). Skin disease activity was positively correlated to LDL-cholesterol (r=0.28; p=0.006). After multiple adjustments, patients with severe joint disease activity had higher body adiposity than patients in remission or low disease activity. Higher skin disease activity was associated with higher intake of trans fat and lower ingestion of omega 6. Conclusion. Higher body adiposity, saturated fat consumption, LDL-cholesterol serum levels had a deleterious role on joint and skin disease activity in patients with PsA.

P84
HIGHER ADIPOSITY, FAT INTAKE AND CHOLESTEROL SERUM LEVELS ARE ASSOCIATED WITH HIGHER DISEASE ACTIVITY IN PSORIATIC ARTHRITIS PATIENTS: IS THERE A LINK AMONG JOINT, SKIN AND FAT?

Leite B.1, Morimoto M.2, Genaro P.S.2, Damasceno N.1, Pinheiro M.M.1
1Universidade Federal de Sao Paulo, Escola Paulista de Medicina, Rheumatology Division, Sao Paulo; 2Universidade do Vale do Paraiba, Dept. of Nutrition, Sao Jose dos Campos, Sao Paulo; 1University of Sao Paulo, Nutrition Dept., Sao Paulo, Brazil

Background. Psoriatic arthritis (PsA) is associated with higher risk of metabolic syndrome (MetS) and cardiovascular disease. However, its role is not well established regarding the relationship between adiposity and disease activity. Aim. To evaluate the link between body composition (BC) measurements, food intake and disease activity in patients with PsA.

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P85
RELATIONSHIP BETWEEN WORK DISABILITY AND FATIGUE, ANXIETY, DEPRESSION AND COMORBIDITIES IN PATIENTS WITH PSORIATIC ARTHRITIS: A PRELIMINARY REPORT

Nas K.1, Saqi S.1, Dağlı A.Z.2, Erkorkmaz U.1, Solak B.4, Tekçeoğlu 1, Kamalni A.1
1Div. Rheumatology and Immunology, Dept. PMR, Faculty of Medicine, Sakarya University, Sakarya, Turkey; 2Div. Rheumatology, Dept. PMR, Faculty of Medicine, Dicle University, Diyarbakar; 4School of Health, Faculty of Medicine, Sakarya University, Turkey

Aim. PsA is chronic inflammatory arthritis associated with axial disease, enthesitis, dactylitis, psoriasis, uveitis, the metabolic syndrome and other less well-defined factors related to long-term inflammation, such as fatigue, anxiety, depression and comorbidities. Work disability (WD) is an important functional outcome measure in arthritis. The aim of this study was to investigate the potential relationship between work disability and fatigue, anxiety, depression and comorbidities.

Methods. Forty patients fulfilling CASPAR (Classification Criteria for Psoriatic Arthritis) criteria for PsA were recruited. WD was assessed with the Work Productivity and Activity Impairment Specific Health Problem (WPAI-SHP) questionnaire. A multivariate logistic regression model was implemented to determine the fatigue severity score, and other covariates associated with work disability. Results. A total of 97 patients with PsA (mean age 46.26±11.5 years) were included. Mean symptom duration was 7.49±10.33 years. Fatigue Severity Score was 3.48±1.27 years. HDO Depression Score was 6.64±0.99 years and HDO Anxiety Score was 6.73±4.37 years. According to multivariate logistic regression model, fatigue severity score was independent risk factor for work disability (work productivity and daily activity) (OR=2.959, p=0.016 and OR=1.942, p=0.043 respectively). 1 unit increase of fatigue severity score, 2.96 times decrease the possibility of work productivity and 1.94 times decrease the possibility of daily activity.

Conclusion. PsA is a chronic inflammatory disease and might be presented with various clinical findings. One of the most important findings in PsA is fatigue because of its negative impact on work productivity and routine daily life.
and all mean higher value associated with lower health. The effect of mSASSS seems to be modest. Regarding healthcare use only the BASFI and/or ASDAS and BASFI, modifiable scores, are negatively associated with QoL and healthcare services demand. Age and BASMI, no modifiable scores, are negatively associated with being employed.

**Figure.** History taking pattern of GP (residents) facing a patient with axial SpA in round 1 and 2.

**References.**

2. L. Diakonhjemmet Hospital, Oslo, Norway; 3. AMC, Rheumatology, Amsterdam, The Netherlands; 4. GHZ, Rheumatology, Gouda, The Netherlands; 5. University of Padova, Rheumatology, Padova, Italy

**Aim.** To evaluate (1) the clinical assessment patterns of GPs and GP residents when facing a patient suspected of having spondyloarthritis (SpA) and (2) the influence of an educational intervention on these clinical assessment patterns.

**Methods.** GPs (residents) were visited in 2 rounds by standardised patients (SPs) simulating either axial or peripheral SpA. In between, an educational intervention on SpA for half of the GP residents was organized. The other half and all GPs served as controls. Participants were visited by the SPs during their regular outpatient clinic and were unaware of the nature of the medical problem and study purpose. After the visit, SPs completed a case-specific checklist inquiring about disease-related items.

Differences in patterns of clinical assessment were explored for the control group and between PFH manifestations.

**Results.** Thirty-eight GP-residents (mean age 27.9 years, 32% male) and 30 GPs (mean age 52.5 years, 80% male) participated. Axial SpA case (Figure): participants who received education were in round 2, as compared to round 1, were more likely to ask questions regarding the presence of extra-articular manifestations and family history of SpA, and to a lesser extent also about the inflammatory character of the complaint.

**Conclusion.** Targeted education can help GPs to improve their history taking and hence pattern recognition of patients suspected for SpA.

**P89 FAMILY MATTERS: IS A POSITIVE FAMILY HISTORY OF SPONDYLOARTHRITIS OF VALUE IN PATIENTS WITH CHRONIC BACK PAIN?**

Ez-Zaitouni Z.1, van Lunteren M.1, Berg J.J.2, Landewé R.3, van Oosterhout M.4, Lorenzini M.5, van der Heijde D.1, van Gaalen F.6

1. UMC, Rheumatology, Leiden, The Netherlands; 2. Diakonhjemmet Hospital, Rheumatology, Oslo, Norway; 3. AMC, Rheumatology, Amsterdam, The Netherlands; 4. GHZ, Rheumatology, Gouda, The Netherlands; 5. University of Padova, Rheumatology, Padova, Italy

**Aim.** To assess whether presence of spondyloarthritides (SpA) manifestations (ankylosing spondylitis (AS), psoriasis, uveitis, reactive arthritis, inflammatory bowel disease; ASAS: axSpA criteria: Assessment of SpondyloArthritis international Society criteria for axial Spondyloarthritis) and family history of SpA is of value in clinical practice.

**Methods.** The SPondyloArthritis Caught Early (SPACE)-cohort includes patients with CBP (≥3 months, ≤2 years, onset ≤45 years) from various rheumatology centers. Patients underwent a full diagnostic work-up including MRI and radiographs of sacroiliac joints, laboratory assessments (e.g., HLA-B27), and assessment of other SpA-features. Patients were asked about the presence of SpA manifestations in first- and second-degree relatives. A positive family history (PFH) was defined as having a positive family history for at least one of the following SpA manifestations: AS, psoriasis, uveitis, IB, and reactive arthritis. We assessed the correlation between PFH manifestations and HLA-B27 positivity and between PFH manifestations and meeting the ASAS axSpA classification criteria.

**Results.** 290 patients with centrally scored imaging and complete information on SpA manifestations in relatives were analysed. Mean age (SD) was 31.4 (8.4) years, 36% of patients were male, and mean symptom duration (SD) was 13.2 (7.2) months. In 48/290 (16.6%) patients AS was reported in first- and second-degree relatives, psoriasis in 49/290 (16.9%), uveitis in 13/290 (4.5%), IB in 26/290 (9.0%), and reactive arthritis in 4/290 (1.4%). Any PFH was reported in 37.9% (110/290) of patients. AS (OR 5.0; 95% CI 2.6-9.7), uveitis (OR 25.2; 95% CI 3.2-196.9), and any PFH (OR 2.7; 95% CI 1.6-4.5) were statistically significantly correlated with presence of HLA-B27. Fulfilment of the ASAS-criteria showed similar results: AS (OR 2.9; 95% CI 1.5-5.5), uveitis (OR 12.4; 95% CI 2.7-57.3), and any PFH (OR 2.1; 95% CI 1.3-3.5). No association was found for psoriasis, IB, and reactive arthritis in both analyses. Multivariate regression analysis showed the same trends (not shown).

**Conclusion.** These findings suggest that in CBP patients only a PFH for AS or uveitis in first- and second-degree relatives is of value in clinical practice.

**Table I.** Univariate regression analysis of the presence of family history manifestations for both HLA-B27 status and the fulfilment of ASAS axSpA criteria in patients with chronic back pain in the SPACE cohort (n=290).

**HLAG27: human leukocyte antigen B27; any FH: any family history manifestation in first- and second-degree relatives; AS: ankylosing spondylitis; IB: inflammatory bowel disease; ASAS: axSpA criteria: Assessment of SpondyloArthritis international Society criteria for axial Spondyloarthritis; OR: odds ratio; 95% CI: 95% confidence interval. P-values under 0.05 were considered significant.**
P90 ETHNICITY AND DISEASE SEVERITY IN ANKYLOSING SPONDYLITIS
Revelle J.1, Ward M.2, Lee M.3, Weisman M.4, Gensler L.5, Rabahr M.6, Brown M.7
1University of Texas-Houston, Houston; 2NIH Clinical Center, Bethesda; 3Cedars-Sinai, Los Angeles; 4University of California, San Francisco, USA; 5Queensland University of Technology, Brisbane, Australia

Objective. To compare clinical and disease severity parameters in ankylosing spondylitis (AS) in three ethnic groups.

Methods. We assessed 925 AS patients (57 Black, 800 White, 63 Hispanics) enrolled in a longitudinal outcome study for parameters associated with functional impairment, disease activity and radiographic severity. Univariable comparisons of clinical characteristics for the three ethnic groups were performed, in two multivariable regression models we compared the baseline Bath Ankylosing Spondylitis Radiographic Index (BASRI) and modified Stokes Ankylosing Spondylitis Spine Score (mSASSS) scores by ethnicity, adjusting for covariates. HLA-B alleles were determined by DNA typing.

Results. Blacks had greater functional impairment (Bath Ankylosing Spondylitis Functional Index) (median 62.5IQR 35.7, 79.4) vs. 27.8 [12.6, 52.2] in whites and 38.1 [15.5, 60.0] in Hispanics (p<0.0001); higher disease activity (Bath Ankylosing Spondylitis Disease Activity Index), (median 5.9 [4.3, 7.7] vs 3.5I1.7, 5.5) in whites and 4.5 [2.9, 6.5] in Hispanics; p=0.0001, erythrocyte sedimentation rate (median 27.0 [9.5, 40.0] in blacks vs 10.0 [5.0, 20.0] in whites and 17.0 [11.0, 29.0], p<0.0001), and C-reactive protein levels (median 1.2 mg/dL [0.4, 2.6] mg/dL vs. 0.4 mg/dL [0.2, 0.9] in whites and 0.9 [0.4, 1.6] in Hispanics, p<0.0001). Baseline BASRI and mSASSS scores were higher in blacks (Mean 9.4 ± 2.2) and median 16.4 [46.0, 55.2], respectively compared to whites (11.2 [41.4] and 6.0 [32.6]) and Hispanics (7.3 [3.1] and 8.1 [3.5, 51.9], p<0.004, 0.007, respectively, and this association became stronger as disease duration increased in both unadjusted and adjusted models. HLA-B27 was present in 62.5% of blacks, compared to 85.3% of whites and 86.7% of Hispanics (p<0.0001).

On multivariable analysis, higher BASRI and mSASSS scores were associated with black ethnicity, after adjusting for disease duration, gender and diabetes as well as TNF usage, smoking status, or education level. BASRI but not mSASSS scores were associated with disability status.

Conclusions. Blacks have more severe disease compared to either whites or Hispanics.

P91 COMPARISON OF THE IMAGING AND CLINICAL ARMS OF ASAS AXIAL SPONDYLOARTHITIS CLASSIFICATION CRITERIA IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS
Sari I., Omar A., Chan J., Bedaiwi M., Ayearst R., Haroon N., Inman R.D.
Division of Rheumatology, University of Toronto, Toronto, Canada

Aim. The ASAS classification criteria have provided new insights in the classification of axial spondyloarthropathy (axSpA). Based on the clinical and imaging diagnosis, patients are categorized into the imaging and clinical arms. There are limited numbers of studies investigating the characteristics and treatment responses of ASAS arms. The objective of our study was to compare clinical features and treatment response of non-radiographic axSpA (nr-axSpA) patients stratified into imaging and clinical subsets.

Methods. Eligible patients who met the criteria for nr-axSpA were selected from a longitudinal observation cohort of axSpA. After identification of the patients, X-rays and MRIs were scored by two rheumatologists. Patients then stratified into the imaging or clinical arms. The imaging arm was further stratified into B27- and B27+ groups. The imaging arm was stratified into the imaging or clinical arms. There were a total of 71 nr-axSpA patients (34 imaging and 37 clinical). Median age and disease durations were 34.9 (8.164) and 7 (1-34) years respectively, 52.1% of the group were males and 80.3% were B27+ patients. Patients were stratified by classification and patients in the imaging arm categorized into B27+ (n=20) and B27- (n=14) subgroups. Comparison of three groups (imaging B27+ vs imaging B27- vs clinical arms) revealed no difference with respect to age, sex, race, and HLA-B27; however, extrarticular features, CRP, BASDAI, quality of life measures and TNFi use. There were a total of 37 (52.1%) patients treated with TNFi. The biologic switch frequency was 48.6%. Rates of biologic non-response and median changes in BASDAI and CRP after 3 months of TNFi treatment were comparable between subgroups (p<0.05).

Discussion and Conclusion. Clinical characteristics of nr-axSpA patients between imaging and clinical arms including response to biologic therapy are comparable. The mandatory positive HLA-B27 in the clinical arm likely constrains the clinical heterogeneity of this population.

P92 FUNCTIONAL INTERACTION OF THE ANKYLOSING Spondylitis ASSOCIATED ENDOPLASMIC RETICULUM AMINO-PEPTIDASE 2 (ERAP2) WITH THE HLA-B*27 PEPTIDOME IN HUMAN CELLS
1Centro de Biología Molecular Severo Ochoa (Consejo Superior de Investigaciones Científicas y Universidad Autónoma), Madrid, Spain; 2Faculty of Biology, Technion, Israel Institute of Technology, Haifa, Israel

Introduction. The first steps of the antigen processing pathway of Major Histo-compatibility Complex Class I (MHC-I) molecules take place in the endoplasmic reticulum (ER). The peptides reaching this compartment are often longer than those optimal for MHC-I binding. In humans, the final cut of MHC-I ligands is carried out by two related aminopeptidases, ERAP1 and ERAP2, which differ in trimming specificity and substrate handling. Yet, the precise role of ERAP2 in shaping MHC-I peptidomes is unknown.

Objectives. To determine the effect of ERAP2 expression on the HLA-B*27 peptidome in live cells.

Material and Methods. HLA-B*27:05-bound peptides were isolated from two ERAP2-negative and one ERAP2-positive lymphoblastoid cell lines expressing functionally undistinguishable ERAP1 variants, by immunoaffinity chromatography and acid extraction. Functional equivalence of ERAP1 variants was established by in vitro peptide digestions. Over 2000-4000 B*27:05 ligands were identified from each cell line and their relative abundance was established by quantitative tandem mass spectrometry and MaxQuant-based analyses.

Results. ERAP2 increases the abundance of nonamers in HLA-B*27:05. The enzyme destroys some, and decreases the abundance of many more, B*27:05 ligands with N-terminal basic residues. These changes did not alter the global affinity of the B*27:05 peptidome.

Discussion. The effects on peptide length presumably result from ERAP2-induced activation of ERAP1, but those on N-terminal residue usage are best explained by direct ERAP2 trimming. The influence of ERAP2 on the B*27:05 peptidome suggests that the relevance of this enzyme in HLA-B*27-positive ankylosing spondylitis is due to its processing of HLA-B*27 ligands and strongly supports a peptide mediated pathogenic mechanism of this disease.

P93 EPIDEMIC AND EXPRESSION ANALYSIS OF ANKYLOSING SPONDYLITIS ASSOCIATION LOCI POINT TO KEY CELL TYPES DRIVING DISEASE
Li Z., Haynes K., Thomas G.P., Kenna T., Leo P., Brown M.A.
1Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane; 2University of Queensland Diamantina Institute, University of Queensland, Brisbane; 3Research Office, Charles Sturt University, Wagga, Australia

Introduction. Susceptibility to ankylosing spondylitis (AS) is primarily genetic; thus far 113 susceptibility variants for AS have been identified. However, most of the AS associated SNPs do not directly affect protein-coding genes. Studies of disease- and trait-associated SNPs suggest they may act by affecting gene regulatory regions in specific cell types or tissues. Therefore, identifying the relevant cell types is crucial for further mechanistic studies.

Material and Methods. We applied several bioinformatics methods to utilize epigenetic, gene and protein expression information to identify the primary relevant cell types through which genetic variants associated with AS operate. In total, there are 113 AS associated loci; 39 of them show genome-wide significance in AS-only analyses, whereas the remainder are genome-wide significant in analyses leveraging pleiotropy with other related diseases (inflammatory bowel disease (IBD), psoriasis, primary sclerosing cholangitis (PSC) and ulcerative colitis (UC)) (1).

Results. Epigenetic analysis suggests that AS-associated SNPs operate primarily through immune cell types including monocytes, CD4+ and CD8+ T cells, NK cells, regulatory T cells, and B cells. Gene expression studies showed enrichment of AS-associated loci in genes specifically expressed in monocytes and NK cells while protein expression study shows protein products of AS associated loci were significantly enriched in CD6+ T cells. Epigenetic analyses also showed evidence that AS-associated signals operate in gut cell types including in mucosa of the small intestine, sigmoid colon and rectum. These findings particularly relate to ileal or colon involvement.

Conclusions. These findings highlight the role of key immune cell types in the mechanism by which genetic associations with AS drive the disease, as well as providing further evidence for the involvement of the gut in the pathogenesis of AS.

Reference
P94
IDENTIFICATION OF DIFFERENTIALLY METHYLATED GENES IN PURIFIED DISEASE RELEVANT BLOOD CELL POPULATIONS IN PATIENTS WITH SPONDYLOARTHITIS

Micieli-Richard C.1,2, Bugge Tingaard A.1, Wang-Renault S.F.1,2, Basato F.1, Dougdados M.1,4, Tost J.1
1Paris Descartes University, Rheumatology Dept., Cochin Hospital, AP-HP, Paris; 2Pasteur Institute, Immunoregulation Unit, Paris; 3Laboratory for Epigenetics, Centre National de Génotypage, CEA – Institute de Génomique, Evry; 4Inserm (U1153), Clinical Epidemiology and Biostatistics, PRES Sorbonne Paris-Cité, Paris, France

Background. Spondyloarthritis (SpA) is a complex disease involving genetic, epigenetic and environmental contributions to disease risk. No comprehensive analysis of genome-wide DNA methylation in disease relevant blood cell populations has so far been performed in SpA.

Objective. This study aimed to perform a genome-wide DNA methylation analysis in sorted CD4 and monocytes from SpA patients compared with controls.

Methods. 24 SpA patients and 16 age and sex-matched controls were analyzed. SpA patients were monocentrically recruited between October 2014 and May 2015 in the department of rheumatology. These patients had an active disease despite NSAIDs intake and were eligible for a TNF-blocker treatment. The mean BASDAI (± SD) was 53±23.7; ASDAS 3.2±1.1 and CRP 13±16.6. Among these patients, 23 fulfilled the ASAS classification criteria (imaging arm) with sacro-iliitis on X-rays (n=16) or objective signs of inflammation on MRI (n=21). Only one patient fulfilled the clinical arm. Genome-wide DNA methylation patterns were analyzed in cell-sorted (MACS) monocytes and CD4 T-lymphocyte populations from SpA patients and controls using the Illumina 450K Infinium Human Methylation 450K BeadChip allowing the simultaneous quantitative analysis of more than 480,000 CpG positions.

