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Abstracts

Invited Lectures

INV2

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

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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 decisive factor that triggers the clinical onset of inflammatory 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.

INV3

IL-17 AS A TRIGGER FOR ARTHRITIS AND JOINT DESTRUCTION

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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-17A is a T cells cytokine and is produced by the newly identified T 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.

INV6

IS THE T2T CONCEPT APPLICABLE TO SPA?

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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 (eg 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 the target 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.

INV8

CAN FIBROMYALGIA BE AN OBSTACLE FOR T2T?

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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 ankylosing 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). CS is characterized by dysregulation of nociceptive and anti-nociceptive neuropeptide function and neural signaling, evidenced by advanced neuroimaging, quantitative sensory testing, and CS-discriminatory patient reported outcome measures (PROs) (1, 2, 3). Concomitant FM (CSS) alters rheumatologic disease presentation, natural history, assessment and treatment outcomes including, potentially, 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 treat-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 enthesitis, and display worse disease activity measures than SpA patients without FM, including BASDAI, BASFI, ASQoL, 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.
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INV10

PATHOPHYSIOLOGY AND TREATMENT OF PSORIASIS

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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

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Introduction. Uveitis is the most common, clinically apparent extra-articular manifestation of spondyloarthritis.
Methods. Literature review and studies in HLA B27/beta$_2$ 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 intestinal microbiome in B27+ Fischer rats. We now report that this model is characterized by a marked increase in IgA coating of specific intestinal bacteria including segmented filamentous bacteria (SFB) and a translocation of gut bacteria to the joint.
Discussion. B27 expression potentiates exaggerated immune responses to SFB and other microbiota. We propose that this dysbiosis results in enhanced bowel permeability and bacterial translocation that contributes to both uveitis and arthritis.
Conclusions. Uveitis is a major clinical manifestation of spondyloarthritis and it is potentially an important clue to pathogenesis.

INV18

THE PATHOGENETIC ROLE OF THE HLA-B27 PEPTIDOME

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Introduction. The joint association of HLA-B*27 and the endoplasmic reticulum aminopeptidases ERAP1 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 ERAP1 variants with high enzymatic activity and ERAP2 expression predispose to AS. Thus, our study addressed the influence of natural ERAP1 polymorphism and ERAP2 expression on shaping HLA-B*27-bound peptidomes.
Methods. HLA-B*27 ligands were isolated from human lymphoid cell lines with distinct ERAP1/ERAP2 backgrounds by affinity chromatography and acid extraction. ERAP1 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-terminal residues to ERAP1 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) ERAP1 polymorphisms associated with increased risk to AS shaped an optimized HLA-B*27 peptidome with increased abundance of nonamers, peptides with ERAP1-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 ERAP1-resistant N-terminal residues compared to peptides found only among non-AS-associated subtypes, 3) ERAP2 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 ERAP1 and ERAP2 have significant effects on the HLA-B*27 peptidome, affecting the expression levels of many natural ligands. The mechanism of ERAP1/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 ERAP1 variant. This leads to an optimized, higher affinity, peptidome in AS-predisposing ERAP1 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 ERAP1 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 ERAP1 activity.
Conclusions. The significant influence of ERAP1 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-B27 folding, stability and NK recognition, may be affected by global alterations in the peptidome.

INV19

THE ROLE OF ERAP1 IN SPONDYLOARTHRITIS IN HLA-B27 TRANSGENIC RATS

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Introduction/Aim. Common variants of the HLA class I B gene (predominantly *HLA-B*27*) predispose to spondyloarthritis, 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-β_2-microglobulin (β_2m) complexes. Common variants of *ERAP1* 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 epistasis. In spondyloarthritis, there are conflicting data on how gain/loss-of-function of *ERAP1* 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 *ERAP1* loss-of-function on the development of spondyloarthritis using HLA-B27/human β_2m transgenic (B27-Tg) rats.

Materials/Methods. Genome editing in fertilized embryos was used to delete 29 nucleotides in the first exon of *ERAP1* (*ERAP1*^{del29}) resulting in a frame shift, premature stop codons, and complete loss of ERAP1 protein expression in cells from *ERAP1*$^{del29/del29}$ animals, with approximately 50% expression in ERAP1 $^{+/del29}$ cells. We generated cohorts of ERAP1$^{+/+}$, ERAP1$^{+/del29}$, and ERAP1$^{del29/del29}$ rats expressing HLA-B27/hβ_2m, HLA-B7/hβ_2m 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$^{+/+}$ or ERAP1$^{+/del29}$ genotypes developed arthritis with a frequency of 32% (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*$^{del29/del29}$ 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*$^{del29/del29}$ rats compared with B27-Tg *ERAP1*$^{+/del29}$ or B27-Tg *ERAP1*$^{+/del29}$ rats. Twelve percent (2/17) of B27-Tg *ERAP1*$^{+/del29}$ females developed arthritis (average arthritis score 0.75), while B27-Tg *ERAP1*$^{+/del29}$ and B27-Tg *ERAP1*$^{del29/del29}$ females remained healthy. Persistent arthritis was not seen in 49 B7-Tg and 48 WT rats of various *ERAP1* 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*$^{del29/del29}$ (7.0) compared to *ERAP1*$^{+/+}$ (5.0) (p<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?

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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*4001, ERAP1, IL-23R) are typically not as strong a risk factor as HLA-B27. Nevertheless, as genetic interaction has been reported between HLA-B27 and other genetic risk factors, combining genetic risk factor testing may improve identification of patients with a high risk of developing axSpA (1, 2).
At the current meeting we will present the first data on the ability of a combined test of HLA-B27/HLA-B*4001 to identify ankylosing spondylitis in two major inception cohorts of patients with recent onset chronic back pain (3). This project is a part of a larger project to study the use of genetic testing in early axSpA.
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INV24

MECHANICS AND STRUCTURAL REMODELING OF THE ENTHESES

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Spondyloarthritis is a chronic disease of the axial skeleton and the peripheral joints. The affected sites are part of the skeleton, the organ that is essential to our existence as it provides a structural framework and support to the body. The peripheral joints and the spine are sites of important biomechanical stress in daily life. Although the driving force behind signs and symptoms in spondyloarthritis is inflammation, biomechanical factors will also contribute. Biomechanical factors likely contribute to signs and symptoms of disease, in particular when a holistic view on the patient is considered. In this era of molecular medicine, the impact of biomechanical stress is sometimes neglected but remains an essential part of the patient burden.
The enthesis, the anatomical site in which tendons, ligaments and capsules insert onto the underlying bone is consider a primary disease location in spondyloarthritis. As a transition tissue with multiple layers conveying its specific strength and resistance, it experiences important biomechanical stress. Biomechanically induced tissue damage has been proposed as trigger for development of inflammation in both axial and peripheral entheses. In the long term, structural damage associated with the disease is also linked to enthesitis as well as osteitis. We hypothesize that, in particular in the spine, inflammation leads to loss of stability mainly due to loss of bone quality and density. New bone formation originating from the entheses is a hallmark of the disease and requires further research.

INV25

NEW MECHANISMS OF BONE REGENERATION

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Inflammatory bone disease results in bone destruction as a result of both enhanced destruction of bone and diminished new bone synthesis. Many inflammatory mediators stimulate osteoclastogenesis and inhibit osteoblast differentiation and matrix production. Methotrexate, the gold standard in the treatment of Rheumatoid Arthritis and other rheumatic diseases, mediates many of its anti-inflammatory effects by increasing local adenosine concentrations at sites of inflammation. Adenosine, acting at its receptors (A1R, A2AR, A2BR and A3R), has a variety of effects on both osteoclasts and osteoblasts. Osteoclast differentiation depends, in part on A1R function whereas A2AR and A2BR stimulation inhibits osteoclast differentiation. In contrast, A2AR and A2BR stimulation promotes osteoblast 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 adenosinergic therapy in the treatment and prevention of inflammatory bone and joint disease.

Oral Presentations

O1

ANTI-IL-17A TREATMENT BLOCKS INFLAMMATION, DESTRUCTION AND NEW BONE FORMATION IN EXPERIMENTAL SPONDYLOARTHRITIS IN HLA-B27 TRANSGENIC RATS

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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-IL17A 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*/IFA 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 83% 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

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

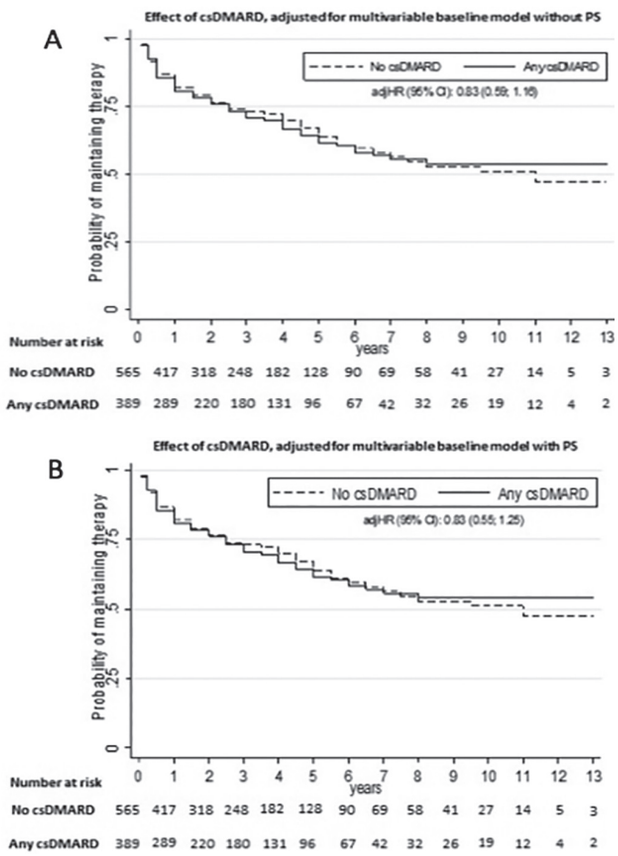

Figure: Drug survival for the first TNFi comparing csDMARD users to non-csDMARD users without PS (A) and with PS-adjustment (B).

O3

DEREGULATED EXPRESSION OF MIRNAS IN PURIFIED DISEASE RELEVANT BLOOD CELL POPULATIONS IN PATIENTS WITH SPONDYLOARTHRITIS

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Background. MiRNAs are thought to regulate over 30% of the total number of human genes. Deregulated miRNA expression has been found in different inflammatory and autoimmune diseases and may have anti- or pro-inflammatory activities based on their specific target mRNAs. Altered miRNA expression has been detected in several inflammatory diseases such as inflammatory bowel disease (IBD) and psoriasis. Although a few studies concerning correlation between Spondyloarthritis (SpA) and miRNA have been published, no systematic studies in specific cell populations have been reported so far.
Objective. As recently published, computational analysis (1) showed a large overlap of active gene regulatory regions with genetic variation associated with SpA for CD4 T cells and CD14 monocytes, we analyzed the miRNA expression pattern in these two purified cell types.
Methods. SpA patients were monocentrically recruited between October 2014 and May 2015 in the department of rheumatology. All included SpA patients fulfilled the ASAS classification criteria with objective signs of inflammation on

MRI and/or CRP for all but one patient. We first analyzed the expression of 360 MiRNAs in cell-sorted (MACS) monocytes and CD4 T-lymphocyte populations from 24 SpA patients and 16 age and sex-matched controls by qPCR using the Exiqon MicroRNA Ready-to-Use Human Panel I on the miRNA-enriched fraction from both CD4+ and CD14+ cell populations.
Results. In CD4 cells 6 miRNAs were found to be differentially expressed including miR-491-3p recently reported to be downregulated in ulcerative colitis and miRNA-26a, a well know inflammation associated miRNA implicated in both allergic inflammation and autoimmune diseases. In monocytes 25 miRNAs were found to be differentially expressed including the paradigmatic anti-inflammatory miRNA mir146a and as the most significantly expressed miRNA, a miRNA involved in the degradation of TNF-α.
Conclusions. The study is the first to analyze miRNA expression in purified disease-relevant blood cell populations in SpA bringing into evidence a number of interesting miRNAs whose deregulation might contribute to the pathogenesis of the disease. Integration with RNA expression data will allow the functional impact of the miRNA expression changes patterns in the blood cell populations allowing to better understand the molecular changes in SpA and potentially identify novel targets for therapeutic intervention.
Acknowledgement. This work was funded by a SIRIUS Research Grant from UCB Pharmaceuticals S.A.
Reference
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O4

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

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Objective. To evaluate the efficacy of golimumab in patients with active peripheral Spondyloarthritis (pSpA) in a very early stage of the disease.
Methods. CRESPA (Clinical REmission in peripheral SPondyloArthritis) is an ongoing monocentric study of golimumab treatment in pSpA patients. Eligible patients were ≥18 years and fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for pSpA. All patients had a symptom duration of less than 3 months. Patients were randomized 2:1 to receive golimumab 50 mg every 4 weeks or matching 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. From week 12 onwards, there was an option to start rescue medication with golimumab 50 mg SC every 4 weeks.
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 (70% (28/40) versus 15% (3/20); $p<0.001$). Overall, improvement in other outcomes were significantly greater in the golimumab group compared to the placebo group (Table I). 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.

Table 1. Disease activity and response criteria at baseline, week 12 and week 24.

	Baseline			Week 12			Week 24		
	Golimumab (n=40)	Placebo (n=20)	p-value	Golimumab (n=40)	Placebo (n=20)	p-value	Golimumab (n=40)	Placebo (n=20)	p-value
Clinical Remission	NA	NA	NA	28 (70%)	3 (15%)	<0.001	30 (75%)	4 (20%)	<0.001
Individual components of pSpARC Criteria									
pSpARC 40%, n (%)	NA	NA	NA	23 (57.5%)	4 (20%)	0.0069	20 (50%)	3 (15%)	0.0112
pSpARC 50%, n (%)	NA	NA	NA	22 (55%)	4 (20%	0.0132	22 (55%)	3 (15%)	0.0048
pSpARC 70%, n (%)	NA	NA	NA	20 (50%)	3 (15%)	0.0112	16 (40%)	3 (15%)	0.0768
TJC, n (%)	5.0 (3.0, 8.0)	4.0 (2.0, 9.5)	0.7643	0.0 (0.0, 2.5)	4.5 (1.0, 11)	0.0012	0.0 (0.0, 2.0)	5.0 (1.0, 7.5)	0.0004
SJC, n (%)	4.0 (2.5, 5.0)	3.0 (2.0, 5.5)	0.3883	0.0 (0.0, 0.5)	2.5 (0.5, 7.0)	0.0002	0.0 (0.0, 1.0)	1.5 (0.0, 6.0)	0.0009
Percentage of patients with enthesitis n (%)	16 (40%)	9 (45%)	0.78	6 (15%)	5 (25%)	0.48	7 (17.5%)	16 (80%)	<.0001
Percentage of patients with dactylitis, n (%)	15 (37.5%)	9 (45%)	0.59	3 (7.5%)	8 (40%)	0.004	7 (17.5%)	12 (60%)	0.0025
Patient Global Pain (0-100mm VAS)	5.5 (4.0, 7.0)	6.5 (4.5, 8.0)	0.20	1.5 (1.0, 4.0)	6.0 (3.0, 7.0)	0.0009	2.0 (0.0 4.0)	6.0 (3.0, 7.0)	0.0006
Patient Global Disease Activity (0-100mm VAS)	7.0 (5.0, 8.0)	8.0 (4.5, 9.0)	0.51	2.0 (1.0, 5.0)	6.0 (4.0, 7.0)	0.0015	1.0 (0.0, 3.0)	6.5 (4.0, 8.0)	0.0008
ESR, mm/h	21.5 (8.5, 41.5)	28.0 (11.0, 60.0)	0.45	3.0 (2.0, 6.0)	17.5 (4.0, 31.0)	0.0016	3.0 (2.0, 8.0)	8.5 (4.0, 21.0)	0.0244
CRP, mg/L	8.8 (3.0, 33.8)	16.8 (4.8, 48.7)	0.35	1.1 (0.6, 2.1)	7.2 (1.7, 20.3)	0.0005	1.0 (0.6, 2.3)	6.5 (1.5, 18.5)	0.0030