Results. In CD4 cells 122 CpGs in 82 promoter regions of genes were found to be differentially methylated using stringent quality thresholds including several genes involved in disease-relevant signaling cascades such as Wnt-signaling and genes in which genetic polymorphisms have previously been associated with susceptibility to SpA. With 158 CpGs located in 86 promoter regions, slightly more genes in which genetic polymorphisms have previously been associated with susceptibility to SpA. With 158 CpGs located in 86 promoter regions, slightly more genes were found to be differentially methylated in monocytes. Differentially methylated loci included again genes in Wnt signaling and bone metabolism, osteoblast or chondrocyte-specific genes as well as genes that have previously been shown to be implicated in related diseases such as psoriasis.

Conclusions. This study suggests a moderate number of promoters whose deregulation might contribute to the pathogenesis of SpA. Integration with RNA expression data will allow defining the functional impact of the DNA methylation patterns in the blood cell populations in order to better understand the molecular changes in SpA and potentially identify novel targets for therapeutic intervention.

P95
ERAPI DIFFERENTIALLY SHAPES THE TWO MAJOR SUBPEPTIDOMES OF HLA-B*51:01: IMPLICATIONS FOR THE PATHOGENESIS OF BECHTEL’S DISEASE

Guasp P.1, Alvarez-Navarro C.1, Gomez-Molina P.1, Martín-Esteban A.1, Marcilla M.2, Barnea E.1, Admon A.2, López de Castro J.A.3
1Centro de Biología Molecular Severo Ochoa (CSIC-UMA), Madrid; 2Proteomics Unit, Centro Nacional de Biotecnología (CSIC), Madrid, Spain; 3Faculty of Biology, Technion - Israel Institute of Technology, Haifa, Israel

Introduction. HLA-B*51:01 is the major risk factor for Bechet’s disease. ERAPI, an aminopeptidase that trims peptides to be loaded onto the MHC-I molecules, is also associated with this disorder in epistasis with HLA-B*51:01, suggesting a role of antigen processing and presentation in Bechet’s disease.

Objectives. To characterize the endogenous HLA-B*51:01 peptidome and its implications for the functional and pathogenic interaction of ERAPI with B*51:01.

Material and Methods. B*51:01 peptide complexes were purified by affinity chromatography. Peptides were isolated by acid extraction and identified by tandem mass spectrometry. Recombinant ERAPI variants with different enzymatic activities were purified and used to digest synthetic peptides. Theoretical MHC-I binding affinities were calculated using predictive algorithms.

Results. B*51:01 binds peptides with Pro or Ala at peptide position 2 (P2), and with Ile or Val at the C-terminal position. The dual preference at P2 generates two subpeptidomes with distinct features. Ligands with Pro showed a preference for ERAPI-susceptible P1, while ligands with Ala showed a strong preference for SpA, which is very resistant to ERAPI. The Pro substrates showed higher affinity for B*51:01 than the Ala substrates.

Conclusions. ERAPI does not trim peptide bonds involving Proline. This feature is crucial, since ligands with Pro cannot be destroyed by ERAPI, while ligands with Ala can be destroyed by over-trimming when the P1 residue is susceptible to this enzyme, favoring peptides with ERAPI-resistant P1 residues. We propose a mechanism in which ERAPI activity directly influences B*51:01 by differentially processing the Ala2 and Pro2 peptides, leading to global alterations in the nature and affinity of the peptide. The correct balance between both subpeptidomes may be crucial for Bechet’s disease susceptibility.

P96
FUNCTIONAL INTERACTION OF ERAPI WITH HLA-B*27 SUB-TYPE-BOUND-PEPTIDOME

Sanz-Braño A.1, García-Medel N.1, Admon A.2, López de Castro A.3
1Centro de Biología Molecular Severo Ochoa (CSIC-UMA), Madrid; 2Faculty of Biology, Technion, Israel

Introduction. Ankylosing spondylitis (AS) is strongly associated with HLA-B*27. Genome wide association studies revealed that the Endoplasmic Reticulum Aminopeptidase (ERA) is a significant risk factor for this disease in HLA-B27 individuals. Thus, ERAPI polymorphism may affect AS susceptibility by altering peptide-dependent features of HLA-B27.

Objectives. To characterize the alterations, and their mechanism, induced in the HLA-B*27:04 and B*27:05 peptidomes expressed in five cells by natural ERAPI polymorphisms predisposing to AS, 2) to analyze the relationship between the peptidomes from subtypes differentially associated with AS and their ERAPI dependency.

Methods. HLA-B*27-bound peptides were isolated from human lymphoid cell lines expressing the same or distinct ERAPI variants and characterized by mass spectrometry. The relative amount of each shared peptide, in any given cell line, was estimated from the respective ion peak areas. ERAPI variants ranging 0 to 100 were assigned to N-terminal flanking and P1 residues based on their susceptibility to ERAPI trimming.

Results. 1) AS-associated ERAPI polymorphisms generated in HLA-B*27:04 an optimized peptidome with more ERAPI-resistant N-flanking and P1 residues, shorter length and higher affinity and thermostability, 2) AS-associated ERAPI polymorphisms generated in HLA-B*27:05 a peptidome with higher molecular weight, more ERAPI-resistant P1 residues, differential use of internal residues and higher affinity, 3) peptides from AS-associated subtypes showed higher dependency on ERAPI compared to non-associated ones.

Conclusions. 1) The mechanism of ERAPI/HLA-B27 interaction is the altered balance between epitope generation and destruction, which is determined by the susceptibility of N-terminal flanking and P1 residues to trimming, by distinct ERAPI variants, 2) the lower discrimination of non-AS-associated subtypes for peptides differing in the susceptibility of their P1 residues to ERAPI is similar to the effect of low-activity variants on the HLA-B*27:04 and B*27:05 peptidomes and suggests that non-AS-associated subtypes are less influenced by ERAPI polymorphism than AS-associated ones.

P97
PRESENCE OF THE HLA-B27+HLA-B*40:01+ HIGH RISK ANKYLOSING Spondylitis GENOTYPE IN EARLY BACK PAIN PATIENTS (RESULTS FROM THE DESIR AND SPACE COHORT)

Bakker P.A.C.1, Hameetman M.1, Ez-Zaitouni Z.1, van Lunteren M.1, Schonkeren J.1, Micieli-Richard C.2, Dougdados M.1, van der Heijde D.1, van Gaalen F.A.1 1Dept. of Rheumatology, LUMC, Leiden, The Netherlands; 2Dept. of Rheumatology, Hôpital Bicêtre, Paris; 3 Dept. of Rheumatology, Hôpital Cochin, Paris, France

Introduction. Susceptibility to spondyloarthritides (SpA) is largely genetically determined, but the presence of HLA-B27 alone is not very specific. Earlier studies have shown the HLA-B27+/HLA-B*40:01+ has a high specificity for ankylosing spondylitis. We studied the prevalence of this genotype in two cohorts of patients with back pain suspected of axial SpA.

Patients and Methods. Patients from the DESIR (inflammatory back pain: ≥3 months, ≥3 years, age≥50) and SPACE-cohort (back pain: ≥3 months, ≥2 years, onset <45 years) were included as cases. Randomly selected healthy blood bank donors from the Netherlands and France were used as controls.

After DNA isolation from whole blood samples, a total of 854 patients (DESIR: 582; SPACE: 272) and 15761 controls (France: 10177; Netherlands: 5584) were genotyped for the presence of both HLA-B27 and HLA-B*40:01 using PCR.

Results. While 3.3% (DESIR) and 4.8% (SPACE) of the early back pain pa-
patients had the HLA-B27+/HLA-B*40:01+ genotype, this was only found in 0.4% of both control groups (table 1). With HLA-B27+ /HLA-B*40:01+ patients as a reference, the OR for HLA-B27+/HLA-B*40:01+ was 19.0 in DESIR (95% CI: 10.7-33.6) and 18.0 in SPACE (95% CI: 8.9-36.3) compared to controls (P<0.0001). In DESIR 42% (8/19) and in SPACE 15% (2/13) of the HLA-B27+/ HLA-B*40:01+ patients already had AS at baseline.

Conclusion. In these two early spondyloarthritis cohorts, the high risk AS genotype (HLA-B27+/HLA-B*40:01+) was found to be increased compared to controls. At baseline, a number of patients had already developed AS. Follow up will reveal if other patients with the high-risk genotype develop AS over time.

Table I. prevalence of the HLA-B27/HLA-B*40:01 genotype in SPACE and DESIR.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Sites (Becton Dickinson-BD) anti-CD66 and anti-CD14 (specific markers for neutrophils, 2 rheumatoid arthritis and 1 juvenile idiopathic arthritis. Venous blood was used to identify protein interactions.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>306 (100.0%)</td>
<td>306</td>
</tr>
<tr>
<td>HLA-B27+</td>
<td>304 (100.0%)</td>
<td>304</td>
</tr>
<tr>
<td>HLA-B27-</td>
<td>2 (0.7%)</td>
<td>2</td>
</tr>
<tr>
<td>HLA-B27+</td>
<td>316 (109.9%)</td>
<td>316</td>
</tr>
<tr>
<td>HLA-B*40:01+</td>
<td>25 (8.2%)</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td>327 (101.0%)</td>
<td>327</td>
</tr>
</tbody>
</table>

P98
INCREASED TOLL LIKE RECEPTOR 2 (TLR2) EXPRESSION ON PERIPHERAL BLOOD MONOCYTES FROM PATIENTS WITH ANTI-TNF INDUCED PSORIASIS SUGGESTS A ROLE FOR A GRAM-POSITIVE INFLAMMATORY TRIGGER


Introduction. Anti-TNF therapy can paradoxically induce immune-mediated inflammatory disorders including psoriasis and streptococcal infection is a possible trigger for such contradictory reactions suggesting the importance of Toll-like receptor (TLR) stimulation. TLR2 and TLR4 are able to activate innate immune receptors for both Gram positive and negative bacteria, respectively. Aim. To evaluate the expressions of TLR2 and TLR4 on peripheral blood from patients under anti-TNF therapy and a new onset of psoriasis.

Patients and Methods. Fifteen patients (10women, 5men), mean age 45±14.03 years (range=14-65 years) and 15 age and sex matched healthy controls were included. Patients developed psoriasis while on anti-TNF therapy (6 infliximab and 9 adalimumab) for different diseases: 6 Crohn’s disease, 6 ankylosing spondylitis, 2 rheumatoid arthritis and 1 juvenile idiopathic arthritis. Venous blood was collected in heparinized tubes for staining with anti-human monoclonal antibodies (Becton Dickinson-BD) anti-CD66 and anti-CD14 (specific markers for neutrophils and monocytes respectively), anti-TLR2 and anti-TLR4. Samples were analyzed by flow cytometry and the FACSCalibur (BD) and results are expressed as total event counts. Statistical analysis was done by Mann-Whitney U-test and P values <0.05 considered significant.

Results. Anti-TNF therapy was used for 20a12.94months (range=0.5-84) prior to new onset psoriasis. Patients had higher TLR2 expression on monocytes (589±301.60 vs 171.53±131, P=0.023) but not on neutrophils (7777.07±3270.57 vs 5993.66±2919.99, p=0.33) compared to controls. TLR4 expression was alike in patients and controls both on monocytes (115.78±159.81 vs ±24.72±39.05, p=0.56) and on neutrophils (2072.85±1414.27 vs 961.93±363.33, p=0.56).

Conclusion. The higher expression of TLR2 on monocytes from patients with paradoxical psoriasis reinforces the idea that Gram-positive bacteria may induce higher inflammatory responses in this clinical manifestation, triggering the innate immune system.

P100
POSITION 97 (P97) OF HLA-B, IMPLICATED IN ANKYLOSING SPONDYLOARTHRITIS PATHOGENESIS, AFFECTS CELL SURFACE FREE HEAVY CHAIN EXPRESSION – EVIDENCE OF INTERACTION WITH BETA 2 MICROGLOBULIN

Chen L., Shi H., Yuan J., Bowness P. Botnar Research Centre, NDORMS, University of Oxford, UK

Background. Polymorphisms of position 97 (P97) of HLA-B have recently been associated with Ankylosing Spondylitis (AS). Mutation of Asparagine (N) at position 97 to Aspartic acid (D) has been reported to decrease HLA-B*27:04 cell surface expression2. We hypothesized that variations of residues at P97 might contribute to AS pathogenesis through altering cell surface HLA-B*27 expression.

Methods. Flow cytometry was used to measure surface expression of HLA-B*27 in C1R and HeLa cells expressing wildtype HLA-B*27 (N97) and six mutants at position 97 (N97T, N97S, N97V, N97R, N97W and N97D). TAP-deficient T cells, Tapasin-deficient 220 cells, ERAP1-silenced and β2m-silenced C1R cells were used to identify protein interactions. β2m-deficient cells were used to study the effect of P97 residues on HLA-B*27 expression.

Results. Mutation of P97 to the AS risk residue Threonine (i.e. N97T) increased surface free heavy chain (FHC) expression in C1R and HeLa cells. This was not seen for the protective residues Serine or Valine, or the non-associated residues Arginine or Tryptophan. The HLA-B*27:N97D mutation reduced HLA-B*27 FHC and classical complex expression2. β2m but not TAP, Tapasin or ERAP1, was required for the reduction of cell surface HLA-B*27 FHC expression observed for HLA-B*27:N97D mutant.

Conclusion. The nature of the P97 residue affects HLA-B*27 free heavy chain and classical complex cell surface expression. β2m association likely plays an important role. The association of P97 amino acid polymorphisms with AS may, at least in part, be explained by its effect on HLA-B*27 free heavy chain cell surface expression.

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MOLECULAR SIZE PROFILE OF SURFACTANT PROTEIN-D IN SPONDYLOARTHRITIS

Munk HL.,1,2 Fakh D.1,2 Sorensen GL1, Tan Q1, Christensen L1, Christensen A.E1, Ejstrup L1, Loft AG1,2 Kyvik K.O.1, Jounblat R.2, Holmskov U1, Junker P.1,2
1Dept. of Rheumatology, Odense University Hospital; 2Dept. of Clinical Research, University of Southern Denmark, Odense, Denmark; 3Laboratory of Immunology, Faculty of Public Health, Leeds University, Fanar, Lebanon; 4Dept. of Cancer and Inflammation Research, Institute of Molecular Medicine; 5Dept. of Epidemiology, Biostatistics and Biodemography, University of Southern Denmark, Odense; 6Dept. of Internal Medicine, Vejle Hospital, Vejle; 7Dept. of Rheumatology, Esbjerg Hospital, Esbjerg; 8Dept. of Rheumatology, Aarhus University Hospital, Aarhus, Denmark; 9Dept. of Biology, Faculty of Sciences II, Lebanese University, Fanar, Lebanon

Introduction. Surfactant protein-D (SP-D), an innate immune defence molecule with immunomodulatory effects, is expressed in lungs and on mucosal surfaces. The molecule consists of subunits ordered as trimers and higher multimers. In healthy adults genes are responsible for the majority of the quantitative variation of SP-D in serum as well as its molecular size distribution. High Molecular weight (HMw) SP-D has anti-inflammatory properties, while low Mw (LMw) variants lacks this capacity.

Aim. To investigate HMw and LMw variants of SP-D in serum among spondyloarthritits (SpA) patients and controls according to the Met11Thr gene polymorphism. Materials and methods. 34 SpA patients with SpA and 34 healthy controls were included. Serum SP-D was measured by ELISA and SNP rs721917 was genotyped. SP-D molecular size distribution was assessed using gel filtration chromatography. Immunohistochemical analysis of the areas where the curves was performed to determine the ratio between HMw and LMw SP-D.

Results. SP-D in SpA was in the normal range, 1092 ng/ml (725:1541) vs. controls, 910 ng/ml (494:1682). The ratio of HMw:LMw serum SP-D was lower in SpA patients, 0.38 (0.18:0.53) compared to controls 1.49 (0.37:3.24) even when adjusting for the Met11Thr polymorphism, gender, age, BMI and smoking.

Conclusions. The molecular size distribution of circulating SP-D in patients with SpA is skewed towards preponderance of small molecular size variants. SpA related disease mechanisms may disrupt the multimeric state of SP-D.

MOLECULAR SIZE PROFILE OF SURFACTANT PROTEIN-D IN SPONDYLOARTHRITIS

Tissue deficiency of the atypical chemokine receptor 6 is associated with the selective increase of gut-derived pro-inflammatory CXCR1-highly6highTL1A+IL-23+cells in the peripheral blood, synovial fluids and bone marrow of AS patients

Ciccia F1, Gugino G1,2, Haroon N1,2, Ranganathan V1, Rizzo A1,2, Alessandro R1, Trillo G1
1University of Palermo, Palermo, Italy, 2University of Toronto, Toronto, Canada, 3Azienda Ospedaliera Villa Sofia Cervello, Palermo, Italy

Background. Gut derived innate lymphoid cells of type 3 (ILC3) are increased in the circulation and inflamed tissues of AS patients. Factors influencing the maintenance of ILC3 in an activated status are not clear. The atypical chemokine receptor 6 is a decoy and scavenger receptor for most inflammatory CC chemokines and acts preventing exacerbated inflammatory reactions. Mice lacking D6 expression in the non-hematopoietic compartment display a significant increase in pro-inflammatory monocytes in the peripheral blood and in secondary lymphoid tissues. The role of D6 and in of human inflammatory disorders has not been investigated.

Objectives. To evaluate whether modulation of D6 expression occurs in the gut, synovia and BM of AS patients and accompanied with a selective increase of pro-inflammatory CXCR1-highly6highTL1A+IL-23+ cells in the circulation and inflamed tissues of AS and to study the effect of these cells in modulating ILC3 differentiation.

Methods. RT-PCR and immunohistochemistry were used to evaluate the expression of D6 in the gut, synovial tissues and bone marrow of AS patients and controls. Different monocyte subsets were analyzed by flow cytometry in the peripheral blood, gut, synovial fluids and bone marrow of AS patients and controls. Confocal microscopy analysis was used to confirm the presence of CXCR1-highly6highTL1A+IL-23+ cells in the gut, synovial tissues and BM of AS patients and controls. Isolated peripheral CXCR1-highly6highTL1A+IL-23+ cells were co-cultured with isolated peripheral ILC3 and changes in ILC3 frequency were evaluated by flow cytometry.

Results. D6 was significantly down-regulated in the ileum, synovial tissues and bone marrow of AS patients compared to controls. D6 expression in the gut and BM was inversely correlated with the frequency of CXCR1-highly6highTL1A+ in the gut and in peripheral blood. D6 down-regulation was accompanied by a complex macrophage signature. Tissue resident CXCR1-highly6highlow macrophages were expanded in the ileum of AS patients compared to controls. A significant increase in the frequency of pro-inflammatory CXCR1-highly6high monocytes producing high levels of TL1A and IL-23 was observed in the ileum of AS patients. In the peripheral blood a statistically significant increase in the frequencies of both bone marrow derived CXCR1lowly6low and intestinal derived CXCR1-highly6highTL1A+IL-23+ monocytes, the latest being also expanded in AS synovial fluids and synovial tissues and bone marrow. Expansion of gut derived CXCR1-highly6highTL1A+IL-23+ monocytes was accompanied by increased TL1A serum levels. Isolated pro-inflammatory CXCR1-highly6highTL1A+ IL-23+CCR7+ monocytes from peripheral blood of AS induced the expansion and activation, evaluated through the production of IL-22 and IL-17, of ILC3.