Descriptive statistics: Median (p25, p75) for continuous variables, percentages for categorical variables. *Except where indicated otherwise, values are the number (%) of patients. pSpARC 40%,50%,70% peripheral SpondyloArthritis 40%, 50% and 70% Remission Criteria; TJC tender joint count; SJC swollen joint count; ESR erythrocyte sedimentation rate, CRP C-reactive proteine, VAS visual analog scale.

O5

KILLER IMMUNOGLOBULIN-LIKE RECEPTORS ARE ASSOCIATED WITH ANKYLOSING SPONDYLITIS

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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 or infectious diseases by shifting activation thresholds of cytotoxic NK cells. We aimed to interrogate patterns in, and statistical interactions between, *KIR* genes and *HLA* alleles in a large population of individuals with ankylosing spondylitis (AS).
Methods. Gene dosages across *KIR* loci were imputed from Immunochip genotype data for 10464 AS cases and 15239 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 *($p=2x10^{-5}$)* 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

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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 SIJs of AS patients have not been performed to date.
Methods. Complete sets of MRI, CT and CR of SIJs of 69 AS patients and 49 age- and gender-matched controls were analyzed. Two blinded readers evaluated the images independently.
Assessment of lesions was performed based on SIJ-quadrants (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 CR/CT, 100 SQ by CT/MRI and 70 SQ by CR/MRI, with 48.9% of SQ detected by CR also seen on CT and 45.4% detected on CT also seen by CR. The corresponding numbers for CT/MRI were 70.9% and 59.9% and for CR/MRI 53.5% and 41.9%, respectively. Disagreement for erosions was found in 144 (26.1%), 108 (19.6%) and 158 (28.6%) SQ, respectively.
Sclerosis was seen in 86 SQ on CR (15.6%), 91 SQ on CT (16.5%) and 63 on T1-MRI (11.4%) and a*nkylosis* was seen in 91 SQ pairs on CR (33,3%), 130 SQ pairs on CT (47,1%) and 106 SQ pairs on MRI (38,4%), with similar agreement and disagreement rates.
In controls, 392 SQ were analyzed. Erosions were found in only 19 (4.8%) SQ and sclerosis in 23 (5.9%) SQ, while no patient showed ankylosis.

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?

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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 (Fig. 1). MRI-SIJ+ at follow-up was seen in 28/168 (16.7%) patients, 14 of which were also positive at baseline; MRI-spine+ was identified in 2/28 (7.1%) and 1/28 (3.6%) patients for the ASAS definition defined by ≥3 and ≥5 inflammatory lesions, respectively. In total, 4 patients had MRI-spine+ and MRI-SIJ-: 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 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.

BASELINE

		MRI of the SI joints		
		Positive	Negative	
MRI of the Spine, cut-off ≥3 inflammatory lesions	Positive	7	2	9
	Negative	36	284	320
	Total	43	286	329

		MRI of the SI joints		
		Positive	Negative	
MRI of the Spine, cut-off ≥5 inflammatory lesions	Positive	2	1	3
	Negative	41	285	326
	Total	43	286	329

FOLLOW-UP

		MRI of the SI joints		
		Positive	Negative	
MRI of the Spine, cut-off ≥3 inflammatory lesions	Positive	2	2	4
	Negative	26	138	164
	Total	28	140	168

		MRI of the SI joints		
		Positive	Negative	
MRI of the Spine, cut-off ≥5 inflammatory lesions	Positive	1	0	1
	Negative	27	140	167
	Total	28	140	168

Fig. 1. Prevalence of positive MRI-ASI 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 definirtion) and ≥5 inflammatory lesions, respectively.

08

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

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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.
Results. 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-17A+ 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±76 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*.

O9

HIGH DOSE NSAIDs AND TUMOR NECROSIS FACTOR INHIBITOR USE SYNERGIZE TOWARDS LESS RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS -– A LONGITUDINAL ANALYSIS

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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 use. The objective of this study was to explore the effect of, and relationship between, both NSAIDs 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, 38%, 29% and 23% had an NSAID index of 0, >0 & ≤50, and >50 respectively. Multivariable results showed an interaction effect for those using 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=0.17, 95%CI 0.05, 0.55, p=0.003).
Conclusion. There is less radiographic progression in AS patients taking higher doses of NSAIDs regularly and using TNFi via effect modification.

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

Variable	Adj. Odds Ratio (95% CI)	p-value
TNFi use * NSAID use interaction effect		0. 034
TNFi use vs. no for NSAID index>50 (high)	0.17 (0.05, 0.55)	0.003
TNFi use vs. no for 0< NSAID index<=50 (low)	0.89 (0.32, 2.51)	0.828
TNFi use vs. no for NSAID no use	0.94 (0.38, 2.33)	0.887
mSASSS baseline ≥4	7.00 (3.68, 13.3)	<.0001
Disease duration>10years	2.65 (1.41, 4.96)	0.003
Male gender	2.26 (1.14, 4.47)	0.019
White race	1.04 (0.50, 2.16)	0.918
Education > college	0.90 (0.39, 2.07)	0.795
current smoking	2.16 (1.01, 4.66)	0.048
# comorbidity≥1	0.72 (0.38, 1.39)	0.330
BASDAI ≥40	0.84 (0.48, 1.47)	0.531
CRP abnormal	1.18 (0.66, 2.10)	0.582
Baseline TNFi use	1.31 (0.67, 2.52)	0.426

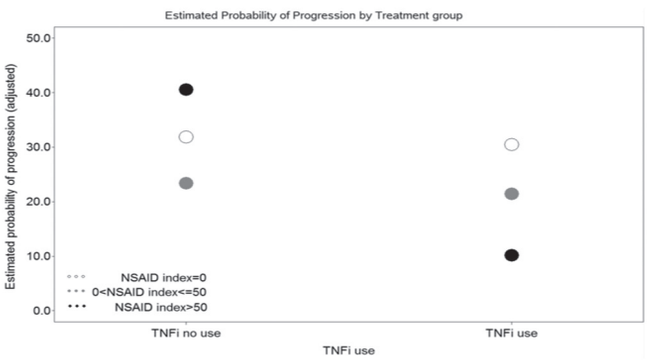

Fig. 1. Estimated probability of progression based on NSAID index and TNFi use.

O10

HLA-B27 HAS MAJOR EFFECTS ON THE INTESTINAL MICROBIOME

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Introduction. Evidence for a discrete intestinal microbiome signature in the terminal ileum (TI) of ankylosing spondylitis (AS) patients, compared to healthy controls, has recently been described. It has been hypothesised that HLA-B27 induces AS by effects on the intestinal microbiome, in turn driving spondyloarthritis by inducing immunological processes, particularly IL-23 production. Here we examine the effect of HLA-B27 on the composition of the intestinal microbiome in healthy individuals using culture independent, 16S rRNA amplicon sequencing.
Methods. 135 intestinal samples from 6 body sites were collected from otherwise healthy persons undergoing routine colorectal screening (age 40-75yrs). All patients were HLA-B typed and biopsies sequenced for the bacterial marker gene 16S rRNA. Sequences were quality controlled, filtered and the distribution of bacteria across the different samples and tissue types was established. Further analysis was conducted using multivariate analysis package MixMC as implemented in R.
Results. 16S sequencing revealed that HLA-B27 genotype (n=10 HLA-B27+ and 85 HLA-B27- samples) influences overall microbial composition with increases in bacterial families *Ruminococcaceae* and *Lachnospiraceae* in the HLA-B27+ samples. Multivariate regression analysis of all samples illustrated distinct clustering of HLA-B27+ from HLA-B27- samples (p=0.0063; PERMANOVA). The TI also showed clear and distinct clustering of HLA-B27+ from HLA-B27- samples driven by a decrease in *Veillonellaceae* (p<0.001) and Clostridiales (p<0.05) and increases in *Bacteroidaceae* (p<0.05) and *Ruminococcaceae* (p<0.05). This is consistent with the microbial signature described in AS cases.
Conclusion. This study shows that healthy HLA-B27+ individuals exhibit shared microbiota changes with AS, indicating a disrupted microbiota may be a primary event in AS pathogenesis rather than secondary to disease or its treatment. These findings support the hypothesis that HLA-B27 operates to cause AS through interaction with the intestinal microbiome, and suggests that therapies targeting the microbiome may be effective in AS prevention and/or treatment.

O11

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

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Background. Recurrent acute anterior uveitis (rAAU) is associated with spondyloarthritis (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 T1W/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 SPARCC/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=6) 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 48% 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 rAUU 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*

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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^{-4}). 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 rs7761118, an intronic SNP of *MAPK14*, and SpA (p=3.5x10^{-7}). Such association appeared to be independent of HLA-B27.
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.

Poster Presentations

P1

ASDAS-BASED REMISSION WAS LESS FREQUENT THAN BASDAI-BASED REMISSION, AND BOTH WERE RELATED TO CRP AND SMOKING IN EARLY AXIAL SPONDYLOARTHRITIS – THE DESIR COHORT

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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 at 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 using 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 uni 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 classified 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, enthesitis, uveitis, IBD, NSAID use, mSASSS. 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 PFIZER France.
Reference
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Table I. Results of multivariate analysis; r: regression coefficient, **p*<0.05; ***p*<0.001; ****p*<0.0001

Remission	ASDAS-R ASDAS <1.3	r,p	BASDAI-R BASDAI <3.6	r,p
M0 N=706	CRP	-0.59***	ESR	-0.04*
	Smoking	-1.5**	Smoking	-0.93*
	Analgesics	1.55***	Analgesics	1.39**
M24 N=577	CRP	-0.6***	BMI	-0.14**
	Smoking	-1.08*	Smoking	-1.16**
	ASDAS clinical	1.76*	ASAS clinical	1.28*
	NSAIDs	-1.4**		
	Analgesics	-2.02***	Analgesics	-1.74***

P2

EVOLUTION OVER THIRTY YEARS OF THE PROFILE OF IN-PATIENTS WITH REACTIVE ARTHRITIS IN A TERTIARY RHEUMATOLOGY UNIT

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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 clinico-biological 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 or 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.

	1984 - 1993	2004 - 2013	p
Number of patients included	15	31	0.4
Number of patients hospitalized	7438	11 823	
Men	13	28	0.6
Median age at diagnosis	37	30	0.9
HLA B27 + (%)	91	63	01
Delay between infection/articular symptoms (days) median	5.5	9	0.6
Leucocytes (giga/l)	9,8	10,6	0.4
CRP (mean) (mg/l)	87,4	90,1	0.9
Evidence of infectious agent (%)	53	61	0.2
TJC / SJC	2.8 / 1.8	3.2 / 2	ns
Dactylitis (%)	13	29	0.3
Enthésitis (%)	40	26	0.5
Extra articular features (%)	47	35	0.4
Axial symptoms (%)	33	29	1
DMARDs use (%)	36	62	0.1
Median delay of DMARD introduction (days)	210	50.5	ns
Biologic agents use (%)	**0**	**45**	**0.005**
Remission at last follow-up (%)	57	47	0.6

P3

WORK STATUS AND RELATED VARIABLES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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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 (BASMI) 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 (WPAI: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 7,24±6,23. In patients with AS according to control group, time lost from work was more due to health problems. Reduction

in work productivity, forced to work out in their daily activities in patient with AS were also more than control group (p<0.05). Reduction in work productivity was associated with BASDAI and depression. Forced to work out in their daily activities correlated with BASFI, BASDAI, anxiety and depression (p<0.05). Patients with AS who used anti-TNF compared to no used anti TNF and there was no significant difference in any parameter of forms of work disability.
Conclusion. Psychological, sociodemographic, and disease-related factors were all found to be related to work status. Depression, in particular, appears to be associated with employment, absenteeism, and presenteeism and should therefore be prioritized in clinical practice.

P4

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

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Aim. The objective 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. Spinal radiographs were scored according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) scoring system. 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 (n=29) as compared to those without progression (n=91): 10.3±8.8 vs. 15.9±13.7 ng/ml, respectively, p=0.002, and in patients with syndesmophyte formation (n=25) as compared to those without syndesmophyte formation (n=95): 10.1±9.6 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 serum level regarding radiographic spinal progression could be confirmed: odds ratio (OR)=1.15 (95% CI 1.02-1.3) for no mSASSS worsening by ≥2 units, and OR=1.28 (95% CI 1.1-1.5) for no syndesmophyte formation, both adjusted for baseline syndemophytes, elevated C-reactive protein (CRP), smoking, body mass index, sex, and NSAIDS intake score.
Conclusions. Higher serum levels of leptin seem to protect patients with 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

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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 COMOrbidities 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) 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

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Background. Peripheral (arthritis, enthesitis and dactylitis) and extra-articular (uveitis, psoriasis and inflammatory bowel disease) disease is common in ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (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 and 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 64.4-76.0%) 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 68.9-84.9%). 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 9.1-13.0%) and IBD (4.1% (95% CI 2.3-6.5%) versus 6.4% (95% CI 3.6-9.7%) were similar in AS and nr-axSpA. The pooled uveitis prevalence was higher in AS (23.0% (95% CI 19.2-27.1%) than in nr-axSpA (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.

P7

ASSESSMENT OF THE PROFILE OF JOINT INVOLVEMENT IN THE SPONDYLOARTHRITIDES IN REGIONS OF DIFFERENT ETHNIC BACKGROUND IN BRAZIL

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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 were associated with 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 (p=0.055) limbs, as well as urethritis (p=0.005), and used more methotrexate (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.