Conclusions. In this study we provide the first demonstration that absence of D6 expression in the gut and in the inflamed tissues of AS patients selectively induced the intestinal accumulation and the re-circulation of pro-inflammatory CXCR1-highly6highTL1A+IL-23+CCR7+ monocytes. We also demonstrate for the first time the increased serum levels of TL1A in AS patients and the ability of CXCR1-highly6highTL1A+IL-23+CCR7+ monocytes in activating ILC3. Since the ability of these cells in promoting ILC3 expansion and activation, these cells may promote a sustained pro-inflammatory status in AS.
P104

BIOMECHANICAL STRESS AS PRIMARY DRIVER FOR INFLAMMATORY ARTHRITIS

Cambrè I., Schryvers N., Verheugen E., Lambrecht S., Jacques P., Elewaut D.
Dept. of Rheumatology, University of Ghent, Belgium

The musculoskeletal system is continuously exposed to biomechanical loading. The main force is focused at the joints and more specific at the enthesis (attachment of tendons to the bone). The entheseal organ, which consists of a collection of tissues adjacent to the enthesis itself, is crucial to dissipate the load over a wide area. Historically, rheumatic diseases (especially Rheumatoid arthritis (RA) and Psoriatic Arthritis (PsA)) were seen as exclusively inflammatory-driven diseases but why systemic inflammation localizes to the joint was not understood. We postulated that biomechanical stress could be a key determinant of the joint localisation.

Therefore we initiated a series of studies on the role of mechanical strain in several models of arthritis.

First, we demonstrated that hind unloading abolishes entheseal inflammation in TNFARE (Spondyloarthropathy (SpA)-like model) and new bone formation in a CAIA (Collagen Antibody Induced Arthritis) model. These findings proved that the key hallmarks of SpA, enthesis and pathological new bone formation, are driven by biomechanical strain. Whereas unloading of diseased TNFARE mice stopped disease progression completely, voluntary running significantly increased disease progression versus mice that have no running wheel available. We also assessed the role of mechanotransduction in the Collagen Induced Arthritis model (CIA). This model features RA and is induced by breaking tolerance to endogenous collagen type II. We thus examined the impact of unloading versus voluntary running. The CIA mice were unloaded during 28 days starting from day 22 (one day after CIA boost injection).

Remarkably the hind paws that were unloaded did not show any sign of inflammation which is in sharp contrast to the hind paws that were loaded (hind paw disease incidence 80%). In accordance the voluntary running group displayed an early onset, higher disease incidence, higher disease progression rate and higher bone erosion % than the regular loaded mice.

We conclude that biomechanical stress is a critical determinant of joint inflammation in a variety of disease models of both RA and SpA. This highlights a crucial role for mechanical strain as trigger for RA and SpA.

P105

ANALYSIS OF GRANZYME AND PERFORIN IN ANKYLOSING SPONDYLITIS IMPLICATES CD8+ T CELL PERFORIN-DEFICIENCY IN JOINT INFLAMMATION

Yao Y., Gracey E., Qiyum Z., Ranganathan V., Imran R.
University Health Network and University of Toronto, Toronto, ON, Canada

Introduction/Aim. Ankylosing Spondylitis (AS) is characterized by chronic joint inflammation, if left unchecked, can lead to profound structural changes in the spine. But the mechanisms which sustain the inflammation have remained unexplained. Although strongly associated with the MHCI allele, HLA-B27, no clear role for CD8+ T cells has been identified. In our recent microarray analysis using RNA from whole blood we found the expression of granzyme (GZM) to be significantly lower in AS than health controls (HC).

Materials and Methods. We proceeded to examine local GZM and perforin (PFN) expression by flow cytometry of mononuclear cells from blood (PBMC) and synovial fluid (SFMC) samples. GZM and PFN levels in AS were then analyzed in the context of the respective patient’s clinical profile including sex, age, treatment, CRP and HLA-B27 status.

Results. We have demonstrated a decrease of PFN+ and GZM+ CD8+ T cells from AS PBMC. AS vs HC: PFN+ T cells 18% vs 28%, p<0.05; GZM+ T cells 1% vs 5%, p<0.05. This observation was subsequently supported by immune bead assay of serum and SF of AS patients, which showed a significant decrease of PFN concentration in SF (4971±268ug/ml) compared to serum (7004±400ug/ml), p<0.0001. Unexpectedly, lower PFN levels were associated with more active inflammation in AS, while GZM levels revealed no such relationship. Serum PFN in AS patients with elevated CRP was 2811±538 ug/ml, and in those with normal CRP was 4488±600 ug/ml, p<0.0001.

Conclusions. Our findings indicate that AS is characterized by a state of decreased PFN expression which could contribute to dysregulation of autoreactive CD8+ T cells. This suggests a mechanistic similarity with hemophagocytic lymphohistiocytosis (HLH) syndrome, an autoinflammatory condition associated with PFN deficiency.

P106

S100A8/S100A9: DRIVERS OF DISEASE IN ARTHRITIS BY MYELOID DEFICIENCY OF A20?

Debuschere K.1,2, Cyper H.1,2, Vogt T.1, Roth J.1, Van Loo G.1,2, Drennan M.1,2, Elewaut D.1
1Ghent University, Dept. of Internal Medicine, Ghent; 2VIB, Inflammation Research Center, Ghent, Belgium; WWU Münster, Inst. Of Immunology, Münster, Germany; 3Ghent University, Dept. of Biomedical Molecular Biology, Ghent, Belgium

Introduction. The ubiquitin-editing enzyme A20 is the best studied regulatory gatekeeper of the pro-inflammatory NF-kappaB signaling pathway. Alterations in A20 lead to a variety of immune-mediated diseases, such as spondyloarthritides. Cell-specific deletion of A20 in the myeloid compartment (A20myeloid-ko) of C57BL/6 mice results in spontaneous development of enthesitis and arthritis driven by a sterile form of inflammation mediated by TLR4/MyD88-signalling. The TLR4-ligands S100A8 and S100A9 are clearly elevated in patients with active rheumatic disease and might thus play an important role in the initiation and progression of spondyloarthritides.

Methods. To explore the role of these S100-DAMPs as upstream ligands of TLR4 in the A20myeloid-ko mice, we crossed the A20myeloid-ko strain onto an S100A9-/- strain which functionality lacks both S100A9 and S100A8. Clinical follow-up, histology and ELISA were performed.

Results. Intriguingly, there were no changes in the arthritic phenotype and in the levels of TNF, IL6 and IL1beta in A20myeloid-ko S100A9-/- compared to A20myeloid-ko S100A9+/-.

Discussion. Inflammation in the knee is not a prominent feature of this model as disease progresses in contrast to the rapid and evident inflammation of the tarso-metatarsal region. The results therefore suggest that these S100-DAMPs might be co-drivers of disease in its initial state, but become redundant later.

Conclusion. While increasing evidence supports a role for S100A8/S100A9 as important biomarkers for disease activity, their role as drivers of disease in spondyloarthritides however may be limited.

P107

GM-CSF TH17 CELLS ARE ENRICHED IN PSORIATIC ARTHRITIS AND ARE DOWNREGULATED BY IL-23

Stober C., Goodall J., Gaston H.
Dept. of Medicine, University of Cambridge, UK

Introduction/Aim. Psoriasis (Ps) is a common chronic inflammatory skin condition affecting 1-2% of the world population and 20-30% of patients have psoriatic arthritis (PsA). Genetic studies demonstrate the importance of TLR4 in the A20myeloid-ko mice, we crossed the A20myeloid-ko strain onto an S100A9-/- strain which functionality lacks both S100A9 and S100A8. Clinical follow-up, histology and ELISA were performed.

Results. Intriguingly, there were no changes in the arthritic phenotype and in the levels of TNF, IL6 and IL1beta in A20myeloid-ko S100A9-/- compared to A20myeloid-ko S100A9+/-.

Discussion. Inflammation in the knee is not a prominent feature of this model as disease progresses in contrast to the rapid and evident inflammation of the tarso-metatarsal region. The results therefore suggest that these S100-DAMPs might be co-drivers of disease in its initial state, but become redundant later.

Conclusion. While increasing evidence supports a role for S100A8/S100A9 as important biomarkers for disease activity, their role as drivers of disease in spondyloarthritides however may be limited.

Discussion. GM-CSF release from PsA PBMC was higher and IFN-γ levels lower relative to HD, and this was significant [p<0.01] when comparing the ratio of IFN-γ to GM-CSF. PsA patients had higher proportions of GM-CSF+ [p<0.05] and fewer GM-CSF+IFN-γ+ [p<0.05], compared to HD. There was also marked enrichment of CD4+GM-CSF+ cells in SFMC [p<0.001]. Almost all CD4+IL-17+ cells expressed CCR6, whereas approximately 50% of CD4+GM-CSF+ cells expressed this Th17-associated chemokine receptor. Whilst IL-23 up-regulates GM-CSF release by Th17, in mice, we showed that IL-17 was increased [p<0.01], but GM-CSF downregulated [p<0.001] by IL-23. IL-23 also increased IL-17 and decreased GM-CSF in naïve CD4+ cells differentiated using Th17-ex panding conditions.

Conclusions. IL-23 and Th17 cells are therapeutic targets in PsA, and mouse models of inflammation suggest that pathogenic Th17 cells release GM-CSF. We reveal that GM-CSF is elevated in patients with PsA, and GM-CSF- cells are enriched in diseased joints. However, only a proportion of GM-CSF+ cells exhibited features of Th17. Furthermore, IL-23 reduced GM-CSF whilst enhancing IL-17. Given that GM-CSF was mainly produced by cells not co-expressing IFN-γ in PsA patients [in contrast to healthy donors], this subset may be pathogenic in PsA and warrants further investigation.

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Poster Presentations
**P108**

**A2O INHIBITION OF STAT1 EXPRESSION IN MYELOID CELLS: A NOVEL ENDOGENOUS REGULATORY MECHANISM PREVENTING DEVELOPMENT OF ENTHESITIS**

De Wilde K.1, Martens A.1,2, Lambrecht S.1, Jacques P.1, Drennan M.B.1, De-busschere K.1, Govindarajan S.1, Coudens J.1, Verheugen E.1, Windels F.1, Lories R.1, McGonagle D.1, Beyaert R.2, van Oo G.2,1, Elevaart D.1,2
1Laboratory for Molecular Immunology and Inflammation, Department of Rheumatology, VIB IRC, Ghent University and Ghent University Hospital; 2Unit of Cellular and Molecular (Patho)physiology, VIB IRC; 3Dept. of Biomedical Molecular Biology, Ghent University; 4Skeletal Biology and Engineering Research Center, KU Leuven, Belgium; 5Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, UK

**Introduction.** A2O is an important endogenous regulator of inflammation. SNP’s in A2O have been associated with various immune-mediated inflammatory diseases, and cell-specific deletion of A2O results in diverse inflammatory phenotypes. Our goal was to delineate the underlying mechanisms of joint inflammation in myeloid-specific A2O-deficient mice (A2O-/- mice).

**Methods.** Bone marrow-derived monocytes/macrophages were derived from A2O-/- and littermate control mice and stimulated with IL-6 or IFN-γ. Luciferase reporter assays, Western blot analysis and qPCR analysis were performed to study the effect of A2O on STAT1/STAT3-dependent signaling and STAT1/STAT3 expression in myeloid cells. The in vivo role of JAK-STAT signaling in the development of enthesitis in A2O-/- mice was assessed following administration of a JAK inhibitor versus placebo control.

**Results.** Enthesitis was found to be an early sign of joint inflammation in A2O-/- mice. A2O negatively modulated STAT1+ (CXCL9, CXCL10, MXI, USP18), but not STAT3-dependent (ICCL2, MCL1, VEGF) target gene expression in myeloid cells by suppressing STAT1 but not STAT3 expression. A2O suppressed STAT1 expression, both in unstimulated conditions and after IFN-γ or IL-6 stimulation.

**Conclusions.** JAK-STAT inhibition in vivo resulted in significant reduction of enthesitis, both clinically and histopathologically.

**P109**

**INVARIANT NATURAL KILLER T CELLS DOMINATE TREGS IN CONTROLLING ARTHRITIS IN TNF-∆ARE MICE**

Venken K.1, Decruy T.1, Jacques P.1, Sparwasser T.1, Kollias G.1, Elevaart D.1
1Laboratory for Molecular Immunology and Inflammation, Dept. of Rheumatology, VIB Inflammation Research Center, Ghent University, Ghent, Belgium; 2Institut für Infektionsimmunologie TWINCORE, Hannover, Germany; 3Biomedical Sciences Research Center Alexander Fleming, Vari, Greece

A better understanding of immunoregulatory networks may significantly contribute to better therapeutic treatments for chronic rheumatic diseases. The goal of this study was to investigate the contribution and potential crosstalk between invariant Natural Killer T (iNKT) cells and CD4+CD25+FOXP3+ regulatory T cells (Tregs) in TNF-∆ARE mice, a model for human Spondyloarthritis. First, we evaluated iNKT responses under steady state conditions in DEREG mice allowing conditional Treg depletion by injection of diphtheria toxin. In the absence of A2O, STAT1 but not STAT3 expression is enhanced leading to STAT1-dependent inflammation. A20 therefore acts as a novel endogenous regulator of STAT1/STAT3-dependent signaling and STAT1/STAT3 expression in myeloid cells by suppressing STAT1 but not STAT3 expression. A2O suppressed STAT1 expression, both in unstimulated conditions and after IFN-γ or IL-6 stimulation.

**Conclusions.** Our data reveal an important and novel interplay between myeloid cells and Tregs to control iNKT cell responses in liver and spleen. These results indicate that Tregs control iNKT cell responses under steady state conditions. Next, we evaluated and compared the onset and progression of peripheral arthritis in TNF-∆ARE mice and iNKT deficient (Jo18+ × TNF-∆ARE REGREG mice by clinical scoring, histopathology and micro-CT analyses of hind paws. Lack of iNKT cells in Jo18+ TNF-∆ARE mice was found to result in a substantial increased disease progression as compared to TNF-∆ARE mice. Rather unexpectedly, Treg depletion did not cause worsening of arthritis in both TNF-∆ARE as well as Jo18+ TNF-∆ARE mice. We found that Treg frequencies in lymphoid organs of TNF-∆ARE mice were increased. Moreover, Tregs were functionally blunted in the joint-draining lymph nodes but not in spleens of TNF-∆ARE mice. Finally, in contrast to the marked difference in joint phenotype, we observed a comparable exacerbated gut pathology in TNF-∆ARE mice deficient in either iNKT or Tregs. Taken together, our findings highlight a particular regulating role for iNKT cells in TNF driven forms of arthritis, independent of a Treg crosstalk. Furthermore, our results indicate that Tregs are particularly prone to site specific functional modulation under conditions of high TNF load.

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**NO RADIOLOGICAL SACROILIAC JOINT PROGRESSION AFTER 2 YEARS OF ETANERCEPT TREATMENT IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: DATA FROM THE EMBARK STUDY**

Dougados M.1,2,3,4, Maksymowych W.1,5, van der Heijde D.1,2, Finger P.1,2,4,1, Bonin R.1,2,4,1, Logeat J.1,2,4,1, Bukowski J.1,2,4,1, Jones H.1
1Paris-Descartes University, Paris, France; 2University of Alberta, Edmonton, Canada; 3Leiden University, Leiden, The Netherlands; 4Pfizer, Collegeville, PA, USA; 5Pfizer France, Paris, France

**Introduction.** Radiological structural changes in the sacroiliac joint (SIJ) over time in non-radiographic axial spondyloarthritis (nr-axSpA) can be evaluated by measuring progression from non-radiographic to radiographic damage status according to modified New York (mNY) criteria and other more sensitive methods. However, the question remains whether anti-tumor necrosis factor therapy can prevent structural progression in nr-axSpA.

**Aim.** To evaluate radiographic progression in SIJ over 2 years of etanercept (ETN) in nr-axSpA.

**Patients and Methods.** Study design: 104-week follow-up of patients enrolled in EMBARK who received ETN 50 mg once a week from baseline to week 12. Patients: Active, NSAID-refractory nr-axSpA. Outcome measures: Pelvic X-rays performed at baseline and week 104; 3 trained readers evaluated films using 0–4 grade scale of mNY radiographic criteria for left and right SIJ. Statistical analysis: x-rays from patients completing 104-week study assessed. Continuous variable: total score 0–8 for left and right SIJ; binary variables: change from non-radiographic to radiographic axSpA, worsening ≥1 grade in ≥1 SIJ and absolute final value ≥2 in worsened joint.

**Results.** Of 215 randomized patients, 169 completed 104 weeks; 161 patients had evaluable x-rays. Only one patient satisfied mNY criteria for radiographic SIJ damage at baseline. Of 160 patients with mNY-negative scores at baseline, none became positive at week 104. Mean score (SD) for total SIJ (scale, 0–8) was 0.87 (0.83) at baseline and 0.88 (0.85) at week 104 (change, 0.01 [0.15]; p = 0.386). No patients had both worsening ≥1 grade in ≥1 SIJ and absolute final value ≥2 in worsened joint.

**Conclusion.** This study suggests that no structural radiological progression in the SIJ occurred after 2 years of etanercept treatment in patients with nr-axSpA, but additional studies using X-rays and MRI should be conducted to further address this question.
THE NATURAL HISTORY OF SACROILIITIS IN YOUNG PEOPLE WITH ENTHESIS-RELATED ARTHRITIS ON BIOLOGIC THERAPY

Bray T.J.P.,1,2 Vendhan K.,1 Atkinson D.,1 Fisher C.,1 Sen D.,1 Ioannou Y.,1 Hall-Craggs M.A.,1
1Centre for Medical Imaging, University College London; 2Arthritis UK Centre for Adolescent Rheumatology, University College London, UK

Introduction. Magnetic resonance imaging (MRI) can provide a wealth of information about inflammation, erosions, fusion and fat metaplasia in the sacroiliac joints (SIJs) of patients with enthesitis-related arthritis (ERA). However, there is currently a lack of information regarding the natural history of imaging findings of axial disease when patients are treated with biologic therapy in young people with ERA. The aim of this study was to evaluate the disease course of patients with enthesitis-related arthritis after biologic treatment using repeat MRI scans before and after treatment.

Materials and Methods. A picture archiving and communication system (PACS) search was used to identify all adolescent and young adult patients aged 12-24 with ERA who had undergone at least three MRI scans of the SIJs, over at least a two-year period, with scans before and after anti-TNF treatment. Each scan was scored for inflammation according to the Spondyloarthritis Research Consortium of Canada scoring system, and for erosions, fat metaplasia and fusion using a recently proposed structural score.

Results. Twenty-two patients were identified for the study. Patients were started on biologics at a mean age of 17y2m, and the mean number of scans per patient was 3.9. Scans were acquired between 3.5 years before starting biologics and 7.8 years after starting biologics. Graphs showing inflammation, erosions, fat metaplasia and fusion over time from biologic start are shown in Figure 1.

Scores for inflammation and erosions were both significantly lower after treatment than before treatment (p<0.001). Fusion and fat metaplasia scores were significantly higher after treatment (p<0.001).

Discussion. These data suggest that ERA patients undergo a reduction in inflammation but a substantial increase in fusion and fat metaplasia after biologic treatment. Biologic therapy has not prevented fusion in these patients, although it is unclear whether fusion is a consequence of the inflammation itself or biologic treatment.

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P113

QUANTITATIVE APPARENT DIFFUSION COEFFICIENT MEASUREMENTS ARE A MORE REPEATABLE MEASURE OF SACRORILIITIS THAN VISUAL SCORING IN YOUNG PEOPLE WITH ENTHESITIS-RELATED ARTHRITIS

Bray T.J.P., Vendhan K., Atkinson D., Punwani S., Fisher C., Sen D., Ioannou Y., Hall-Craggs M.A.

Centre for Medical Imaging, University College London; Arthritis UK Centre for Adolescent Rheumatology, University College London, UK

Introduction. Visual scoring of short tau inversion recovery (STIR) magnetic resonance images (MRI) is widely used for assessing sacroiliitis (1). However, current scoring systems contain a number of subjective elements including assessment of depth and brightness of inflammation, and the number of inflamed joint quadrants. Furthermore, observers can only make binary choices for each joint quadrant. Quantitative apparent diffusion coefficient (ADC) measurements (2) are based on pixel values in the image itself and are therefore intrinsically objective. This study aims to compare the repeatability (3) of visual STIR scoring and quantitative ADC measurements.