P8

SCREENING FOR ANTIBODY TARGETS AS NOVEL CANDIDATE BIOMARKERS FOR THE DIAGNOSIS OF ANKYLOSING SPONDYLITIS USING CDNA PHAGE DISPLAY

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Aim. Diagnosis of ankylosing spondylitis (AS) is often delayed as specific serological tests and pathognomic clinical features are lacking. Although there is no consensus about the involvement of the humoral immune response in the etiology of AS, emerging evidence suggests plasma cells and antibodies to be involved in the disease course. Therefore, we aim to identify novel antibody markers for AS diagnosis.
Materials and Methods. A cDNA phage display library was constructed from synovium of three rheumatoid arthritis (RA) patients. This RA cDNA display library was screened for antibody reactivity present in pooled plasma of 10 early AS patients by successive rounds of serological antigen selection (SAS). The resulting antibody targets identified by SAS were further characterized by screening for antibody reactivity present in pooled and individual plasma samples of AS patients and healthy controls using phage enzyme-linked immune sorbent assay (ELISA).
Results. Our preliminary data demonstrate antibody reactivity in AS plasma, indicated by the enrichment of specific displayed peptides. Sequence analysis of the enriched antibody targets resulted in 67 different peptides which encode both known and novel, artificial peptide sequences. Screening of individual plasma samples by phage ELISA resulted in the detection of 21 antibody targets that only showed antibody reactivity in early AS patients and not in healthy controls.
Discussion. Antibody reactivity against these 21 antibody targets will be validated in a large number of plasma samples of AS patients, rheumatic controls and healthy controls to establish the true value of these antibodies as diagnostic biomarkers for AS.
Conclusion: We identified antibody reactivity against 21 antibody targets in plasma of early AS patients which might have the potential to be used as novel biomarkers for the improved diagnosis of AS.

P9

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

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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 (0.72, 0.36-1.07), BASFI (1.00, 0.76-1.23) and ASQoL (2.21, 0.94-3.49). 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.

P10

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

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Introduction. Ankylosing spondylitis (AS) may substantially impact on both performance and ability to remain in work. The AS Work Instability Scale (ASWIS) 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 0.7-55.7) 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 within this time (versus 3%: 3.2, 0.9-10.7).
Discussion. 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 predictive power of the ASWIS, however; even in the short-term, this instrument may identify those requiring occupational assessment, potentially opening up pathways for intervention.

P11

INCREASED SMOKING EXPOSURE IS ASSOCIATED WITH INCREASED DISEASE SEVERITY IN AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER FOR ANKYLOSING SPONDYLITIS (BSRBR-AS)

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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 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 (ASQoL).
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).
Discussions. 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

	N	BASDAI	BASFI	BASMI	Spinal VAS	ASQoL
Ever smoker / never-smoker	524/408	1.04 (0.72, 1.36)	1.34 (0.98, 1.69)	0.61 (0.36, 0.87)	1.11 (0.74, 1.49)	2.71 (2.01, 3.41)
Current smoker / ex-smoker	177/347	0.90 (0.43, 1.37)	1.21 (0.67, 1.74)	0.50 (0.12, 0.88)	0.87 (0.30, 1.43)	2.47 (1.42, 3.52)
Heavy smoker / light smokers [1]	64/108	0.29 (-0.46, 1.03)	0.55 (-0.32, 1.43)	0.34 (-0.34, 1.02)	0.84 (-0.04, 1.73)	1.21 (-0.49, 2.9)

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

P12

DEVELOPMENT AND EVALUATION OF THE COMBINED ANKYLOSING SPONDYLITIS SPINE SCORE (CASSS) FOR THE ASSESSMENT OF SPINAL RADIOGRAPHIC OUTCOME

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Objective. To develop a combined AS spine score (CASSS) in which the cervical facet joint score is combined with the mSASSS, and to investigate the additional value of the CASSS in the evaluation of spinal radiographic progression in AS patients.
Methods. Baseline and 4-year radiographs from 98 consecutive AS patients treated with TNF-α inhibitors in the GLAS cohort were scored by two readers; vertebral bodies according to mSASSS (0-72) and cervical facet joints according to the method of de Vlam (0-15). The CASSS was calculated by summing up the total scores of both methods (range 0-87) and was compared to mSASSS (gold standard) using three aspects of the OMERACT filter: feasibility, discrimination, and truth.
Results. *Feasibility:* Scoring cervical facet joints took a few minutes; no additional radiographs were necessary. The mSASSS could be calculated in 94 (96%) and CASSS in 91 (93%) patients.
Discrimination: Both scoring methods had very good inter-observer reliability (ICC's status scores >0.99, progression scores 0.92). Measurement error was similar for mSASSS and CASSS, smallest detectable change was 1.8 and 1.9, resp. Sensitivity to change was moderate for both methods with a standardized response mean of 0.59 for mSASSS and 0.63 for CASSS.
Truth: The use of CASSS resulted in 41 (46%) patients with higher baseline scores and 22 (25%) with higher progression scores compared to mSASSS. Baseline damage of facet joints was moderately correlated with damage of vertebral bodies (rho=0.49). Radiographic progression of facet joints was not correlated with progression of vertebral bodies (rho=0.16).
Conclusions. According to the OMERACT filter, mSASSS and the new CASSS performed similar in respect to feasibility and discrimination. Additionally, the CASSS showed better truth value since it provides a broader range of structural changes and captures more AS patients with progression which is very important in the evaluation of radiographic outcome in this heterogeneous and slowly progressing disease.

P13

ASSESSING PHYSICAL ACTIVITY IN AXIAL SPONDYLOARTHRITIS PATIENTS: MODIFICATION OF THE SQUASH

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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, semi-structured, in-depth interviews concerning the SQUASH domains in relation to the disease were performed with 9 professional axSpA experts (e.g. rheumatologists, rehabilitations 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).
Conclusions. 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

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Aim. It is often difficult to differentiate psoriatic arthritis (PsA) from osteoarthritis (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 obtained. Soluble markers of cartilage metabolism (COMP, hyaluronan), metabolic syndrome (adiponectin, adipsin, resistin, HGF, insulin, leptin) and inflammation/ immune response (CRP, IL-1b, -6, -8, TNF-α, MCP-1, NGF) were assayed in the samples using Luminex multiplex assay. Marker levels in serum were compared 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 univariate 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 differed 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 following 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 .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 consistently identified MCP-1 as a PsA marker. Further validation of the model including COMP, resistin, MCP-1 and NGF showed an AUROC of 0.98.
Conclusion. A panel of 4 biomarkers (COMP, resistin, MCP-1, NGF) may distinguish PsA from OA.

P15

PLASMA CALPROTECTIN IN SPA-PATIENTS, A BIOMARKER FOR PERIPHERAL ARTHRITIS

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Introduction. Spondyloarthritis (SpA) is a rheumatic disease with axial and peripheral inflammatory arthritis. Inflammatory biomarkers as SR and CRP are weakly 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 synovitis or inflammatory back pain by questionnaire. Symptomatic relatives were investigated, and included if they fulfilled the ESSG-criteria. 387 SpA-patients were included. 273 patients with inflammatory back-pain had x-ray and MRI of SI-joints. 235 patients, 51 symptomatic relatives and 74 healthy relatives were tested for Plasma- Calprotectin. Statistic testing with SPSS Chi square test or Students t-test.
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 are correlated to inflammatory markers. Calprotectin is correlated to BMI and swollen joint count but not to BASDAI, BASFI or MHAQ.

Calprotectin	**N**	**Calprotectin nG/mL Mean**	**t-test**
Healthy relatives/ SpA-patients	74/235	460/719	0,308
Symptomatic relatives/ Spa-patients	61/235	520/719	0,515
Male	158	812	0,097
Female	202	501	
Correlations with Calprotectin in spa-patients	235 t	Spearmans rho	Chi-square test
Body mass index		0,164	**0,013**
Age		-0,105	0,111
Disease duration		0,050	0,480
SR		0,421	**0,000**
Crp		0,725	**0,000**
Hb		-0,249	**0,000**
Trc		0,545	**0,000**
Lkc		0,050	0,457
Tender joint count		0,057	0,437
Swollen joint count		0,250	**0,002**
Basdai		-0,044	0,504
Basfi		0,003	0,962
MHAQ		0,024	0,745

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

P16

ASDAS PERFORMANCE IN PATIENTS WITH SPONDYLOARTHRITIDES FROM DIFFERENT BRAZILIAN REGIONS

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Aim. To analyze the capacity of Ankylosing Spondylitis Disease Activity Score (ASDAS) to measure disease activity in spondyloarthritides (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-Reactive 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 (SPARCC), 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 studied 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 enthesitis: BASDAI (Curitiba with p<0.0001; PA with p<0.0001; Manaus with p<0.0001), VHS (Curitiba with p=0.0001; PA with p=0.0007 ; Manaus with p=0.007),BASFI (Curitiba with p=0.0002; PA with p<0.0001; Manaus with p=0.02), MASES (Curitiba with p=0.006 ; PA with p=0.01; Manaus with p=0.007), SPARCC (Curitiba with p=0.007; PA with p=0.001 ; Manaus with p=0.004), and ASQoL (Curitiba with p<0.0001 ; PA with p=0.0002 ; Manaus with p=0.0004).
Conclusion. 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

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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=2214pg/ml, IQR 2103-2618pg/ml) compared to those with no evidence of bony fusion (median=3042pg/ml, IQR 2321-3607pg/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.

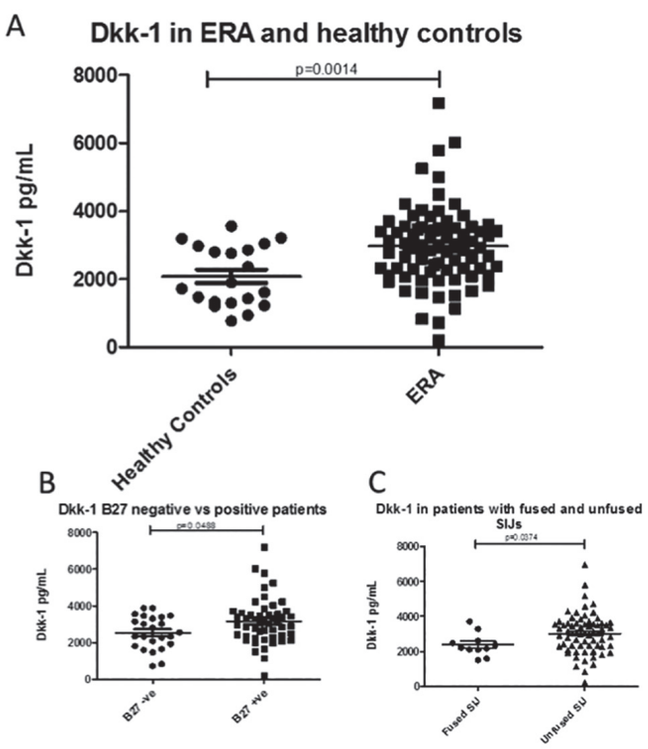

Fig. 1. A. Dkk-1 levels were significantly higher in patients with ERA compared to healthy controls. **B.** Levels were higher in patients with ERA who were HLA-B27 positive compared to negative. **C.** Patients with SIJ bony fusion had significantly lower levels than those with no bony fusion.

P18

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

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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 Aesku. 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 (1.49±2.81 (IgApositive) versus 0.69±1.85 (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 the receptor of macrophage migration inhibitory factor (MIF), which is upregulated in axial spondyloarthritis and stimulates osteoblasts. Potentially, 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.

P19

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

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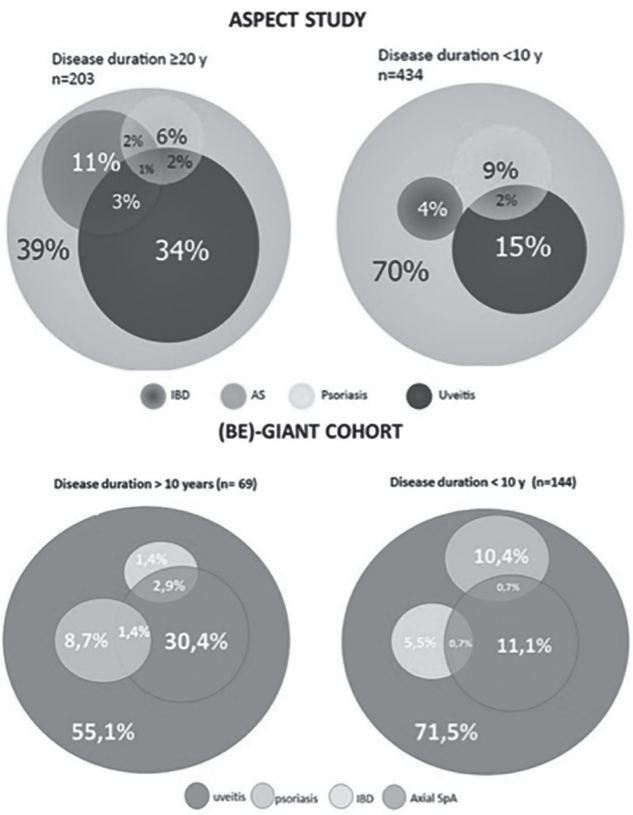
Background. The prevalence of extra-articular manifestations (EAMs) in ankylosing spondylitis (AS) is well-known. However, as the diagnosis of axial spondyloarthritis (AxSpA) is now made much earlier in the disease the prevalence of the EAMs may be different. Moreover, the introduction of anti-TNF therapy 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 (Be-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.



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P20

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

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Introduction/Aim. Antibodies against CD74 are associated with long established axial SpA. InterSpA is 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 are 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 SPONDILOARTHRITIS: IMPLICATIONS FOR THE CLINICAL PRACTICE

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Introduction. Pathogenesis and early diagnosis of enteropathic spondyloarthritis (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-catenin signalling 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-IgGs serum levels are novel biomarkers that may be helpful in the early diagnosis of axial spondyloarthritis in IBD patients with articular symptoms.