Materials and Methods. Ten adolescent patients aged 12-24 with axial enthesitis-related arthritis (ERA) and ten controls with mechanical back pain underwent conventional MRI and diffusion-weighted MRI. Measurements were performed by two experienced musculoskeletal radiologists with expertise in spondyloarthritis imaging. STIR images were assessed using the Spondyloarthritis Research Consortium of Canada scoring system (1). Sacroiliac joint ADC measurements were performed using multiple linear regions-of-interest placed across the sacroiliac joint, as previously described (2). (Figure 1).

Results. Bland Altman 95% limits of agreement were ± 770 x 10^-6 mm^2/s (9.9% of the mean) for quantitative ADC measurements, and a 6.4 (31% of the mean) for visual STIR scoring. Intraclass correlation coefficients were 0.988 for ADC, and 0.906 for STIR scoring.

Discussion. These data suggest that quantitative ADC measurements are more repeatable (3) than visual scoring as a measure of inflammation in ERA. DWI can be acquired and analysed more quickly than STIR images, and image analysis requires minimal expertise. Quantitative image analysis techniques may lower the threshold for using imaging biomarker data in the clinic, and could be used for both adults and children with spondyloarthritis. However, joint immaturity may reduce the accuracy of ADC measurements in younger or pre-adolescent patients.

References

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ENTHESITIS, SYNOVITIS AND TENOSYNOVITIS DETECTED BY ULTRASONOGRAPHY IN PATIENTS WITH PSORIASIS: DIAGNOSTIC VALUE OF PASE AND EARP QUESTIONNAIRES AND PREDICTORS VARIABLES

Reina D., Vidal D., Cerdá D., Estrada P., García Díaz S., Navarro V., Peramiquel L., Roig D., Torrente V., Coroninas H.

1Dept. of Rheumatology, Hospital de Sant Joan Despí Moisés Broggi, Barcelona; 2Dept. of Dermatology, Hospital de Sant Joan Despí Moisés Broggi, Barcelona, Spain

Objective. The aim of this study was to assess the diagnostic quality of the PASE and EARP questionnaires in the ultrasonographic detection of enthesitis, synovitis and tenosynovitis. It also aimed to determine the possible predictor variables for these findings.

Methods. Cross-sectional study to evaluate the diagnostic validity of the PASE and EARP questionnaires in a total of 96 consecutive patients. Double blind clinical examination and echographic assessment were performed. A ROC model analysis for the questionnaires was established using echographic findings as reference variable. The optimal diagnostic point was determined following a Youden analysis model from the obtained data, calculating sensitivity and specificity along with predictive values, likelihood ratio (LR) and diagnostic odds ratio (OR). A logistic regression analysis was used to determine possible predictor variables of enthesitis, synovitis and tenosynovitis.

Results. For the EARP questionnaire the analysis showed an AUC of 0.66 in synovitis at the Youden point of 3.5. Sensitivity 66.7% and specificity 60.8%. For the PASE questionnaire the analysis showed an AUC of 0.69 in enthesitis and 0.71 in tenosynovitis. Sensitivity 81.0% and specificity 60.8% for enthesitis and 100% and specificity 57.1% for tenosynovitis.

Conclusion. The PASE and EARP tests had a diagnostic performance for enthesitis, synovitis and tenosynovitis that followed the expected pattern when the prevalence of findings is low. In these cases, the tests increase their negative predictive value, being particularly interesting in ruling out the disease.

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ABOUT HALF OF THE PATIENTS WITH ANKYLOSING SPONDYLITIS ALREADY HAVE RADIOGRAPHIC CHANGES IN T SPINE AT THE POINT OF DIAGNOSIS - CROSS SECTIONAL STUDY, BY WHOLE SPINE CT

Lee S.H., Choi J.Y., Song R., Lee Y.A., Hong S.J., Yang H.Y.

Kyung Hee University, Seoul, South Korea

Background. Ankylosing spondylitis (AS) is a chronic inflammatory disease, which destructs spine. After involvement of sacroiliac joint, inflammation usually spreads from lower L spine to C spine. But it is hard to evaluate radiographic changes in T spine due to air in lung by X-ray.

Objectives. We performed this study to find out how many patients have radiographic changes in T spine at first visit and if bone spurs of vertebral bodies are associated with radiographic changes in facet joints in spine.

Methods. We enrolled the patients who were diagnosed as AS by modified NY criteria in Kyung Hee university hospital at Gangdong in Seoul, South Korea from Mar 2008 to Dec 2015. After diagnosis, we performed a whole spine CT in each patient according to the routine protocol of our clinic to evaluate the radiographic involvement of spine. Total 1,170 patients were enrolled and analyzed.

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Mean age was 33.0±10.0 years and mean disease duration was 10.5±9.3 years. 34.1% of patients had at least one bone spur and 26.3% had at least one lesion in facet joints in L spine. In T spine, 47.2% of patients had at least one bone spur, 28.2% had at least one lesion in facet joints. 32.8% had at least one lesion in CVJs.

Each radiographic change is associated with one another (p<0.00). These all radiographic changes were significantly more frequently observed in the patients with old age and long disease duration at the point of diagnosis (p=0.00). The lesion of CVJs and facet joints in T spine were observed more frequently in male than female significantly (respectively p=0.02; 0.00). 19.2% of the patients had radiographic changes in T spine without in L spine.

Conclusions. At the point of diagnosis, many patients already had radiographic changes in T spine. We suggest if radiographic change of T spine is included in radiographic progression score system such as mSASSS, we can more sensitively detect radiographic progression even in a short interval.

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BACK PAIN IS RELATED TO MRI-LESIONS IN PATIENTS INCLUDED IN THE SPACE COHORT
de Hooge M.1, de Bruin L.2, de Beer L.3, Bakker P.1, van den Berg R.1, Ramiro S.1, van Gaalen F.1, Fagerli K.1, Landewé R.1, van Oosterhout M.1, Ramondu R.1, Huizinga T.1, Bloem J.2, Reijnierse M.2, van der Heijde D.1
1LUMC, Rheumatology, Leiden; 2LUMC, Radiology, Leiden, The Netherlands; 3Diakonhjemmet Hospital, Rheumatology, Oslo, Norway; 4AMC, Clinical Immunology and Rheumatology, Amsterdam; 5GHZ, Rheumatology, Gouda, The Netherlands; 6University of Padova, Rheumatology, Padova, Italy.

Introduction/Aim. For clinicians, it is relevant to know whether a relationship between MRI-lesions and pain localized at the same site exists. We investigate possible associations of pain with MRI-lesions originating from either axSpA or degeneration in patients with chronic back pain (CBP).

Materials and Methods. Patients with CBP (≥3 months, ≤2 years, onset <45 years) from the SPondyloArthritis Caught Early cohort indicated sites of pain (thoracic, lumbar, buttck). Average MRI-scores from two sets of two readers (for axSpA and degenerative lesions separately) were used.

Results. Readers were blinded for patient characteristics and clinical outcome. On MRI of the sacroiliac joint (MRI-SI) and MRI of the spine (MRI-spine), inflammatory and fatty lesions, erosions and ankylosis/synovialphathies were scored. Each vertebral unit was scored for disc degeneration, high intensity zone (HIZ), herniation, Schmorls’ nodes and Modic changes.

Associations between MRI-SI lesions and buttck pain were investigated by logistic regression analysis. Associations between axSpA/degenerative MRI-spine lesions and thoracic/lumbar pain were investigated by generalized estimating equations.

Conclusion. In 348/342 patients MRI-spine/MRI-SI was available (126 males, 127 fulfilling ASAS-criteria, mean age 29.4 years). Pain was localized in thoracic spine (35.6%), lumbar spine (35.6%), and buttck (35.6%). On MRI-SI, inflammatory lesions (OR 1.06, p=0.04) and erosions in patients <25 years (OR 1.16, p=0.04) were associated with buttck pain.

Modic type 1 lesions in patients >35 years (OR 5.19, p=0.02) and herniation in various subgroups (OR ranged 2.07–4.66) were associated with pain.

Conclusion. Specific degenerative lesions on MRI-spine are associated with pain at the same location in given subgroups. Inflammatory lesions on MRI-SI are associated with buttck pain.

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THE CHARACTERISTICS OF ANDERSSON LESIONS (Spondylodiscitis) BASED ON WHOLE SPINE MAGNETIC RESONANCE IMAGING IN ANKYLOSING SPONDYLITIS
Kim T.H.1, Nam S.W.1, Lee S.W.2, Kim S.K.1, Shin K.C.3, Song Y.A.3, Lee S.H.3
1Division of Rheumatology, Dept. of Internal Medicine, Arthritis and Autoimmunity Research Center, Catholic University of Daegu School of Medicine, Daegu; 2Division of Rheumatology, Dept. of Internal Medicine, Seoul National University College of Medicine, Seoul; 3Dept. of Radiology, Hanyang University Hospital for Rheumatic Diseases, Seoul; 4Dept. of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea

Introduction/Aim. Andersson lesions could cause debilitating pain and functional impairment in ankylosing spondylitis (AS) patients. The objective of this study was to identify the characteristics of Andersson lesions using whole spine magnetic resonance imaging (MRI) in AS.

Materials and Methods. A total of 62 patients with AS who had taken whole spine MRI were retrospectively enrolled in this study. Regional distribution in the entire spine and within the individual discvertebral unit (DVIU) during the central, peripheral, and diffuse disc types of Andersson lesion was assessed. We compared the number of DVIUs with Andersson lesion with clinical and radiographic indices such as erythrocyte sediment rate (ESR), C-reactive protein (CRP), BASDAI, BASFI, and modified Stoke Ankylosing Spondylitis Spine Score (mSASSS).

Results. Fifty-three patients (85.5%) had at least one Andersson lesion. We found a total of 129 DVIUs with Andersson lesions (9.0%) in the entire spine levels. Andersson lesion at the lower thoracic spine (from T7-8 to T12-L1) was most commonly detected than other spine levels. Among the total 151 Andersson lesions, 41 lesions were identified at the central, 26 lesions at the anterior peripheral, 44 lesions at the posterior peripheral, and 40 lesions at the diffuse disc types. However, the number of Andersson lesions did not correlate with ESR, CRP, BASDAI, BASFI, and mSASSS in AS patients (p>0.05 in all).

Conclusion. Our study indicates that presence of Andersson lesion in AS patients is clearly underestimated. MRI provides more increased opportunity to detect earlier Andersson lesions than conventional radiography.

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CURRENT SMOKING, ITS INTENSITY AND DURATION, IS ASSOCIATED WITH FAT METAPLASIA ON MRI IN PATIENTS WITH SPONDYLOARTHRITIS
Maksymowych W.P.1, Wichuk S.1, Chiowchanwisawakit P.1, Zheng Z.2, Lambert R.G.2, Connor-Spady B.3, Spady D.3, Pedersen S.J.4
1Division of Rheumatology, University of Alberta, Edmonton, Canada; 2Department of Medicine, Mahidol University, Bangkok, Thailand; 3PLA General Hospital, Beijing, China; 4Dept. of Radiology, University of Alberta, Edmonton, Canada; 5Copenhagen Center for Arthritis Research, University of Copenhagen, Denmark

Introduction/Aim. Prospective MRI data indicates that ankylosis develops following an intermediary phase of fat metaplasia, which follows resolution of inflammation in subchondral bone and at sites of erosion, when it is termed backfill. We aimed to determine whether smoking influences the propensity to develop fat metaplasia as a potential mechanism for its association with progression in SpA.

Methods. MRI scans were scored independently by 2 readers and adjudicated by a third reader. MRI inflammation was assessed on T1W scans using the SPARC SJI and 23-DVU scores while structural lesions were assessed on TIW scans using the SPARC SSS score for SJI fat, erosion, backfill, ankylosis, and the FASSS score for spinal fat. Univariate and multivariate regression assessed associations between smoking (current Yes/No, <10/≥10 years), past, never, pack per day, pack years) and MRI parameters.

Results. MRI scans were available on 250 cases in the prospective cohort. In univariate analyses, current but not previous smoking, especially intensity (from 0.25 to 1 pack/day) and duration of current smoking (≥10 years vs <10), was associated with spinal (FASSS: p=0.03) and SIJ fat (SSS backfill: p=0.01; SSS fat ≥2: p=0.03), SJI ankylosis (p=0.01), and spinal inflammation (SPARC 23-DVU p=0.02). In multivariate models that included age, sex, B27, smoking, ASDAS, and selected according to the best goodness of fit (AIC), current smoking (intensity and/or duration) was independently associated with SJI fat and ankylosis.

Conclusion. Current, but not past smoking, and its intensity and duration is associated with the degree of fat metaplasia and ankylosis on MRI of the SJI suggesting an influence on the tissue response to inflammation.
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WHAT PREDICTS ABSENCE OF SPINAL DAMAGE IN PATIENTS WITH SPONDYLOARTHRITIS AFTER PROLONGED DISEASE?

Maksymowych W.P.1, Wichuk S.1, Chiowchanwisawakit P.1, Lambert R.G.1, Pedersen S.J.1
1Rheumatology, University of Alberta, Canada; 2Medicine, Mahidol University, Bangkok, Thailand; 3Radiology, University of Alberta, Canada; 4Copenhagen Center for Arthritis Research, University of Copenhagen, Denmark

Introduction/Aim. The majority of patients with AS develop new bone in the spine although disease may remain isolated in the SII. A new hypothesis has proposed that MRI can identify a “progressive phenotype” in early SpA characterized by the appearance of fat metaplasia in the SII. We aimed to determine whether MRI lesions in the SII are associated with absence of spinal damage.

Methods. AS patients (n=431) were prospectively assessed for clinical, lab, and imaging outcomes. MR scans were assessed by SPARCC SIJ and SSS scoring methods for inflammation and structural lesions. Absence of spinal damage was pre-specified as no syndesmophytes or ankylosis on cervical and lumbar spine radiographs after ≥10 years from onset of symptoms and for the entire duration of follow up. Patients with and without spinal damage were matched for age and symptom duration. Univariate and multivariate conditional logistic regression assessed which demographic, clinical, and imaging variables were associated with absence of spinal damage.

Results. The group with no damage had fewer males (p=0.004), lower CRP (p=0.02), and lower MRI scores for fat (p=0.03) and ankylosis (p=0.003). Definite ankylosis (SSS score ≥2 by both readers) was evident in 20.7% of cases in the no damage group versus 53.3% of those with damage (p<0.007). A multivariate model that included gender, ASDAS, and MRI lesions indicated that lower scores for backIII and ankylosis were associated with no damage (OR[95%CI]=0.81[0.69-0.99] and 0.89[0.82-0.96], respectively). When all definite MRI features (SSS score ≥2 by both readers) were included in the model, definite SII ankylosis was significantly less likely in those without spinal damage (OR[95%CI]=0.24[0.08-0.70]).

Conclusion. The absence of radiographic damage in the spine after prolonged disease is associated with the lack of fat metaplasia and ankylosis in the SII on MRI supporting the hypothesis that fat metaplasia identifies a progressive phenotype.

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THE DETECTION OF SACROILIITIS BY CT ENTEROGRAPHY MAY BE USEFUL IN THE EVALUATION OF CROHN’S DISEASE

Lage R.C.1, Tavares W.C.2, Resende G.G.1, Kakehashi A.M.1
1Unit of Rheumatology, Dept. of Locomotor System, Federal University of Minas Gerais; 2Unit of Radiology, Clinics Hospital, Federal University of Minas Gerais and Ecoal medicina diagnostica, Belo Horizonte, Brazil

Introduction/Aim. Computed tomography enterography (CTE) is a useful tool to assess the presence, extension and inflammatory activity of intestinal Crohn’s disease (CD). The sacroiliac joints (SII) are not routinely examined by radiologists, when performing CTE. The aim of the present study was to determine the prevalence of sacroiliitis in CTE images of patients with suspected or established CD.

Materials and Method. We evaluated the CT images of 62 consecutive patients who underwent CTE examination to clarify the diagnosis of suspected Crohn’s disease or to search for intestinal complications of established disease. CT scans were performed with neutral oral contrast and intravenous iodized contrast. Abdominal images were obtained in high-resolution scheme. SII changes were described by a radiologist, as previously defined by the modified New York criteria.

Results. Forty-one (66%) patients were male, and the mean age was 47 (15 to 85) years. At the study entry, 23 (37%) patients had a previous diagnosis of CD and 39 (63%) had suspected CD. CTE changes consistent with CD were described in 29 (46.8%) patients, and 31 (50%) had a definite diagnosis of CD after image analysis. In patients with confirmed CD, sacroilitis (SII) was detected in nine (29%), while SII was found in only one (3%) patient without the diagnosis of CD (p=0.01). Of the 10 patients with SII, nine (90%) had a definite diagnosis of CD.

Conclusion. CTE may play a role in the detection of SII and may contribute to the diagnosis of axial spondyloarthritis (SpA) associated with CD. On the other hand, the detection of SII by CTE may improve confidence in the diagnosis of CD in doubtful cases, but further studies with a larger sample are needed to confirm this hypothesis.

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THE PREVALENCE OF INFLAMMATORY AND STRUCTURAL LESIONS ON MRI OF THE SACROILIAC JOINTS IN PATIENTS WITH VERY EARLY PERIPHERAL SPONDYLOARTHRITIS

Varkas G.1*, Carron P.1, Cypers H.2, Van Pael L.1, Elewaut D.1, Jans L.1, Van Bosch F.1
1Dept. of Rheumatology Ghent University Hospital; 2Dept. of Radiology Ghent University Hospital; 3VIB Inflammation Research Center, Ghent University, Ghent, Belgium

*equal contribution to the manuscript

Objective. To assess the prevalence of inflammatory and structural lesions on the sacroiliac joints (SII) in patients with peripheral spondyloarthritis (PSpA) in a very early stage of the disease.

Methods. Baseline data originated from the double-blind RCT with golimumab in 60 patients (CRESPA), who were diagnosed with PSpA and had a symptom duration <3 months. MRI SII was performed at baseline. Peripheral arthritis, dactylitis or enthesitis combined with ≥1 SpA feature (uveitis, psoriasis, IBD, preceding infection, HLAB27 or sacroiliitis on imaging) was necessary for inclusion. However, all patients already fulfilled the classification criteria without data on imaging of the SII. Bone marrow edema (BME) of the SII was quantified using the Spondyloarthritis Research Consortium of Canada (SPARCC) scoring system. Besides BME of the SII, all MRIs were also scored for other inflammatory lesions such as enthesitis and capsulitis. Structural MRI lesions of the SII such as subchondral sclerosis, erosions, periarticular fat and ankylosis were also assessed. Hip evaluation consisted of the presence of joint effusion, BME, enthesitis and cortical aberrations.

Results. Although not the reason for encounter, 7 out of 60 patients reported ever having inflammatory back pain (IBP) at inclusion or in the past, with median Visual analogue scores (VAS) of 2.0 (range 0.0-9.0) for back pain. Overall, 35% of patients (21/60) exhibited BME of the SII and fulfilled the definition of a positive MRI by ASAS, with median SPARCC score of 8.0 (range 2.0-37.0). Only 3 out of 7 patients with IBP exhibited BME on MRI SII. Therefore, almost 80% of patients (18/21) with active sacroiliitis did not exhibit symptoms of IBP. Median VAS back pain in patients with sacroiliitis compared to patients without sacroiliitis respectively reached 2.0 and 1.0 (P=NS). Pelvic enthesitis was present in 23.8% (5/21) of patients with an ASAS positive MRI SII and in 10.3% (4/39) of patients with negative MRI. None of the patients exhibited enthesitis of the L5 spinous process, iliac crest, anterior superior iliac spine or ramus pubis. None of the patients exhibited thorax enthesitis. MRI features of patients fulfilling ASAS criteria for a positive MRI and patients not fulfilling these criteria are presented in Table I.

Table I. Comparison of MRI features of inflammatory and structural changes of the sacroiliac joints, the pelvis and the hip in 60 peripheral SpA patients in very early disease.