P22

OXIDATIVE STRESS EVALUATED BY DISULFIDE/THIOL HOMEOSTASIS IN PATIENTS WITH PSORIATIC ARTHRITIS

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Introduction/Aim. Inflammation and angiogenesis were shown to be interrelated processes.
Oxidative stress may be one of the pathogenic mechanisms of angiogenesis seen in inflammation.
Hypoxia could be a driving factor for both angiogenesis and joint destruction in arthritis with the increase in reactive oxygen species. Therefore in the present study we measured the thiol levels and disulfide/thiol homeostasis to evaluate oxidative status in patients with psoriatic arthritis (PsA).
Materials and Methods. In total 71 consecutive patients with PsA (49 female [69%]; with a mean age of 42.1 ± 10.1 years) and age and sex matched 36 healthy control subjects (23 female [64%]; with a mean age of 39.6 ± 9.7 years) were included in the study. Disulfide/thiol homeostasis was measured using a fully automatic analysis method. First reducible disulfide bonds were reduced to compose free functional thiol groups. All thiol groups containing native and reduced

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), DAS28 and BASDAI scores were 1.2±1.9, 2.9±1.2 and 3.2±2.3 respectively in our PsA patients. Serum native thiol (267.7±89.7 vs 300.8±62.7µmol/l) and total thiol levels (304.9±54.8 vs 324.7±40.7µmol/l) were found to be significantly decreased in the PsA 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 µmol/l), disulfide/native and disulfide/total thiol ratios were increased in the PsA group, this increase did not reach statistical significance. In PsA patients native thiol levels were negatively correlated with age and patient reported pain (VAS).
Conclusions. Serum thiol levels decreased significantly in PsA 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

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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 (32.8%) 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 golimumab). Other therapies in use were azathioprine, sulphasalazine and mesalazine.
Twenty-five (21%) IBD patients mentioned peripheral (joint pain and enthesopathy) symptoms and 33 (28%) IBP. Fifteen of these 33 patients had radiological (Xr or MRI) evidence of sacroiliitis. Seventeen (16%) patients who denied axial complaints had radiographic changes suggestive of sacroiliitis.
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 rheumatic 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

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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 BASFI 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

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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 Assessment of Spondyloarthritis International Society (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.

P26

REGIONAL REGISTRY AS A TOOL FOR IMPROVEMENT OF MANAGEMENT OF ANKYLOSING SPONDYLITIS: EVALUATION OF PSYCHOLOGICAL STATE

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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 anxiety and 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 41,17% 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.

P27

FECAL CALPROTECTIN AS A NEW DIAGNOSTIC TOOL IN DIAGNOSING SPONDYLOARTHROPATHIES

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Introduction. Spondyloarthropathies (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%[1]. 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, Bülhmann) was performed among patients consulting the department of rheumatology of the OLV Hospital Aalst and with clinical suspicion of SpA. Patients were asked to quit the intake of NSAIDs 2 weeks before collection of the sample. Fecal 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.

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P28

PREVALENCE OF OSTEOPOROSIS IN AN ANKYLOSING SPONDYLITIS COHORT

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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.

P29

SERUM AMYLOID A LEVELS IN PSORIATIC ARTHRITIS PATIENTS – A MARKER OF DISEASE ACTIVITY?

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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 SPARCC 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

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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/cm^2) 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. Out of 126 SpA patients, 63 (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 levels (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 44%, $p=0.02$) was observed. In SC group, FN-BMD was negatively associated with disease duration and CRP (r= -0.30 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 osteoproliferation.

P31

SPONDYLOARTHRITIS PREVALENCE IN EUROPE, A EULAR-ENDORSED SURVEY

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Background. The spondyloarthritis (SpA) prevalence has shown a trend to increase in the last two decades, in line with better recognition of the disease as well as the use of new classification criteria (1).
The need to estimate and compare the SpA prevalence across Europe was recognized.
Objectives. to estimate the SpA prevalence in several European countries: France, Turkey, Lithuania and Serbia by using identical methodology and sampling; to standardize the results with reference to the European Standard Population by direct method of standardization.
Methods. A two-step approach was taken. First, a unique detection Questionnaire, covering self-reported diagnosis, SpA classification criteria (ESSG 1991), personal and family history for SpA (2), previously translated and validated for each of the participating countries, was administered to a population sample. A two-stage sampling was carried out on seven areas covering 20 counties in France, seven geographical regions covering 25 administrative provinces in Turkey, two largest cities - Vilnius and Kaunas in Lithuania and two geographical regions covering four counties in Serbia.
Diagnoses were confirmed by rheumatologists. Results were standardized by age and sex using the European Standard Population, defined as EU-27+EFTA, 2010 estimates.
Results: Detection Questionnaire was administered by telephone on 15219 persons in France (3), 6558 in Lithuania (4) and 6213 in Serbia (1), with 64.7%, 64.7% and 63.3% response rate, respectively. In Turkey, Questionnaire was administered face-to face on 4012 persons. Diagnoses were confirmed for 29 cases in France (37.9% male), 18 in Turkey (16.7% male), 27 in Lithuania (55.6% male) and 16 in Serbia (37.5% male). Estimates of the SpA prevalence standardized for age and sex are given in Table I.

Table I. Age- and sex- standardized SpA prevalence (95% CI) for France, Lithuania, Turkey and Serbia, age ≥18 years.

	Men	Women	Total
France	0.29 (0.12-0.47)	0.31 (0.16-0.45)	0.30 (0.19-0.41)
Lithuania	1.38 (0.68-2.09)	0.39 (0.16-0.63)	0.89 (0.78-1.00)
Turkey	0.17 (0.00-0.36)	0.57 (0.28-0.87)	0.37 (0.18-0.56)
Serbia	0.38 (0.06-0.71)	0.32 (0.10-0.54)	0.35 (0.17-0.54)

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.
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P32

HLA-B27/hB2m DROSOPHILA A NEW MODEL TO STUDY HLA-B27 IMPLICATION IN SPONDYLOARTHRITIS

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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 mechanism. To understand HLA-B/hB2m intracellular trafficking, localization and consequence of its expression, we developed HLA-B2705, HLA-B0702 (control) and human Beta-2-microglobulin (hB2m) transgenic Drosophila.
Methods. Gateway Technology was used for developing transgenic HLA-B/human B2m 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-B0702/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/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 comportment of HLA-B subtypes.

P33

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

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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" $CCR2^{+}CD43^{low}$ monocytes both in the central and peripheral compartments. Antibiotic treatment of B27 rats reduced ileitis and decreased the number of circulating $CCR2^{+}CD43^{low}$ 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 $CCR2^{+}CD43^{low}$ monocytes. This reduced inflammation in B27 rats in turn affects BM osteoclast precursors and reduces their potential to differentiate into mature osteoclasts.
Conclusions. We have provided 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 INDUCIBLE COSTIMULATOR (ICOS) IN SPONDYLOARTHRITIS ANIMAL MODEL

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Background/Aim. HLA-B27/hβ2m transgenic rats (B27 rats), a model of spondylarthritis (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 (F344). 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

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Background/Aim. Spondyloarthritis (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 or absence of recombinant IL-27. Effector T cells and Tregs were cultured 3 days with coated anti-CD3. Naive T cells were cultured 6 days with coated anti-CD3 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-10 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 pathogenic in SpA, these results suggest that IL-27 may be a new promising therapeutic tool for SpA.

P36

WANT SIGNALING MODULATORS EXPRESSION BY FLS IN INFLAMMATORY JOINT DISEASES

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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 an 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 (r=0.76; $p<0.01$) in synovial fluid and higher levels of IL22 and sFRP3 were observed among TNF-α inhibitors users ($p=0.01$). 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/FRZB by FLS in both *in vitro* and *ex vivo* models. This finding links IL22 to local inhibition of Wnt signaling, with consequent blockade of osteogenesis and the potential to contribute also to the resorptive damage. Furthermore, the FLS presents as a source of this inhibitor in synovial fluid, assigning this cell to another bone injury mechanism.