<table>
<thead>
<tr>
<th>Inflammatory lesions of the SII, n (%)</th>
<th>ASAS MRI + (n=21)</th>
<th>ASAS MRI – (n=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BME</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>16/21 (76.2)</td>
<td>5/39 (12.8)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>7/21 (33.3)</td>
<td>34/39 (87.2)</td>
</tr>
<tr>
<td>Capsulitis</td>
<td>5/21 (23.8)</td>
<td>1/39 (2.6)</td>
</tr>
<tr>
<td>Chronic lesions of the SII, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sclerosis</td>
<td>1/21 (4.8)</td>
<td>0/39 (0.0)</td>
</tr>
<tr>
<td>Fat metaplasia</td>
<td>2/21 (9.5)</td>
<td>4/39 (10.3)</td>
</tr>
<tr>
<td>Erosions</td>
<td>3/21 (14.3)</td>
<td>8/39 (20.5)</td>
</tr>
<tr>
<td>Antkylosis</td>
<td>2/21 (9.5)</td>
<td>0/39 (0.0)</td>
</tr>
<tr>
<td>Pelvic enthesitis, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symphysis</td>
<td>1/21 (4.8)</td>
<td>0/39 (0.0)</td>
</tr>
<tr>
<td>Iliac painfulness</td>
<td>2/21 (9.5)</td>
<td>0/39 (0.0)</td>
</tr>
<tr>
<td>Posterior superior iliac spine</td>
<td>3/21 (14.3)</td>
<td>0/39 (0.0)</td>
</tr>
<tr>
<td>Greater trochanter</td>
<td>0/21 (0.0)</td>
<td>2/39 (5.1)</td>
</tr>
<tr>
<td>Glenoid posterior</td>
<td>1/21 (4.8)</td>
<td>0/39 (0.0)</td>
</tr>
<tr>
<td>Hip, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint effusion/ BME</td>
<td>4/19/0 (21.1)</td>
<td>0/40/3 (0.0)</td>
</tr>
<tr>
<td>1/21 (4.8)</td>
<td></td>
<td>1/40 (2.5)</td>
</tr>
<tr>
<td>1/21 (4.8)</td>
<td></td>
<td>1/40 (2.5)</td>
</tr>
<tr>
<td>Bony changes of the cortex</td>
<td>1/21 (4.8)</td>
<td>0/39 (0.0)</td>
</tr>
</tbody>
</table>

Conclusion. Even in early diagnosed peripheral SpA patients, over 1/3 exhibited BME suggestive of acute sacroiliitis and structural lesions of the SI joints. Our findings underscore the importance of sacroiliitis as the cornerstone feature within the SpA-concept, even in asymptomatic patients.
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PREDICTORS OF SUSTAINED REMISSION ON TNF-ALPHA INHIBITOR IN AN OBSERVATIONAL COHORT OF PATIENTS WITH ANKYLOSING SPONDYLITIS: THE ROLE OF MRI PARAMETERS OF INFLAMMATION AND STRUCTURAL DAMAGE

Pedersen SJ1, Wichuk S1, Chiowchanwisawakit P1, Zheng Z1, Lambert RG1, Bernatsky S2, Conner-Spady B1, Spady D1, Maksymowych WP2
1Copenhagen Center for Arthritis Research, Glostrup Hospital, University of Copenhagen, Denmark; 2Division of Rheumatology, University of Alberta, Edmonton, AB, Canada; 3Dept. of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand; 4PLA General Hospital, Beijing, PR China; 5Dept. of Radiology and Diagnostic Imaging University of Alberta, Edmonton, AB; 6Dept. of Medicine, McGill University, Quebec, Canada

Introduction/Aim. Sustained clinical remission is one of the key benchmarks for treatment of AS over the long term. We aimed to determine the factors predictive of sustained clinical remission on anti-tumor necrosis factor alpha (anti-TNF-α) therapy and the role of MRI parameters of inflammation and structural damage at baseline and after treatment.

Patients and Methods. In the Follow-up Research Cohort in AS (FORCAST), AS patients from Northern Alberta attending community and academic practices are assessed for clinical and laboratory outcomes every 6 months, radiography at baseline and 2 years, MRI at baseline, at 3-6 months for patients starting anti-TNF-α, and annually. MRI inflammation was assessed using Spondyloarthritis Research Consortium of Canada (SPARCC) Sacroiliac Joint (SIJ) and 23-DVU Spine scores while structural change was assessed independently using the SPARCC SIJ Structural Scores (SSS) for fat metaplasia, erosion, backfill, ankylosis, and the Fat Ankylosing Spondylitis Spine Score (FASSS) score for fat metaplasia.

Sustained clinical remission was defined as ASDAS<1.3 at two consecutive 6-monthly visits. We used univariate and multivariate logistic regression to assess patient demographics, smoking, B27, NSAID utilization, and baseline CRP, ASDAS, mSASSS, SPARCC scores, SSS, and FASSSS scores, adjusted for duration of follow up. We also assessed attainment post-treatment of CRP<6mg/L, ASDAS<1.3, and SPARCC MRI remission (SIJ <2 and spine <3) as predictors of future remission.

Results. We assessed 316 patients on anti-TNF therapy of mean (SD) age 41.2 (12.5) years, 78% males, mean (SD) symptom duration 18.7 (11.1) years, and mean (SD) duration of follow up of 1704 (961.4) days, of whom 144 had MRI evaluation. 98 (31.0%) achieved sustained ASDAS remission after mean (SD) follow up of 848.3 (682.4) days. In univariate analyses, patients attaining ASDAS remission were younger (p<0.0001), had shorter disease duration (p<0.0001), lower baseline ASDAS (p=0.01), were not current smokers (p=0.01), had definite SIJ erosion (p=0.01) but low spinal fat metaplasia (FASSS<5) (p=0.01) and SIJ ankylosis scores (p=0.01), and post-treatment scores indicating SPARCC MRI remission of inflammation (p=0.02), and normalized CRP (p=0.01). In multivariate analyses adjusted for duration of follow up, age, current smoking, baseline ASDAS, and normalized CRP were the strongest clinical predictors. The best models (in terms of R-squared values) included age, sex, ASDAS, current smoker, duration of follow up, and an MRI structural parameter (SSS erosion or ankylosis).

Conclusion. Current smoking is negatively associated with attainment of sustained remission to anti-TNF. Sustained remission is more likely in patients attaining normalized CRP, in the presence of definite SIJ erosion, and in the absence of SIJ ankylosis.

Adjusted R² Significant OR [95% CI] p-value

<table>
<thead>
<tr>
<th>Variable</th>
<th>Basic Model age, sex, ASDAS, current smoker, duration of follow up</th>
<th>Basic Model plus post-treatment CRP&lt;6</th>
<th>Basic model plus SSS erosion a2</th>
<th>Basic model plus SSS ankylosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>age</td>
<td>0.12</td>
<td>0.17</td>
<td>0.38</td>
<td>0.39</td>
</tr>
<tr>
<td>Baseline ASDAS</td>
<td>0.95 [0.92-0.98]</td>
<td>0.33 [0.14-0.80]</td>
<td>0.34 [0.14-0.84]</td>
<td>0.34 [0.13-0.92]</td>
</tr>
<tr>
<td>Current Smoking</td>
<td>0.009</td>
<td>0.33 [0.14-0.80]</td>
<td>0.019</td>
<td>0.033</td>
</tr>
<tr>
<td>Post-treatment CRP&lt;6</td>
<td>0.016</td>
<td>0.33 [0.14-0.80]</td>
<td>0.013</td>
<td>0.019</td>
</tr>
<tr>
<td>Baseline ASDAS</td>
<td>0.34 [0.14-0.84]</td>
<td>0.34 [0.14-0.84]</td>
<td>0.34 [0.13-0.92]</td>
<td>0.34 [0.13-0.92]</td>
</tr>
<tr>
<td>SSS erosion a2</td>
<td>8.86 [1.57-50.0]</td>
<td>8.86 [1.57-50.0]</td>
<td>8.86 [1.57-50.0]</td>
<td>8.86 [1.57-50.0]</td>
</tr>
<tr>
<td>SSS ankylosis</td>
<td>0.08 [0.07-0.98]</td>
<td>0.08 [0.07-0.98]</td>
<td>0.08 [0.07-0.98]</td>
<td>0.08 [0.07-0.98]</td>
</tr>
</tbody>
</table>

*Within first year of treatment.

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PREDICTORS OF SURVIVAL ON TNF-ALPHA INHIBITOR IN AN OBSERVATIONAL COHORT OF PATIENTS WITH ANKYLOSING SPONDYLITIS: THE ROLE OF MRI PARAMETERS OF INFLAMMATION AND STRUCTURAL DAMAGE

Pedersen SJ1, Zheng Z1, Wichuk S1, Chiowchanwisawakit P1, Lambert RG1, Bernatsky S2, Conner-Spady B1, Spady D1, Maksymowych WP2
1Copenhagen Center for Arthritis Research, Glostrup Hospital, University of Copenhagen, Denmark; 2Division of Rheumatology, University of Alberta, Edmonton, AB, Canada; 3Dept. of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand; 4PLA General Hospital, Beijing, PR China; 5Division of Rheumatology, University of Alberta, Edmonton, AB, Canada; 6Dept. of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand; 7Dept. of Radiology and Diagnostic Imaging University of Alberta, Edmonton, AB, Canada

Introduction/Aim. There has been no data reported evaluating MRI parameters of inflammation and structural damage. We aimed to identify factors influencing survival on anti-TNF therapy in real world practice specifically focusing on the role of MRI parameters of inflammation and structural damage.

Patients and Methods. In the Follow-up Research Cohort in AS (FORCAST), AS patients from Northern Alberta attending community and academic practices are assessed for clinical and laboratory outcomes every 6 months, radiography at baseline and 2 years, MRI at baseline, at 3-6 months for patients starting anti-TNF therapy and annually. MRI inflammation was assessed using Spondyloarthritis Research Consortium of Canada (SPARCC) Sacroiliac Joint (SIJ) and Spine scores while structural change was assessed independently using the SPARCC SIJ Structural Score (SSS) for fat metaplasia, erosion, backfill, ankylosis, and the Fat Ankylosing Spondylitis Spine Score (FASSS) score for fat metaplasia. MRI scans were scored independently by 2 readers and adjudicated by a third reader according to pre-specified rules. We used Kaplan-Meier plots, log rank tests and univariate and multivariate Cox regression analyses to assess the effects of patient demographics, smoking, B27, NSAID utilization, and baseline CRP, ASDAS, mSASSS, SPARCC scores, SSS and FASSSS scores on drug survival. We also assessed early attainment post-treatment of CRP<6mg/L, ASDAS<1.3, and SPARCC remission (SIJ <2, Spine <3) as predictors of anti-TNF survival.

Results. We recruited 480 patients on anti-TNF, mean (SD) age 41.0 (12.7) years, 74.4% males, mean (SD) symptom duration (11.6) years, mean (SD) survival on first anti-TNF 1228.1 (1036.9) days. The number discontinuing first-time anti-TNF prescription was 126 (26.3%) after mean (SD) follow up of 814.8 days from first prescription date, of which 28% was for lack of efficacy (LOE), and 17% for adverse events. There were 45 primary and 82 secondary failures. 125 patients had MRI at baseline and 100 had at least one follow up MRI. Univariate analysis showed that male sex (HR 0.57, p=0.02), and CRP<6mg/L (HR 0.56, p=0.02) were significant predictors of drug survival. Early attainment of SPARCC SIJ remission was the best MRI predictor of drug survival (HR 0.58, p=0.14). In multivariate analysis of clinical predictors, SPARCC SIJ <2 [adjusted OR=2.1 [1.02-4.74]; p=0.043] was a significant predictor.

Conclusion. From an extensive array of patient demographic and disease severity variables, attainment of normalized CRP or low disease activity state within first year of starting an anti-TNF was most strongly associated with survival on treatment. Early attainment of MRI inflammation may also be a factor but this requires further study with larger sample size.

Table. Multivariable Cox Regression.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio</th>
<th>p-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.82</td>
<td>0.47</td>
<td>0.48-1.41</td>
</tr>
<tr>
<td>Gender</td>
<td>1.01</td>
<td>0.29</td>
<td>0.99-1.03</td>
</tr>
<tr>
<td>Baseline CRP</td>
<td>0.99</td>
<td>0.035</td>
<td>0.98-1.00</td>
</tr>
<tr>
<td>CRP&lt;6 post-treatment*</td>
<td>0.46</td>
<td>0.008</td>
<td>0.26-0.82</td>
</tr>
<tr>
<td>ASDAS&lt;1.3 post-treatment*</td>
<td>0.54</td>
<td>0.027</td>
<td>0.32-0.93</td>
</tr>
</tbody>
</table>

*Within first year of treatment.
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CAN STRUCTURAL PROGRESSION ON MRI OF SACROILIAC JOINTS IN PATIENTS WITH PSYANDOLOPATHIES BE RELIABLY DETECTED AND WHAT TYPE OF CALIBRATION IS NECESSARY TO ACHIEVE THIS?

Pedersen S.J.1, van den Berg R.2, Navarro V.2,3, Wichuk S.4, Marin J.4, de Hooge M.S.M.2, Lambert R.G.4, van der Heijde D.4, Maksmowych W.P.1
1Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; 2LUMC, Leiden, The Netherlands; 3University Hospital La Paz, Madrid, Spain; 4University of Alberta, Edmonton, Canada; 5University of British Columbia, Canada

Introduction/Aim. Assessment of structural lesions of the SJJ on MRI may be a helpful tool to monitor disease progression but requires evidence that change in such lesions can be reliably detected and the type of calibration necessary to achieve this. We aimed to assess reliability of detection of structural lesions and the impact of calibration using either a standardized web-based training module or a set of DICOM-based reference MRI scans.

Patients and Methods. In this international multicenter study, 5 readers without exposure to the application of scoring methods for structural lesions in the SJJ reviewed either a web-based training module (n=3) or DICOM-based reference MRI scans (n=2). Both calibration methods used the SPARC-SJJ Structural Score (SSS). Baseline and 2-year T1W scans from 30 patients with axial SpA blinded to time point and STR scan were assessed. Interobserver reliability for structural changes was calculated by ICC and comparisons made with predefined expert readers (n=3).

Results. Mean (SD) reduction in SSS erosion score was significantly greater for expert readers (-1.46 (4.05)) and for DICOM-trained readers (-1.40 (3.42)) than for web-based module trained readers (-0.47 (1.56)). Mean (SD) increase in SSS backfill score was significantly greater for expert readers (0.82 (3.87)) than for web-based module trained readers (-0.06 (1.67)). ICC differed between groups mainly for 2-year change in erosion and backfill. Although reliability was superior for DICOM-trained readers, substantial reliability with expert readers was attainable following training with the web-based module.

Conclusion. Structural lesions in the SJJ on MRI are often heterogeneous in appearance and their evolution may not be reliably detected without the more rigorous approach to calibration using DICOM scans.

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SUBCLINICAL UNGUAL DYSTROPHY IN PATIENTS WITH PSORIASIS WITHOUT JOINT INVOLVEMENT: IS THERE ANY ROLE FOR NAIL ULTRASOUND?

Kleere B.N.C.1, Luz K.R.1, Soares P.O.M.1, Ohe E.M.D.1, Pinheiro H.H.C.1, Perio A.M.2, Pinheiro M.M.2
1Rheumatology Division, Federal University of Sao Paulo (Unifesp) EPM, Sao Paulo; 2Rheumatology Dept., Federal University of Sao Paulo (Unifesp) EPM, Sao Paulo, Brazil

Background. The joint involvement is observed in approximately 30% of patients with psoriasis (Ps). However, no clinical, lab or by imaging strategy is well established to identify them before progression to psoriatic arthritis (PsA). Aim. To assess the association among the nail involvement and distal interphalangeal extensor enthesopathy (DIP-ExE), evaluated by ultrasound (US), with the subclinical joint involvement, including arthritis, enthesis and dactylitis in patients with Ps.

Patients and Methods. A total of 89 patients with active Ps were included in this cross-sectional study and were compared with 21 healthy controls, paired for sex, age and ethnicity. After evaluation by a dermatologist, including the PASE and the PEST questionnaires, as well as PASI, BSA and NAPSI, the patients were classified in two groups, according to clinical nail involvement (CNI).

Moreover, they were also evaluated by a rheumatologist, regarding enthesis, dactylitis, axial complaints and peripheral arthritis, in order to apply the CASPAR criteria (2006). A third-blind physician performed a global and complete US evaluation, including 1246 enthesis, synovial thickness in 1958 joints, 1 active skin lesion and 2 bed-nails, according to OMERACT (2010), using the MyLab60 ® (Esaote, Italy). P<0.05 was set as statistically significant.

Results. There was no significant difference concerning time of disease, comorbidities, life habits and PASE in patients with CNI when compared to those with no nail dystrophy. However, patients with CNI (67.4%) had higher number of tender and swollen joints. The presence of nail power-Doppler (N-Pd) and the DIP-ExE was observed in 65-70% of patients with CNI (p<0.035). The nail US identified 58.6% of subclinical nail dystrophy and 70.6% had also positive N-Pd (p<0.001).

Conclusions. Our results showed that the nail US was able to identify subclinical nail dystrophy and DIP-ExE in almost 60% of patients with active Ps, but no nail or joint clinical involvement, suggesting that it could be used for early screening of patients with increased risk of developing PsA.

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STUDY OF INTRACELLULAR BEHAVIORS OF HLA-B*27 SUBTYPES ASSOCIATED OR NOT WITH SPONDYLOPORTHIDES

Jah N.1,2, Chiochica G.1,2, Breban M.1,2, André C.1,2
1INSERM U1173 Inflammation and infection, France, Faculty of Health Sciences Simone Veil, Montigny-le-Bretonneux; 2University of Versailles Saint-Quentin-en-Yvelines, Paris; 3Service de Rhumatologie, Ambroise Pare Hospital, University of Versailles Saint-Quentin-en-Yvelines, Boulogne, France

Aim. Mechanisms underlying the striking association of spondyloarthropathies (SpA) with the MHC class I molecule HLA-B27 remain poorly understood. SpA-like disease develops spontaneously in B*2705 transgenic rats in correlation with high HLA-B27 expression levels. This study was undertaken to examine the consequences of expressing HLA-B27 alleles which are differently associated with SpA.

Methods. HeLa cells were transfected with complementary DNA encoding for HLA-B proteins fused to yellow fluorescent protein. We studied the composition and nature of HLA-B-containing intra-cellular vesicles by antibodies staining HLA–B proteins fused to yellow fluorescent protein. We studied the composition and nature of HLA-B-containing intra-cellular vesicles by antibodies staining HLA–B proteins fused to yellow fluorescent protein. We studied the composition and nature of HLA-B-containing intra-cellular vesicles by antibodies staining HLA–B proteins fused to yellow fluorescent protein. We studied the composition and nature of HLA-B-containing intra-cellular vesicles by antibodies staining HLA–B proteins fused to yellow fluorescent protein.

Our results showed that the nail US was able to identify subclinical nail dystrophy and DIP-ExE in almost 60% of patients with active Ps, but no nail or joint clinical involvement, suggesting that it could be used for early screening of patients with increased risk of developing PsA.

Results. With increased expression, all HLA-B proteins accumulated in cytoplasmic vesicles. We observed comparable staining of those vesicles with HC10 antibody (anti-class I heavy chain) for all HLA-B alleles. In contrast, we ob-
served differential staining with BBM1 antibody that binds to beta-2-microglobulin (β2m): the SpA-associated HLA-B27 subtypes formed vesicles that were stained significantly more with BBM1 than the non-associated HLA-B8, B27, and HLA-B*0702 alleles. On the other hand, we observed no staining of theses vesicles with EEA1 (early endosomes marker), Rab7 (late endosomes marker), LC3 (autophagosomes marker) and Rab6 (Golgi marker) antibodies.

However, we found positive staining with endoplasmic reticulum (ER) markers (BiP and Calreticulin) suggesting that the HLA-B-containing vesicles belong to the ER. Consistent with such interpretation, those cytoplasmic vesicles were still observed using live-cell imaging of HeLa cells transfected with HLA-B after treatment with nocodazole or brefeldin-A that inhibit ER exit.

Conclusion. It appears that under conditions of high expression, HLA-B molecules accumulate in cytoplasmic vesicles that belong to the ER. Moreover, our data indicate different composition of HLA-B-containing cytoplasmic vesicles, depending on the allele: vesicles formed with HLA-B27 subtypes associated with SpA contained significantly more β2m than those formed with non-associated alleles.

This report establishes a correlation between the level of predisposition to SpA conferred by HLA-B alleles and their biochemical behaviors.

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PREVALENCE OF HIP ARTHRITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TNF INHIBITORS

Konsta M., Nurmohamed M.T., van Denderen J.C., Visman I., van der Horst-Bruinssma I.E.

Dept. of Rheumatology, VUMc, Amsterdam, The Netherlands

Introduction. Hip involvement is the most frequent extra spinal arthritic manifestation of Ankylosing Spondylitis (24% to 36%) and a common cause of disability, leading to total hip replacement (THR) in 5% of AS patients.

Aim. 1. To examine the prevalence of hip arthritis in AS; 2. To identify possible risk factors of its development; 3. To identify possible gender difference in hip arthritis in AS.

Materials and Methods. 241 AS patients (162 men, age: 48.6±11years (meansSD), disease duration: 23.6±11.2 years) were included in this cross-sectional study. The patients received initially: etanercept (n=117), adalimumab (n=89) infliximab (n=25), or golimumab (n=10). Anteroposterior X-rays of the pelvis, obtained before anti-TNF treatment initiation, were scored according to BASRI-hip scoring system. In parallel, the lateral X-rays of cervical and lumbar spine were scored using the mSASSS. The patients’ disease activity and functional limitation were recorded by BASDAI, ASDAS-CRP, ASDAS-ESR, BASFI and BASMI. Mann-Whitney, two-sample t-test and logistic regression analysis were applied.

Results. Hip involvement was assessed clinically (pain, reduced range of motion and intermalleolar distance) and radiographically, as BASRI-h score ≥2 at baseline anteroposterior pelvis X-rays.

After 7.2±4.4 years, 8/205(3.9%) patients, with hip involvement at baseline, underwent total hip replacement (4 bilateral, 4 unilateral). Thus, the BASRI-hip score although remained unchanged after 2.6±0.7 years (1.05±0.98 vs. 1.33±0.99, p=NS), increased significantly at follow-up end (1.13±0.99, p<0.0001), compared to baseline. AS males had a significant increase in BASRI-hip score at the two intervals (1.12±0.96 vs. 1.14±0.98, p=0.017), compared to females, who had significant increase only at follow-up end. In contrast, the mean JSW remained unchanged at the three time points (4.2±0.8 vs. 4.1±0.7), in patients with and without hip arthritis, and males vs. females. In contrast the mSASSS-score raised significantly during the follow-up period [4(0-21) vs. 7.5(1-27) vs. 9(2-29), median-IQR, p<0.0001], regardless of gender and presence of hip involvement.

Conclusions. Despite the lack of a control group, our results suggest that long-term anti-TNF treatment inhibits radiographic progression of hip arthritis in AS. The new scoring system may contribute to detect minor changes in contract to BASRI-hip score rough estimation.
DYSBIOSIS AND ZONULIN UP-REGULATION ALTER GUT EPITHELIAL AND VASCULAR BARRIERS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Ciccio F.1, Guggino G.1, Rizzo A.1, Luchetti M.M.1, Milling S.1, Cyper H.1, Fasano A.1, Elewaut D.2, Trelo G.2
1University of Palermo, Palermo; 2Azienda Ospedaliera di Palermo, Italy

Background. The aim of this study was to investigate the role of ileal bacteria in modulating local and systemic immune responses in Ankylosing Spondylitis (AS).

Methods. Ileal biopsies were obtained from 50 HLA-B27+ AS patients and normal subjects. Silver stain was used to visualize bacteria. Ileal expression and tissue distribution of tight and adherens junction proteins were investigated by TaqMan real-time (RT-PCR) and immunohistochemistry. Serum levels of lipopolysaccharide (LPS), LPS-binding protein (LPS-BP), intestinal fatty acid-binding protein (iFABP) and zonulin were assessed by ELISA. Monocyte immunological functions were studied in in vitro experiments. In addition the effects of antibiotics on tight junctions in HLA-B27 transgenic (TG) rats were assessed.

Results. Adherent and invasive bacteria were observed in the gut of AS patients with higher bacterial scores significantly correlated with gut inflammation. Impairment of the gut-vascular barrier was also present in AS, accompanied by significant up-regulation of zonulin, and associated with high serum levels of LPS, LPS-BP, iFABP and zonulin. In in vitro studies zonulin altered endothelial tight junctions while its epithelial release was modulated by isolated AS ileal bacteria. AS circulating monocytes displayed an anergic phenotype partially restored by ex vivo stimulation with LPS+CD4+ and their stimulation with recombinant zonulin induced a clear M2 phenotype. Antibiotics restored tight junction function in HLA-B27 TG rats.

Conclusions. Bacterial ileitis, accompanied by increased zonulin expression and damaged intestinal mucosal- and gut-vascular barriers, characterize the gut of AS patients and are associated with increased blood levels of zonulin, LPS, LPS-BP and i-FABP. Bacterial products and zonulin influence monocyte behavior.

MICROSCOPIC GUT INFLAMMATION IN SPA IS A PROGNOSTIC FACTOR FOR INITIATION AND RESPONSE TO ANTI-TNF δ THERAPY

Cypers H.1,2, Varkas G.1,2, De Vos M.3, Cuvelier C.A.4, Van den Bosch F.1, Elewaut D.1,2
1Dept. of Rheumatology, Ghent University Hospital; 2Unit for Molecular Immunology and Inflammation, VIB IRC Ghent University; 3Dept. of Gastroenterology, Ghent University Hospital, Belgium; 4Dept. of Pathology, Ghent University, Belgium

Aim. Microscopic gut inflammation is frequently present in spondyloarthritis (SpA) and is associated with more severe disease. However, the relevance of this subclinical inflammation for therapeutic decision-making in SpA is unknown. In this study we evaluated the effect of microscopic gut inflammation on anti-TNF-δ initiation and response to anti-TNF-δ therapy.

Patients and Methods. 126 newly diagnosed axial and peripheral SpA patients from the Ghent Inflammatory Arthritis and spoNdyliits cohort (GIANT) were included. All patients underwent an ileocolonoscopy at baseline to assess the presence of microscopic bowel inflammation. The rate of anti-TNF-δ initiation was assessed performing survival analysis. Response to anti-TNF-δ therapy was evaluated in axial SpA by assessment of ASDAS scores after 3 and 6 months.

Results. Of the 126 SpA patients assessed, 43 (34.1%) had been started on anti-TNF-δ therapy. Microscopic gut inflammation at baseline, present in 47 (37.3%) patients, was significantly linked to the rate at which anti-TNF-δ therapy was started (log rank p=0.025). Other baseline factors associated with anti-TNF-δ initiation were BASDAI BASM, past or present enthesitis and BASMI. However, the association between gut inflammation and anti-TNF-δ initiation remained significant after adjustment for these factors. ASDAS response to anti-TNF-δ was assessed in 35 axial SpA patients of which 15 had microscopic gut inflammation. Significant more patients with gut inflammation showed a clinically important ASDAS improvement (≥1.1 as defined by ASAS) under anti-TNF-δ therapy (p=0.034), and this association remained significant after correction for age, sex or CRP.

Conclusion. Microscopic gut inflammation in SpA seems to be a risk factor for more extended and progressive disease resulting in a higher need for biologic therapy. It also might be a predictor of better response to anti-TNF-δ therapy.
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RESPONSE TO TREATMENT WITH NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN PATIENTS WITH ANKYLosing Spondylitis and Non-Radiological Axial Spondylo-Arthritis

Cherentsova I.A., Ottea E.N.
Postgraduate Institute for Public Health Workers, Khabarovsk, Russia

Objective. To evaluate the activity level and functional status in patients with ankylosing spondylitis (AS) and non-radiological axial spondyloarthritis (nr-axSpA) in response to the treatment with non-steroidal anti-inflammatory drug (NSAIDs).

Material and Methods. 153 patients, mean age was 34.3±0.8 years, 106 (69.2%) males, 47 (30.8%) females were examined. The patients were divided into two groups: group 1 (n=119) – patients with a confirmed diagnosis of ankylosing spondylitis, group 2 (n=34) - patients with non-radiological axial SpA. The disease was diagnosed according to the modified New York criteria in the first group, second – to the ASAS classification criteria for axial SpA. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to assess activity. Examination included: HLA-B27.

All patients were taking NSAIDs, a type of a medication had been chosen taking into consideration personal tolerance and accompanying or underlying diseases. The local ethics committee approved the study protocol, and all patients gave informed consent for participation. In the beginning and the end of the research, BASDAI was evaluated.

Results. The mean age in the first group was 36.4±0.9, nr-axSpA - 27±1.0 years. The mean age when the first symptoms appeared and a diagnosis was made, were 21.5±0.5 and 21.7±1.2 years respectively (p=0.05). In all patients axial variant prevailed (AS - 64 (53.7%), nr-axSpA - 23 (76.7%)). HLA B27 was positive in 102 (85.9%) patients AS and 30 (88.2%) nr-axSpA. Patients of the first and second groups were predominantly men (AS - 82 (68.9%), nr-axSpA - 24 (80.0%)). The median BASDAI was in patients with AS 4.0±0.1, in twelve months 2.4±0.1 (-40.0%, p<0.01), nr-axSpA - 3.4±0.2,15±0.04 (-55.5%, p<0.01).

Discussion. We did not reveal any clinical or demographic differences in both groups. At the background of receiving NSAIDs, the percentage of activity lowering in patients with nr-axSpA was two times higher. Conclusion. The therapy onset at the non-radiological stage of the disease will help to suppress progression of the disease and achieve remission.

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USE OF CONVENTIONAL SYSTEMIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS BEFORE, DURING, AND AFTER TNFI THERAPY FOR PSORIATIC ARTHRITIS IN THE UK: CAPTURE STUDY

Bishop-Bailey A.1, Coope H.2, McHugh N.2 on behalf of the CAPTURE Study Investigators.
1pH Associates Ltd, Marlow; 2Novartis Pharmaceuticals Ltd, Frimley/Camberley; 3Royal National Hospital Rheumatic Diseases, Bath, UK

Introduction. The availability of Tumour Necrosis Factor inhibitor (TNFi) therapies has increased treatment options for UK clinicians managing patients with psoriatic arthritis (PsA). Most patients will have received non-TNFI therapies (including conventional systemic disease-modifying antirheumatic drugs [csDMARDs]) before transitioning to TNFi. This real world CAPTURE study evaluated PsA management with TNFi during standard clinical care in the UK NHS, and here the use of csDMARDs before, during, and after TNFi therapy is reported.

Methods. CAPTURE was a retrospective observational study of 141 consenting patients from 11 NHS centres. Patient eligibility: documented diagnosis of PsA managed with PsA or PsA with psoriatic arthritis (PsA). Most patients will have received non-TNFi therapies (including conventional systemic disease-modifying antirheumatic drugs [csDMARDs]) before transitioning to TNFi. The real world CAPTURE study evaluated PsA management with TNFi during standard clinical care in the UK NHS, and here the use of csDMARDs before, during, and after TNFi therapy is reported.

Results. CAPTURE was a retrospective observational study of 141 consenting patients from 11 NHS centres. Patient eligibility: documented diagnosis of PsA managed with TNFi during standard clinical care in the UK NHS, and here the use of csDMARDs before, during, and after TNFi therapy is reported.

Conclusions. The use of concomitant csDMARDs in patients with PsA managed on TNFi (despite little evidence to support combination therapy1), along with their use following permanent TNFi discontinuation, are suggestive of a need for alternative therapeutic options to be made available to UK clinicians managing patients with PsA.

Acknowledgment. CAPTURE study was sponsored by Novartis Pharmaceuticals UK Ltd and managed by pH Associates Ltd.

Reference

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SECUKINUMAB IMPROVES MINIMAL DISEASE ACTIVITY RESPONSE RATES IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: DATA FROM PHASE 3 FUTURE-2 STUDY

Mease P., Coates L.C.1, Kirkham B.2, McLeod L.D.3, Mpofu S.4, Karyekar C.5, 6, Gandini K.6
1University of Washington, Seattle, USA; 2University of Leeds, Leeds; 3Guy’s and St Thomas’ NHS Foundation Trust, London, UK; 4RTI Health Solutions, Research Triangle Park, USA; 5Novartis Pharma AG, Basel, Switzerland; 6Novartis Pharmaceuticals Corporation, East Hanover, USA

Introduction. Minimal disease activity (MDA) is gaining acceptance as a validated composite measure for achieving disease control in psoriatic arthritis (PsA). This post-hoc analysis assessed MDA response rates with secukinumab, a fully human anti-IL-17A monoclonal antibody, through 52 weeks in FUTURE-2 study.

Materials and Methods. 397 patients with active PsA were randomised to subcutaneous secukinumab (300mg, 150mg, or 75mg) or placebo; details of study design, efficacy and safety results are published. MDA was assessed in overall population and in patients stratified by prior anti-TNF therapy (anti-TNF-naive and anti-TNF-IR [inadequate response/intolerance]) and disease duration (≤2 years versus >2 years since diagnosis). Observed data are shown. 75mg data are not reported. Results. In total, 23/100 (23%) and 27/97 (28%) patients achieved MDA at Week-16 with secukinumab 150mg and 300mg, respectively, versus 9/88 (10%) in placebo; these responses were sustained through Week-52. In anti-TNF-naive cohort, higher proportion of patients achieved MDA at Week-16 with secukinumab 150mg (20/63 [32%]) or 300mg (22/65 [34%]) versus placebo (8/58 [14%]), with response rates sustained through Week-52. Lower rates were observed in anti-TNF-IR patients. Proportion of patients achieving MDA at Week-16 and Week-52 in overall population was greater for those ≤2 years versus those >2 years since diagnosis. Observed data are shown. 75mg data are not reported. Conclusions. The therapy onset at the non-radiological stage of the disease will help to suppress progression of the disease and achieve remission.
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IS IT POSSIBLE TO INTERRUPT ANTI-TNF THERAPY USING A TAPERING STRATEGY IN PATIENTS WITH ANKYLOSING SPONDYLITIS ACHIEVING CLINICAL RESPONSE?

Navarro-Compán V., Plasencia C., Monjo I., Peiteado D., Villalba A., Balsa A., Martín-Molea E., de Miguel E. Dept. Rheumatology, University Hospital La Paz, Madrid

Introduction. Discontinuation of anti-TNF therapy in patients with ankylosing spondylitis (AS) leads to the appearance of flare within a few months in most cases. However, evidence is based on studies only including patients suddenly interrupting anti-TNF therapy.

Aim: First, to assess the frequency of patients with AS interrupting anti-TNF therapy after achieving clinical response in clinical practice; second, to investigate whether or not interrupting anti-TNF therapy after a progressive tapering strategy is successful to maintain clinical response in patients with AS.

Patients and Methods. Retrospective analysis of a prospective longitudinal cohort including patients with AS under anti-TNF therapy in a tertiary hospital. Patients achieving and maintaining clinical response during ≥6 months after initiating anti-TNF therapy started a tapering strategy reducing progressively anti-TNF dose. After this, patients who maintained clinical response during the tapering strategy interrupted this therapy and were followed during 12 months. In case of flare, the same treatment was reintroduced. The frequency and clinical efficacy of anti-TNF therapy discontinuation after a tapering strategy was evaluated.

Results. In total, 186 patients with AS received anti-TNF therapy. Only 10 (5.4%) patients interrupted the treatment due to clinical remission. Median (IQR) time until flare was 4 (3-10) months. After reintroducing anti-TNF therapy, all patients achieved clinical response.

Conclusions. In patients with AS, discontinuation of anti-TNF therapy due to clinical remission in clinical practice is very uncommon. Even if a tapering strategy is used before, discontinuation of anti-TNF therapy leads to the appearance of flare within a few months in most cases.

Results. A total of 174 (67%) prevalent cases and 84 (33%) incident patients were included, all of them receiving/starting an anti-TNF agent. Table I shows the results (mean ±standard deviation or relative frequencies) for the characteristics of patients included in both groups. Compared to prevalent cases, the group of incident cases had shorter disease duration at the beginning of the first administered anti-TNF therapy, less proportion of males and patients with HLA-B27.

Table I. Characteristics at baseline visit of all patients included in REGISPONSERBIO.

<table>
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<tr>
<th>Characteristic</th>
<th>Total N=258</th>
<th>Prevalent N=174 (67%)</th>
<th>Incident N=84 (33%)</th>
<th>p value</th>
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<tr>
<td>Age (years)</td>
<td>40±13</td>
<td>42±13</td>
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<td>Disease duration (years)</td>
<td>13±10</td>
<td>14±10</td>
<td>11±9</td>
<td>0.04</td>
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</tbody>
</table>

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IS THE PATTERN OF PATIENTS WITH AXIAL SPONDYLOARTHRITIDES STARTING BIOLOGICAL THERAPY CHANGING OVER-TIME? RESULTS FROM REGISPONSERBIO?


Introduction. During the last decade, the progress experienced in clinical research in the field axial spondyloarthritis (axSpA) has been extraordinary. The repercussion of this progress on the pattern of patients with axSpA initiating intensive treatment is unclear.

Aim. To evaluate if the pattern of patients with axSpA starting anti-TNF therapy is changing over-time.

Patients and Methods. Baseline data from all patients included in REGISPONSERBIO were analysed. REGISPONSERBIO is a Spanish multicenter, prospective registry (3 year-follow-up, with clinical controls every six months) of patients with axial SpA (ASAS criteria) under biological treatment. During the inclusion period (September 2013-December 2014), a total of 258 patients were recruited in 17 centers. These patients were classified in two groups: a) prevalent cases (patients receiving biological treatment prior to baseline visit) b) incident cases (patients who started on biological therapy at the inclusion in the registry). Collected data included demographic and disease characteristics, disease activity, function, metrology, quality of life, biological treatment at the time of inclusion in the registry and concomitant treatments. For this study, characteristics between prevalent and incident cases were compared using t-Student and chi-square tests.

Results. A total of 174 (67%) prevalent cases and 84 (33%) incident patients were included, all of them receiving/starting an anti-TNF agent. Table I shows the results (mean ±standard deviation or relative frequencies) for the characteristics of patients included in both groups. Compared to prevalent cases, the group of incident cases had shorter disease duration at the beginning of the first administered anti-TNF therapy, less proportion of males and patients with HLA-B27.
positive, a higher frequency of patients with non-radiographic axSpA and more patients receiving concomitant treatment with NSAIDs. However, no differences were observed with regard to the degree of disease activity.

Conclusions. The profile of patients with axSpA starting biological therapy is changing overtime. Currently, patients with axSpA initiate intensive treatment earlier, which may have a repercussion in the evolution of the disease.

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IMPACT OF AEROBIC FITNESS ON AXIAL SPONDYLOARTHRITIS ACTIVITY: A META-ANALYSIS OF CONTROLLED STUDIES

Verhoeven F., Guillot X., Prati C., Tordi N., Demouoge C., Wendling D.
University Teaching Hospital, Besançon, France

Introduction. The current recommendations for management of spondyloarthritis suggest a significant part of physical therapy with supervised exercises. Benefit of physiotherapy and spa-therapy is known for long time, but impact of aerobic fitness on the disease is not clear.

The objective of this study is, after a systematic review of the literature and meta-analysis, to evaluate the impact of an aerobic fitness program on disease activity (BASDAI) and function (BASFI).

Methods. A systematic review of the literature was performed on the PubMed and Embase databases with the following keywords: ("Ankylosing spondylitis" OR "Spondyloarthritis") AND ("Physical activity" OR "Aerobic fitness").

The diagnosis axial spondyloarthritis was based on the modified New York and/or the ASAS criteria. Aerobic fitness was defined as an exercise performed at 50–90% of the maximal heart rate or between 50% and 80% VO2 pick.

Results. 520 abstracts were identified and 93 analysed. 8 studies fulfilled the selection criteria and 6 finally included because of the presence of a control group.

Both groups were similar in terms of age, sex, disease duration. Aerobic fitness program showed a positive impact on the BASFI (WMD: -0.25 [95% CI -0.83; 0.32]) (I2: 0% , p=0.41). Aerobic exercise does not provide in the intervention group a positive impact on the BASFI (WMD: -0.31 [95% CI -0.73; 0.11]) (I2: 0% , p=0.79). When compared to a control group, aerobic fitness does not provide a more positive impact on the BASFI (WMD: -0.41 [95% CI -1.09; 0.27]) (I2: 0% , p=0.62).

Conclusion. Aerobic exercise did not provide beneficial effects in axial SpA, neither on disease activity nor on physical function when compared to a control group.

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CERTOLIZUMAB PEGOL FOR THE TREATMENT OF AXIAL SPONDYLOARTHRITIS: 4-YEAR OUTCOMES FROM THE RAPID-AXSPA TRIAL

van der Heijde D.1, Dougados M.2, Landewé R.3, Sieper J.4, Maksymowycz W.5, Rudwaleit M.6, Van den Bosch F.7, Braun J.3, Mease P.J.8, Davies O.9, Hoepken B.10, Peterson L.11, Deodhar A.12, 1Leiden University Medical Centre, Leiden, The Netherlands; 2Cochin Hospital, Paris, France; 3Amsterdam and Atrium Medical Center, Heerlen, The Netherlands; 4University Hospital Charité, Berlin, Germany; 5University of Alberta, Edmonton, Canada; 6Klinikum Bielefeld, Bielefeld, Germany; 7Ghent University Hospital, Ghent, Belgium; 8Rheumazentrum Ruhrgebiet, Herne, Germany; 9Swedish Medical Center and University of Washington, Seattle, USA; 10UCB Pharma, Slough, UK; 11UCB Pharma, Monheim, Germany; 12UCB Pharma, Raleigh, USA; 13Leiden University Medical Centre, Leiden, The Netherlands

Introduction/Aim. RAPID-axSpA (NCT01087762) investigated efficacy and safety of certolizumab pegol (CZP) in patients with axial spondyloarthritis (axSpA), including ankylosing spondylitis (AS) and non-radiographic (nr-)axSpA patients. Here we report 4-year efficacy and safety data.

Patients and Methods. RAPID-axSpA was double-blind, placebo-controlled to Week (Wk) 24, dose-blind to Wk48 and open-label thereafter. Patients had active axSpA and fulfilled ASAS criteria. Patients randomized to CZP (200mg Q2W/400mg Q4W) continued on assigned dose to Wk204. Efficacy data for patients originally randomized to CZP (combined doses) are presented as observed cases and with imputation (NRI for categorical measures, LOCF for continuous). Safety set contained patients treated with ≥1 CZP dose to Wk204.

Results. 218/325 patients were randomized to CZP, of whom 65% completed Wk204 (AS: 67%; nr-axSpA: 63%). In the open-label period, 9.2% of patients withdrew through adverse events (AEs) and 1.4% through lack of efficacy. From Wk24 to Wk204, the proportion of patients achieving ASAS20/40/PR was maintained in patients completing Wk204, as was efficacy in all outcomes (Table). Improvements were similar for AS and nr-axSpA (Table) and both CZP dose regimens (data not shown). The safety set (N=315) had 981 patient-years (PY) total CZP exposure, with an AE rate/100PY of 292.9. No new safety signals were identified from Wk96 to Wk204, and no deaths reported over 4 years.

Conclusion. CZP efficacy was maintained in axSpA patients over 4 years with no new safety signals. Treatment responses were similar in AS and nr-axSpA patients.
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ENTEROPATHIC SPONDYLOARTHRITIS: TREATMENT AND OUTCOME IN A 2-YEAR PROSPECTIVE STUDY

Chimenti M.S., Conigliaro P., Triggiani P., Cedola F., Onali S., Calabrese E., Petruzziello C., Ruffa A., Biancone L., Perricone R., Cedola F., Perricone R.

Medicina dei Sistemi”, University of Rome Tor Vergata, Rome; “Rheumatology, Allergology and Clinical Immunology Dept. of “Medicina dei Sistemi”, University of Rome Tor Vergata, Rome; “Rheumatology, Allergology and Clinical Immunology Dept. of “Medicina dei Sistemi”, University of Rome Tor Vergata, Rome, Italy

Background. Spondyloarthritides (SpA) are a distinct group of diseases with similar clinical features and a common genetic background. SpA frequently occur in combination with inflammatory bowel disease (IBD).

Objective. Aim of the study was to prospectively evaluate the effect of treatment and outcomes in a cohort of IBD patients with SpA (enteropathic SpA, ESpA) who concomitantly referred to a combined gastro-rheumatologic outpatient clinic for 2 years.

Methods. 127 ESpA patients [M:F=1:8, age 46.6±13.4 years, n=84 Crohn disease, n=43 Ulcerative Colitis] were enrolled. CRP, ASDAS-CRP, DAS-CRP, BASDAI, BASFI, HAQ and treatments were evaluated at baseline (T0) and after 3/6/12/18/24 months.

Results. Axial(ax)-ESpA occurred in 37% of cases with 59.6% non-ax SpA. Diagnostic delay was lower in peripheral than ax-ESpA (7.4 vs 4.3 years, p 0.03). Prevalence of patients on Coxibe or HCQ was higher at all the time points comparing to T0 (p<0.01). At T18 and T24, treatment with mesalazin was reduced while assumption of anti-TNF (adalimumab and golimumab) were higher than T0 (p<0.01). In both ax- and peripheral-ESpA, Coxibe were higher at T3/6/12/18/24 while anti-TNF were higher in ax-ESpA at T12/18/24 compared to T0 and T12 in peripheral-ESpA (p<0.001). In all axESpA CRP, DAS, ASDAS, and BASDAI were lower at T12 than T0 (p<0.05). In particular, CRP and HAQ were reduced at T18 (p<0.05) and T24 (p<0.01); while CRP, BASDAI, and BASFI were lower at T24 than T0 (p<0.01). In ax-ESpA, BASFI was lower at T12, CRP at T18 and T24, and BASDAI, BASFI and HAQ at T24 compared with T0 (p<0.05). In peripheral-ESpA, CRP was reduced at T6/12/18 (p<0.01), DAS and HAQ at T24 compared with T0 (p<0.05).

Conclusion. A combined approach may improve treatment strategies and clinical outcome in ESpA patients.
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PATIENT-REPORTED QUALITY OF LIFE IN PATIENTS WITH BASELINE OBJECTIVE SIGNS OF INFLAMMATION AND ACTIVE NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS TREATED WITH GOLIMUMAB: RESULTS OF THE OPEN-LABEL EXTENSION OF A RANDOMIZED, DOUBBLE-BLIND STUDY

Maksymowycz W.P.1, Dougdas M.2, Sieper J.,1 Braun J.,1 Bergman G.,1 Curtis S.P.1, Trontcheva A.,2 Philip G.,2 Huycck S.2, van der Heijde D.2

1University of Alberta, Edmonton, AB, Canada; 2Paris-Descartes University, Paris, France

Introduction/Aims. In an open-label extension (OLE) of a 16-week, randomized, double blind (DB), placebo (PBO)-controlled, phase 3 study (GO-AHEAD; NCT1453725) in patients with nonradiographic axial spondyloarthritis (nr-axSpA) (1), we assessed quality of life (QoL) in patients with objective signs of inflammation at baseline.

Methods. Patients GLM 50mg Q4W during the 44-week OLE (36-week efficacy period; 8-week safety follow-up). QoL evaluations in patients with objective inflammation (MRI sacroiliitis+ and/or C-reactive protein upper limit of normal) included Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL), 36-item Short Form Health Survey (SF-36), and EuroQol Group 5 Dimensions Health Questionnaire (EQ-5D) and Health State (0–100 VAS), and Work Productivity and Activity Impairment (WPAI) at weeks 16 and 52 and the Patient’s Global Disease Assessment (PGDA; 0–10cmVAS) at weeks 16, 20, 24, 32, 40, and 52.

Results. There were 153 patients with objective inflammation at baseline who were treated in the OLE (GLM=76; PBO=77). At week 52, patients continuing GLM and those switched from PBO to GLM demonstrated improvement in QoL parameters (Figure) Mean (SD) change from baseline in Overall Work Impairment scores were -21.2 (24.7) (GLM) and -8.4 (28.5) (PBO) at week 16; at week 52, mean (SD) changes were -31.1 (27.2) (PBO/GLM). Among patients with objective inflammation before treatment in the DB phase, those who continued GLM in the OLE had continued benefits in QoL and work productivity, and those who switched to GLM in the OLE from the DB phase had notable improvement in QoL and work productivity.

Reference

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EFFECT OF SECUKINUMAB ON SPINAL RADIOGRAPHIC CHANGES THROUGH 2 YEARS IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS OF THE PHASE 3 STUDY, MEASURE-1

Braun J.1, Baraliakos X.1, Deodhar A.2, Baeten D.1, Sieper J.,1 Emery P.3, Talloczy Z.1, Martin R.1, Richards H.B.1

1Rheumazentrum Ruhrgebiet, Herne, Germany; 2Oregon Health & Science University, Portland, USA; 3University of Amsterdam, Academic Medical Center, Amsterdam, The Netherlands; 4Charité University Medicine Berlin, Berlin, Germany; 5University of Leeds, Institute of Rheumatic and Musculoskeletal Medicine, Leeds, UK; 6Novartis Pharmaceuticals Corporation, East Hanover, USA; 7Novartis Pharma AG, Basel, Switzerland

Introduction. Inhibition of radiographic spinal changes represents a main goal of therapy in active ankylosing spondylitis (AS). Here, we report effects of secukinumab on radiographic progression up to 104 weeks in MEASURE-1 trial (NCT01358175).

Materials and Methods. 371 patients with active AS were randomised to secukinumab or placebo. Details of study design have been published elsewhere (1). Lateral radiographs of cervical and lumbar spine performed at baseline and Week 104 were read centrally applying the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Patients initially randomised to secukinumab, who had X-rays available at baseline and Week 104 (n=168), were included in this analysis. Observed data are shown.

Results. Secukinumab data were pooled for both the 150mg and 75mg doses as there were no major differences in radiographic results between the doses. Mean (SD) mSASSS at baseline was 10.2±16.6; mean change from baseline at Week 104 was 0.30±2.53. Approximately 80% of patients showed no radiographic progression from baseline to Week 104 (Figure). New syndesmophytes were found in 5% patients who were without syndesmophytes at baseline. Approximately 70% of patients with syndesmophytes at baseline developed no additional syndesmophytes through Week 104. Overall, baseline mSASSS and mean mSASSS change at Week 104 were higher in males, those with baseline syndesmophytes, or elevated baseline CRP levels.

Conclusions. In secukinumab-treated patients, mean change in mSASSS was low, with no major difference between doses. Changes were higher in patients who were male, had baseline syndesmophytes, or elevated baseline CRP. No radiographic progression was observed in ~80% of patients receiving secukinumab over 104 weeks.

Reference

Disclosure of Interest:
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DA: Grant/research support from: Abbvie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Consultant for: Abbvie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer, UCB

DB: Grant/research support from: Abbvie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, Consultant for: Abbvie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer, UCB

SJ: Grant/research support from: Abbvie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB, Consultant for: Abbvie, Boehringer Ingelheim, Janssen, Novartis, Pfizer, Lilly, Pfizer, and UCB
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SECUKINUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS: COMPARATIVE EFFECTIVENESS RESULTS VERSUS ADALIMUMAB UP TO 48 WEEKS USING A MATCHING-ADJUSTED INDIRECT COMPARISON

McInnes I.B., Nash P., Mease P., Thom H., Hunger M., Gandhi K., Mpofu S., Jugl S.
1University of Glasgow, Glasgow, UK; 2University of Queensland, Brisbane, Australia; 3Swedish Medical Center and University of Washington, Seattle, WA, USA; 4University of Bristol, Bristol, UK; 5Mapi Group, Munich, Germany; 6Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; 7Novartis Pharma AG, Basel, Switzerland

Background. Matching-adjusted indirect comparison (MAIC) can assess relative efficacy in the absence of direct comparison or a continuous common placebo arm. MAIC adjusts for differences in patient characteristics at baseline, reducing the effective sample size (ESS) for the therapy arm in one trial, but matching this with the population of the therapy arm from another trial, simulating head-to-head comparison.

Objectives. To assess the relative efficacy of secukinumab (SEC) versus adalimumab (ADA) in adults with active psoriatic arthritis (PsA).

Methods. Patient-level data from the SEC arms of the FUTURE2 trial were weighted to match patient baseline characteristics for the ADA arm of ADEPT. Logistic regression was used to determine weights for age, sex, race, methotrexate-use, presence of psoriasis (≥3% body surface area), mean PASI score, dactylitis, enthesitis, mean HAQ-DI and previous biologic therapy. Sensitivity analysis included BASDI score adjustment. Weighted outcomes from MEASURE2 (ESS n=72) were re-weighted to match baseline characteristics of the ADA arm in ATLAS (n=208). Logistic regression was used to determine weights for age, sex, mean BASFI score, mean CRP level, and prior biologic use. Sensitivity analysis included BASDAI score adjustment. Weighted outcomes from MEASURE2 (ESS n=34) were compared with outcomes from ATLAS at weeks 12, 16, 24 and 52.

Results. SEC had higher mean ACR20/50/70 responses than ADA, with statistically significant higher responses at week 24 and higher, but non-significant responses at week 52 versus ADA. Sensitivity analysis supported these findings.

Conclusions. In this first MAIC in AS, symptomatic improvement measured by ASAS20/40 response was statistically significantly higher with SEC versus ADA at week 24. Potential limitations include differences in study designs such as early-escape criteria, disease duration, imputation methods and small ESS. Further research is suggested.
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SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE ANKYLOSING SPONDYLITIS: 2-YEAR RESULTS FROM A PHASE 3 TRIAL WITH SUBCUTANEOUS LOADING AND MAINTENANCE DOSE (MEASURE-2)


1NIHR Leeds Musculoskeletal Biomedical Research Unit, LHT and Institute of Rheumatology, Leeds University, Leeds, UK; 2Low Country Rheumatology, Articularis Healthcare, Charleston; 3University Clinic Benjamin Franklin, Berlin, Germany; 4Altoona Center for Clinical Research, Dunscaville, USA; 5Hospital Universitario Marqués de Valdecilla, Santander, Spain; 6McGill University, Division of Rheumatology, Montreal, Canada; 7Novartis Pharmaceuticals Corporation, East Hanover, USA; 8Novartis Pharma AG, Basel, Switzerland

Introduction. Secukinumab improved signs and symptoms of ankylosing spondylitis (AS) over 52 weeks in the MEASURE-2 study (NCT01649375). Here we report long-term efficacy and safety of secukinumab through 104 weeks.

Materials and Methods. 219 subjects with active AS were randomised to subcutaneous secukinumab 150mg, 75mg and placebo. Details of the study design have been published elsewhere.

Results. 60/72 (83.3%), 57/73 (78.1%) and 57/74 (77%) subjects completed 104 weeks of treatment with secukinumab 150mg, 75mg and placebo, respectively. Secukinumab 150mg significantly improved all endpoints at Week 16 versus placebo, except ASAS partial remission; 5mg dose did not achieve statistical significance (1). ASAS20/40 response rates at Week 104 were 71.5/47.5% with both secukinumab doses. Improvements in ISCRAP, ASAS50/66, BASDAI, SF-36 PCS and ASAS partial remission were sustained through Week 104 with secukinumab. In TNF-inhibitor-naive (TNFi-naive) subjects, ASAS20/40 response rates at Week 104 were 71.5/47.5% with both secukinumab doses. For ASAS remission rates, the difference between secukinumab 150mg and 75mg was 3.3/3.1% respectively. Corresponding rates in TNF-inhibitor-naive responder (IR) subjects were 85.0/50.0% and 68.8/43.8%. Exposure-adjusted incidence rates for serious infections/infestations, IBD, malignant/unspecified neoplasms and deaths were 0.8/0.5, 0.4/0.3 and 0.3/0.3 per subject-years, respectively. No cases of TB, opportunistic infections or suicidality-related adverse events were reported.

Conclusions. Secukinumab provided sustained improvement through 2-years in signs and symptoms of AS with improved physical function in both TNF-α-naive and TNF-α-IR patients. Safety profile was consistent with previous reports.

Reference


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REDUCTION IN SPINAL RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS PATIENTS RECEIVING PROLONGED TREATMENT WITH TNF INHIBITORS

Maas F.1, Arends S.1,2, Brouwer E.1, Essers L.1, van der Veer E.1, Eide M.3, van Ooijen P.M.A.1, Wolf R.1, Veeger N.J.G.M.1, Boetsma H.1, Wink F.R.2, Spoorenberg A.2,3,4,5

1Rheumatology and Clinical Immunology, UMC, Groningen; 2Rheumatology, MCL, Leeuwarden; 3Rheumatology, MUMC, Maastricht; 4Laboratory Medicine, UMC, Groningen; 5Radiology, UMC, Groningen

Objective. To evaluate the course of spinal radiographic progression up to 8 years of follow-up in a large cohort of AS patients treated with tumor necrosis factor-alpha (TNF-α) inhibitors.

Methods. Consecutive patients from the Groningen Leeuwarden AS (GLAS) cohort who started with TNF-α inhibitors between 2004-2012 were included. Baseline and biannual radiographs were randomized with radiographs of TNF-α naive AS patients and scored in chronological time order according to mSASSS. Generalized estimating equations with different time functions were used to investigate whether spinal radiographic progression followed a linear or non-linear course. The estimated mean 2-year progression rates were calculated based on the time model with the best fit. Primary analysis was performed in patients with complete data over 4, 6, and 8 years. Sensitivity analysis was performed after single linear imputation of missing radiographic data.

Results. 188 patients were included: 70% male, mean age 42±11 years, median symptom duration 14 (IQR: 7-23) years, and median mSASSS 2.5 (IQR: 0.0-11.9) during the first 4 years. During the first 4 years, spinal radiographic progression followed a linear course (mean mSASSS progression rate was 1.7 units for both 0-2 and 2-4 years). A deflection from a linear course was found in patients with complete and imputed data over 6 and 8 years of follow-up (mean mSASSS progression rate reduced from 2.5 units over 0-2 years to 0.8 units over 6-8 years). The non-linear time model remained statistically significant after adjustment for patient characteristics (e.g. baseline damage, gender). Primary and sensitivity analyses revealed the same results.

Conclusions. This large observational cohort study in AS patients receiving TNF-α inhibitors in daily clinical practice showed a reduction in spinal radiographic progression after more than 4 years of follow-up.

P150

ESPECIALLY ANKYLOSING SPONDYLITIS PATIENTS AT RISK OF POOR RADIOGRAPHIC OUTCOME SHOW DIMINISHED SPINAL RADIOGRAPHIC PROGRESSION DURING LONG-TERM TREATMENT WITH TNF INHIBITORS

Maas F.1, Arends S.1,2, Wink F.R.2, Boetsma H.1, Brouwer E.1, Spoorenberg A.1,2,3,4,5

1Rheumatology and Clinical Immunology, University Medical Center Groningen; 2Rheumatology, Medical Center Leeuwarden, The Netherlands

Introduction. In AS, spinal radiographic progression shows a very heterogeneous course. Our aim was to investigate which patient characteristics are of influence on the course of spinal radiographic progression in AS patients treated long-term with TNF-α inhibitors.

Methods. Consecutive patients from the Groningen Leeuwarden AS (GLAS) cohort who started TNF-α inhibitors, with baseline and biannual spinal radiographs until 6 years of follow-up were included.

Radiographs were scored using mSASSS by two independent readers. Generalized estimating equations (GEE) were used to explore the associations between baseline characteristics and radiographic data per time. The course of radiographic progression was investigated with different time functions (linear and non-linear), stratified for the significantly associated patient characteristics.

Primary analysis was performed in patients with complete radiographic data. Sensitivity analysis was performed after single linear imputation of missing radiographic data.

Results. 80 AS patients reached 6 years of follow-up (mean mSASSS 8.2±12.9) of which 53 patients had complete radiographic data at all 2-year time points. Baseline syndesmophytes, male gender, older age, longer disease duration, current smoking status, and higher BMI were significantly associated with more radiographic damage over time. Baseline syndesmophytes was the only independent risk factor. GEE analysis in patients with these characteristics revealed that mSASSS progression followed a non-linear course; mean mSASSS progression rate reduced from maximal 3.0 units over 0-2 years to minimal 1.2 units over 4-6 years. A linear course with low progression scores of approximately 1 mSASSS...
unit over the 2-year intervals was found in patients without risk factors. Sensitivity analysis revealed similar findings.

Conclusion. AS patients who are at risk of poor radiographic outcome showed the largest but diminishing spinal radiographic progression over time during long-term treatment with TNF-α inhibitors. Only little and linear progression was observed in patients without risk factors such as no syndesmophytes, no smoking and normal BMI.

P151

HOW ENTHESITIS AND DACTYLITIS IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS PATIENTS RESPOND TO ANTI-TNF TREATMENT?


Introduction/Aim. Enthesitis and dactylitis are common features of spondyloarthritis that may lead to a loss of functionality. This study’s aim was to determine their distribution and their response to anti-TNF treatment in a real-world registry.

Methods. This analysis included AS and PsA patients treated with infliximab or golimumab from BioTRAC, an ongoing, prospective registry of patients. The paired sample t-test and McNemar test were used to compare the enthesitis count, and the presence of dactylitis overtime, respectively.

Results. A total of 260 AS and 261 PsA patients were enrolled with a mean age at baseline of 46.1 ± 50.0 years, respectively. Enthesitis was present at baseline, 6-months, and 12-months among AS (28.1%, 21.7%, 22.4%) and PsA patients (32.2%, 19.9%, 22.6%). Dactylitis was reported at baseline and 6 months, respectively, in AS patients (6.2%, 2.2%), and a higher proportion in PsA patients (30.7%, 12.7%). At 6 months of treatment 69.0% of PsA patients with dactylitis at baseline had no dactylitis, 4.6% developed dactylitis. Presence of enthesitis in all anatomical sites, and dactylitis in hands or feet, was significantly associated with higher HAQ in AS and PsA patients. Treatment with IFX or GLM for 12 months was associated with higher HAQ in AS and PsA patients. Treatment with IFX or GLM for 12 months was associated with higher HAQ in AS and PsA patients.

Conclusion. Although a lower proportion of AS patients had dactylitis, both dactylitis and enthesitis were associated with higher functional disability in AS and PsA patients. Treatment with IFX or GLM for 12 months was associated with significant reduction in the mean enthesitis and dactylitis count.

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MINIMAL DISEASE ACTIVITY AMONG PSORIATIC ARTHRITIS PATIENTS IN A REAL-LIFE REGISTRY


Background. Minimal disease activity (MDA) is defined as the fulfillment of ≥5 of the following criteria: TJC28<4, SJC28<1, PASI16, pain (VAS) ≤15 mm, PGA (VAS) ≤20 mm, HAQ≤0.5, and tender entheses point ≤1. This analysis’ aim is to assess the contribution of each criterion in preventing the achievement of MDA at 6 and 12 months.

Methods. BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA. This analysis included PsA patients treated with infliximab or golimumab. Modified MDA (mMDA) was evaluated by removing patient-reported outcomes, one criterion at a time, and mMDA achievement was defined as patients who met ≥6 criteria.

Results. 223 PsA patients were included with a mean age of 49.8 years. MDA was achieved by 11.7%, 43.5%, and 44.8% at baseline; at 6 and 12 months of treatment, respectively. At 6 months of treatment the proportion of patients who achieved mMDA increased to 54.3% for pain removal, 52.2% for PGA removal, 50.7% for HAQ removal; while the removal of objective measures did not increase in substantial manner the percentage of patients achieving mMDA. At 12 months, the proportion of patients achieving mMDA upon removing HAQ was 58.1%, pain: 57.1%, PGA: 55.2%, TJC: 50.5%, SJC: 48.6%, PASI: 46.7%, and enthesitis was 45.7%. The highest proportion of mMDA achievement at 6 and 12 months of treatment was observed upon the removal of patient reported pain, PGA and HAQ.

Conclusion. The results of this analysis revealed that the most common limiting factors in achieving MDA are patient reported outcomes. Elimination of each of these criteria from the MDA formula would result in as many as 13% additional cases of MDA.

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DRUG SURVIVAL FOR ANTI-TNF TREATMENTS IN A UK COHORT OF AXIAL SPONDYLOARTHRITIDES PATIENTS

Yahya F., Cavill C., Berry-Jenkins J., Boyle C., Bond D., Sengupta, R., Royal National Hospital for Rheumatic Diseases, Bath, UK; University of Bath, Bath, UK

Introduction and Aim. The use of anti-TNF therapy has provided good outcomes for patients with axial spondyloarthritis (axSpA). However, these drugs are structurally different and have different mechanisms of action. As a result, a sub optimal treatment response or the development of side effects may result in the discontinuation of the treatment drug. The aim of this study was to analyse the drug survival of anti-TNF treatments used in axSpA patients based on a UK cohort.

Materials and Methods. A retrospective analysis of AxSpA patients who fulfilled ASAS Classification criteria, aged 18 years or above, receiving anti-TNF treatment at the Royal National Hospital for Rheumatic Diseases (RNHRD) Bath was undertaken. Data were collected from review of patients’ medical notes. The initial anti-TNF prescribed is described as the index biologic.

Results. Data from 261 patients, who had commenced an index biologic agent, were analysed. N=45 (17.2%) switched to a second biologic, and N=6 (13.3%) to a third biologic. The overall survival duration for index biologic (85.6 months, 95% CI: 75.6-95.6) was better than second-line biologic (50.8 months, 95% CI: 36.3-65.3) (p<0.05) (Figure 2). The longest mean drug survival was observed in Etanercept (75.6 months 95% CI: 64.7-86.5) and Adalimumab (74.9 months 95% CI: 64.9-85.0) (p=0.94) (Figure 3).

Discussion. Drug survival for index anti-TNF was significantly better than second-line treatments. No significant differences were found between Adalimumab and Etanercept, which were the 2 most frequently used anti-TNF drugs in this cohort.

Appendix:

Fig. 1. BASDAI response 6 months after starting anti-TNF.
**P154**

**IMPACT OF METHOTREXATE DOSE ON ADA LiMUMAB EFFICACY IN PSORIATIC ARTHRITIS: A SUBANALYSIS OF ADEPT**

Aletaha D.1, Li Y.2, Hojnik M.1, Ganz F.1

1Rheumatology, Medical University of Vienna, Vienna, Austria; 2Immunology, AbbVie Inc., North Chicago, IL, USA

**Aim.** To explore the efficacy of adalimumab (ADA) in combination with different MTX doses in PsA patients in ADEPT during the placebo (PBO)-controlled and open-label extension (OLE) periods.

**Methods.** This post-hoc analysis evaluated the dose-response relationship between clinical outcomes and MTX dosage in PsA patients. For this analysis, patients were grouped by MTX dose (no MTX; low-dose:<15mg/wk; medium-dose:15mg–20 mg/wk; high dose:>20mg/wk) either at baseline or start of OLE. Efficacy endpoints analyzed in as observed population were ACR20/50/70, PASI75, Minimal Disease Activity (MDA), and Disease Activity index for Psoriatic Arthritis (DAPSA) scores. The mean change from baseline in modified Total Sharp Score (mTSS) and HAQ-DI were also analyzed.

**Results.** Of 313 patients randomized in the ADEPT trial, 50% were receiving MTX at baseline (75 ADA, 81 PBO). At week 24, patients receiving ADA compared with PBO achieved numerically higher ACR20/50/70, PASI75, and MDA responses, irrespective of MTX dose. In addition, ADA-treated patients in all subgroups achieved greater inhibition of structural progression (mTSS) and improvement in DAPSA and HAQ-DI scores compared with the PBO subgroup. There was a tendency towards higher clinical response rates with higher doses of MTX, but the rates for ADA monotherapy were higher than the combination groups. At wk 144, patients who continued to receive ADA maintained their responses regardless of MTX dosage. Furthermore, during the OLE, MTX dosage did not significantly impact ACR or PASI response rates compared with ADA monotherapy. However, a trend towards greater inhibition of radiographic progression was observed with higher MTX doses.

**Conclusions.** ADA monotherapy was as effective as ADA in combination with different doses of MTX in reducing disease activity in PsA patients. There was numerically less long-term radiographic progression in patients initially treated with ADA in combination with high MTX dose. Further prospective controlled studies would help clarify the significance of this observation.

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**P155**

**DRUG SURVIVAL OF TNF-INHIBITORS THERAPY IN DIFFERENT KINDS OF JUVENILE SPONDYLOARTHRITIS: SINGLE CENTER EXPERIENCE**

Nikishina I.P., Kostareva O.M., Arsenyeva S.V., Kaleda M.I., Shapovalenko A.N., Nasonova V.A. Research Institute of Rheumatology, Moscow, Russian Federation

**Background.** Juvenile spondyloarthritids (JSpA) is a distinct part of juvenile arthritis group which includes 3 main conditions: juvenile onset of ankylosing spondylitis (JAS), enthesitis-related arthritis (ERA), juvenile psoriatic arthritis (JPsA). Biologics provided excellent progress in JSpA therapy for the last 15 years. Drug survival is a general marker of the treatment success as it depends on its efficiency and safety.

**Objective.** To compare drug survival of biologics depending on the subtype in JSpA patients (pts) in real clinical practice of single center.

**Method.** The study involved a prospective cohort of JSpA pts treated by different TNF-inhibitors in our clinic from 2004 to 2016. Analyze included drug survival with Kaplan-Meier, reasons of withdrawals and adverse event (AE) rates.

**Results.** 177 JSpA pts, treated with one or more biologics were analyzed. At the start of biologics pts average age was 13.19 years (range 3.5-17.9), mean disease duration was 50.4 months (range 2-240), JSpA subtypes were as follows: ERA - 106(60%), JAS - 48(26%), JPsA - 23(13 %). 149(83%) were HLA-B27positive. 24(13,4%) had uveitis. In total, 205 treatment series, including 79 for etanercept (183 patient-years PY), 73-adalimumab (160 PY), 53-infliximab (182 PY) were evaluated.

There were 62 cases of withdrawals. Reasons for withdrawals were AE in 7.32% (95%CI 4.9-11.72), inefficacy ≤0.73% (95%CI 1.7-15.71), others – 11.71% (95% CI 8-16.83), basically due to organizational difficulties of biologics access in adult life. AE were developed after at mean 1.63 years (range 0.74-3.36). AE were included: etanercept – 3 cases of uveitis de novo (1.62 per 100 PY); infliximab – 6 infusion reactions (3.3 per 100 PY), 1 psoriasis de novo, 1 severe skin disorder, 1 toxic hepatitis, 2 tuberculosis; adalimumab – 2 psoriasis de novo, 1 tuberculosis. AE as a reason of Infliximab withdrawal was observed more often than under adalimumab or etanercept (18.9% vs 2.74% and 3.8% respectively, p<0.05). Long-term drug survival of TNF-inhibitors was 78% for ERA, 64% for JAS and 57% for JPsA. Drug survival for etanercept were 95% and 35% after 1 and 5 years, infliximab – 90% and 38%, adalimumab – 97% and 32%, respectively.

**Conclusions.** Drug survival of TNF-inhibitors in JSpA pts seemed to be better for etanercept, especially in ERA subtype. Infliximab mostly withdrawn due to AE and inefficacy, but adalimumab cancelled more often because of organizational reasons, especially in adult life.
INFLUENCE OF SULFASALAZINE COMEDICATION IN SWITCHING AND RESPONSE TO ANTI-TUMORAL NECROSIS FACTOR IN ANKYLOSING SPONDYLODYSPLASIA


Aim. Recently, comedication with methotrexate or use of any DMARD (except sulfasalazine) was associated to better anti-TNF retention in spondyloarthritis (SpA). However, data on the possible occurrence of co-therapy for clinical response and remission was not provided. The aim of this study was to determine in a long-term follow-up the influence of comedication in ankylosing spondylitis (AS) patients with peripheral or pure axial involvement on anti-TNF switching, clinical response and remission.

Patients and Methods. Data from an ongoing longitudinal electronic database of patients with active anti-TNF therapy between June 2004 and August 2013 were assessed. Demographic and clinical parameters, disease activity and treatment responses by Ankylosing Spondylitis Disease Activity Score (ASDAS) remission (<1.3) and inactive/moderate (<2.1) were analyzed to characterize the switch of TNF inhibitors.

Results. Among 117 AS patients treated with anti-TNF, 69 patients (55%) were prescribed only one anti-TNF, 48 (41%) switched to another anti-TNF (58% failure and 42% side effects) and 13 (11%) to third anti-TNF (60% failure and 40% side effects). At the final assessment, 42 patients still under the first anti-TNF (non-switcher group) achieved lower levels of ASDAS (1.5±0.7 vs. 2.0±1.0, p<0.05) and BASFI index before surgery - 5,48±2,39, 6 months - 2,78±2,31, 1 year - 2,32±1,60 points. No complications after surgery were recorded.

Conclusion. Hip endoprosthesis joints in patients with SpA is effective not only in improving functional ability and pain relief, but also a reduction of disease activity. Dynamic rheumatologist observation in perioperative period leads to positive dynamics in relation to the activity of SpA and quality of life of patients during the first year after surgery.
Results. We noted a highly significant reduction of the secretion of IL-1ra, IL-1β, and MIP-1β in response to selected stimuli after treatment with TNF-blockers. We also tested whether there is a correlation between the responses of immune cells to specific stimuli and the clinical response to TNF-blockers. We found that axSpA patients who secreted the highest levels of inflammatory cytokines and chemokines in response to specific immune stimuli before initiation of anti-TNF therapy had the best therapeutic responses.

Conclusions. Our results show that anti-TNF therapy induces specific changes in immune responses to selected stimuli. Our data also indicate that analyzing immune responses in patients before therapy is a promising strategy to develop biomarkers predicting therapeutic efficacy of TNF-blockers.

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SIGNIFICANTLY REDUCED RECURRENCE RATE OF ACUTE ANTERIOR UVEITIS IN ANKYLOSING SPONDYLITIS DURING TREATMENT WITH GOLIMUMAB

Heslinga S.C.1, Nurmoohamed M.T.1, Gerards A.2, Griep E.N.3, Koehler C.4, Kok M.R.5, Schlieder A.6, Verhoef M.1, Van der Horst-Bruinsma I.E.1

1Amsterdam Rheumatology and Immunology Center, Amsterdam; 2Vlieland Hospital, Schiedam; 3Antonius Hospital, Sneek; 4Gele Hospital, Apeldoorn; 5Maassstad Hospital, Rotterdam; 6Medical Centre Leeuwarden, Leeuwarden; 7MSD The Netherlands, Haarlem, The Netherlands

Background. Acute anterior uveitis (AAU) is common in ankylosing spondylitis (AS). Golimumab, a tumor necrosis factor alpha (TNF-α) blocker, has proven to be effective in the treatment of AS. At present, the effect of golimumab on the recurrence rate of AAU in AS is unknown.

Objectives. To investigate the effect of golimumab treatment on the recurrence rate of AAU attacks in AS patients.

Methods. Consecutive AS patients were enrolled. All patients were treated with golimumab 50mg once a month for 12 months. During treatment, all occurring AAU attacks were assessed. The historic presence of AAU attacks was assessed from the year before baseline for non-biologically treated patients, or the year before the first treatment with a TNF-α blocker in case of a switch from another TNF-α blocker to golimumab.

Results. In total, 93 patients (65% male) were evaluable, with a mean age of 44±13 years and a median disease duration of 7 (0-53) years. Six patients (7%) had a prior history of AAU with a total of nine attacks in the year prior to the first TNF-α blocker use (9.8/100 patient years). During golimumab treatment, the rate of recurring AAU attacks was reduced to two new attacks (2.2/100 patient years), a significant reduction of 78% (p<0.001). These two AAU attacks occurred in two separate patients, of whom one had no history of AAU.

Conclusion. Treatment of AS patients with golimumab leads to a significant decrease in disease activity. Simultaneously, the rate of recurring AAU attacks decreased significantly during golimumab treatment.

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P161
SMOKING RELATED WITH DISEASE RESPONSE AND AGE AT DIAGNOSIS IN ANKYLOSING SPONDYLITIS

Rusman T.1, Nurmoohamed M.T.1-2, Visman I.1, van der Horst-Bruinsma I.E.1

1Amsterdam Rheumatology Immunology Center, Dept. of Rheumatology VU University Medical Center
2Amsterdam, The Netherlands

Introduction/Aim. Limited data are available on the influence of smoking, Body Mass Index (BMI), alcohol consumption and physical activity on disease activity and response to TNF inhibitors in ankylosing spondylitis (AS). This study aims to determine whether these factors influence age at diagnosis, disease activity and response to TNF inhibitors.

Patients and Methods. Consecutive AS patients (fulfilling the modified New York criteria) who started or switched TNF treatment were included in a prospective, observational cohort. Data on disease activity Ankylosing Spondylitis Disease Activity Score (ASDAS)) were collected at baseline, 6, 12 and 24 months after start of treatment. Lifestyle factors, with a p<0.005 in relation to age at diagnosis and ASDAS were subsequently entered in the overall regression model.

Results. In total 312 AS patients were included with a mean follow-up of 18.9 months (6-24). The majority 172 (55%) improved on TNF treatment whereof, 86 patients (27.7%) showed a clinical important improvement (decrease in ASDAS >1.1) and 86 (27.7%) a major clinical improvement (decrease in ASDAS >2.2). In multivariate analysis, age at diagnosis was negatively influenced by a positive smoking status, being physical active and having a normal BMI (Figure 1). No risk factors were related to the change in ASDAS during treatment. No relation between alcohol consumption and disease onset or treatment response was found.

Conclusion. Smoking, being physical activity and normal BMI were associated with an earlier age at diagnosis. A significant improvement of the ASDAS at both 1 and 2-year follow-up under TNF treatment was found, confirming the efficacy of TNF inhibitors in a real life cohort. However, contrary to the expectations no relations were found between lifestyle factors and disease activity.

Figure 1. Lifestyle related factors influencing the age at diagnosis in AS patients.
Development of Recommendations on the Content, Organisation and Positioning of Exercise Therapy for Axial Spondyloarthritis in the Netherlands

van Weelij S.F.E.¹, van der Giesen F.J.¹, Kat Y.¹, de Jong S.², Vliet Vlieland T.P.M.¹
¹Leiden University Medical Center, Leiden; ²Dutch Arthritis Foundation, Amsterdam, The Netherlands

Introduction. In national and international recommendations, exercise therapy is advised for optimal treatment of axial-SpA. However, there is no consensus on the practical implementation of these general recommendations. Research in the Leiden region showed large variation in treatment of axial-SpA patients. This has adverse effect on the quality of exercise therapy interventions for these patients. Consensus on the practical implementation could improve this by giving direction on indicators, content and therapeutical practices.

Aim. Development of recommendations on the content, organisation and positioning of exercise therapy for axial-SpA.

Methods. 1. A survey of literature and formulation of draft clinically relevant questions;
2. First expert-group meeting to determine definite questions. This group consists of a representation of patients, rheumatologists, physical and exercise therapists, policy makers, scientists and special interest groups.
3. Perform additional literature review to answer questions and formulate draft recommendations.
4. Second expert-group meeting to evaluate concept recommendations and determine level of evidence.
5. Field of consultation in which the level of support is determined through a Delphi method.
6. Final consensus statement with recommendations

Results. Early May, the first meeting with 24 experts took place in which 18 clinical relevant questions were discussed, concerning targets for treatment and a framework for the therapeutic process for exercise treatment (indication, referral, assessment, analyses, treatment-plan, intervention and evaluation).

Conclusions. The first meeting has led to a clear starting point for the additional literature research and draft recommendations. The implementation of the final recommendations, in the form of directives is explored, with the ultimate aim of improving the quality of care for axial-SpA patients.

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