P37

WINDOW OF OPPORTUNITY: CIRCULATING OSTEOBLAST PRECURSORS WERE DECREASED AFTER INFLIXIMAB THERAPY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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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 multilayering 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 S red staining of circulating osteoblast precursors, 3) total procollagen type 1 N-terminal propeptide (P1NP) as osteoprogenitor marker, osteocalcin as mature osteoblast marker in patients with AS and in healthy controls at baseline and 14 weeks after infliximab therapy in AS patients.
Results. The serum level of P1NP (osteoprogenitor marker) was significantly higher in patients with AS than in the controls ($p=008$), 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

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Introduction. Morning stiffness is a prominent clinical feature in spondyloarthritis suggesting that circadian rhythms play a role in spondyloarthritis 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 Arntl-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 ($Bmal1^{f/f}$) were crossed with Prx1-cre mice to delete Bmal1 in mesenchymal cells of the embryonic limb bud. Phenotype 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 ($Bmal1^{f/f}$.Dermo1-cre) and in tendon/tendon progenitor cells ($Bmal1^{f/f}$.Scx-cre).
Results. Bmal1 germline mutant mice and $Bmal1^{f/f}$.Prx1-cre 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 upregulated in Achilles tendons of $Bmal1^{f/f}$.Prx1-cre mice. Bmal1 deletion in Scx+ cells, but not in Dermo1+ osteochondroprogenitor cells, induced Achilles tendon ossification to the same degree as Prx1-cre 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.

P39

WHICH CELLS CORRESPOND TO TYPICAL SIGNALS FOR FATTY AND INFLAMMATORY LESIONS SEEN ON MRI IN AS?

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Background. The occurrence of bone marrow edema (BME) and fat metaplasia detected by MRI were shown to be significantly associated with syndesmophyte formation in patients with ankylosing spondylitis (AS). The cell type responsible for the fat signal seen in MRI has not been defined to date.
Aim. To histologically analyze the cells seen in fatty lesions (FL) as detected by MRI in spinal biopsies of AS patients and compare them with controls.
Methods. Spinal biopsies from vertebral edges of patients with AS and controls who underwent surgery for spinal deformity or spinal stenosis were prospectively collected. All patients had spinal STIR- and T1-weighted MRIs available exactly from the area of biopsy, and all biopsies were taken from areas that had a fat signal on MRI. The biopsies were analysed blinded to patients' diagnosis. Histomorphological analyses were performed to detect normal bone marrow, fat cells, inflammatory cells and fibroblasts. Histologic results were compared with MRI findings.
Results. Biopsies mostly obtained from the lower thoracic and the lumbar spine of 13 AS patients (mean age 56.3 years, mean disease duration 26 years) and 6 controls (mean age 53.4 years) were available.
Similar proportions of AS patients, (12/16, 75%) and non-AS patients (4/6, 67%) had vital bone marrow.
Fat cells were found in all 13 biopsies obtained from AS patients from the area of the fat signal vs. only 2 non-AS patients (33%), while inflammatory cells were found in 9 AS patients (56.3%), all of which also had BME on MRI, vs. 3 non-AS patients (50%). Fibroblasts were seen in 3 AS (18.9%) and 2 non-AS patients (33%).
Discussion. The underlying cell types of FL and BME as detected by MRI in these long standing AS patients were fatty and inflammatory cells. The main difference between AS and non-AS patients was the proportion of biopsies containing fat cells. This suggests that fat cells are responsible for the MRI signal, at least in patients with longstanding ankylosing spondylitis.

P40

ASSOCIATION BETWEEN IMPROVEMENT IN ENTHESOPATHY AND QUALITY OF LIFE: RESULTS FROM ANTI TNF-NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS IN TWO PHASE 3 USTEKINUMAB TRIALS

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Aim. Assess changes in enthesopathy & function/health-related QoL (HRQoL) in anti-TNF-naïve patients with PsA receiving ustekinumab (UST).
Methods. Adult patients in 2 Ph3 trials (n=747 anti-TNF naive) with active PsA (≥5 SJC&≥5 TJC;CRP≥0.3mg/dL) despite DMARD &/or NSAIDs were randomized to UST45mg, 90mg,or PBO at wks0,4, & q12wks. Stable concomitant MTX was permitted but not mandated. At wk16, patients with <5% improvement in TJC & SJC entered blinded early escape (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 (enthesopathy at BL, but not at wk24), worsened (enthesopathy at wk24, but not at BL) & unchanged. Patients with enthesopathy assessment missing at either time point were included in unchanged category; those with enthesopathy data missing at both time points were excluded. EE patients were excluded from this analysis.
Improvements in HRQoL (using SF-36 PCS&MCS & physical function (HAQ-DI) were assessed by enthesopathy response category.
Results. 591 anti-TNF-naïve patients from both trials were included; 45% of patients were female, mean age 47yrs, 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 enthesopathy had greater improvement in functioning & HRQoL, vs those who did not ($p< 0.05$). When the analysis was restricted to those who achieved ACR 20, patients with improvement in enthesopathy 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-naïve patients with PsA in 2 UST trials. Some, not all, improvement may be explained by improvements in peripheral arthritis.

P41

MONITORING SEROLOGIC RESPONSE TO HBV VACCINATION IN SPONDYLOARTHRITIC PATIENTS TREATED WITH TNF BLOCKERS

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Introduction. According to the WHO data, HBV vaccination has an efficacy of 95% and a duration of protection of at least 20 years. Until now the evolution of immune response to HBV vaccination in patients with SpA treated with TNF blockers has not yet been assessed.
Aim. To evaluate the effect of antiTNF therapy on the evolution of immune response to HBV vaccination in SpA patients and to identify potential effect modifiers on immune response.
Materials and Methods. Study type: Prospective observational study.
Patients. Patients with SpA treated with antiTNF with previous response to HBV vaccination.
Procedures. Determination of AbHBs at least one year after vaccination. Levels › 10 mUI/Ml were considered protective.
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. 11 patients were included. The average age was 49.36 years old. The median of time from SpA diagnoses was 15 years. The average of antiTNF treatment time was 58.91 months.
4 patients maintained immune response to HBV vaccination. A decrease in levels was observed in all patients. Persistence of protective levels of antibodies was independent of the use of synthetic immunosuppresants, associated causes of immnunosuppression, time from vaccination and biological therapy way of administration. We found significant differences regarding vaccine dose and levels of antibodies reached after vaccination.
Conclusions. In our study, the proportion of patients who maintained immune response to HBV vaccination was low. Related factors to persistence of protective levels of antibodies were the vaccine dose and the levels of antibodies reached after vaccination.
This study is limited by the small sample size. It would be useful to continue our investigation in order to ameliorate the vaccination standards of our patients.

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

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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 disease in patients at risk for spondyloarthritis (SpA).
Aim. To describe GP's ability to recognize symptoms suggestive of SpA.
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 relieve 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 psoriasis (83.6%) and inflammatory bowel disease (72.1%). GPs less often ask about other SpA related symptoms such as uveitis (61.8%), enthesitis (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).

Signs of inflammatory disease	Peripheral	Axial
Insidious onset of complaints, n (%)	53 (29.0)	90 (49.2)
Symptom duration>3 months, n (%)	57 (31.2)	93 (50.8)
Pain improved with exercise, n (%)	25 (13.7)	38 (21.3)
Pain not relieved by rest, n (%	30 (16.4)	40 (21.9)
Pain relieved by NSAIDs, n (%)	160 (87.4)	150 (82.0)
Morning Stiffness>30min, n (%)	141 (77.1)	138 (75.4)
Nocturnal Pain, n (%)	Not Applicable	143 (78.1)
Alternating Buttock Pain, n (%)	Not Applicable	37 (20.2)

P43

THE PREVALENCE OF AXIAL AND PERIPHERAL SPONDYLOARTHRITIS IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW & META-ANALYSIS

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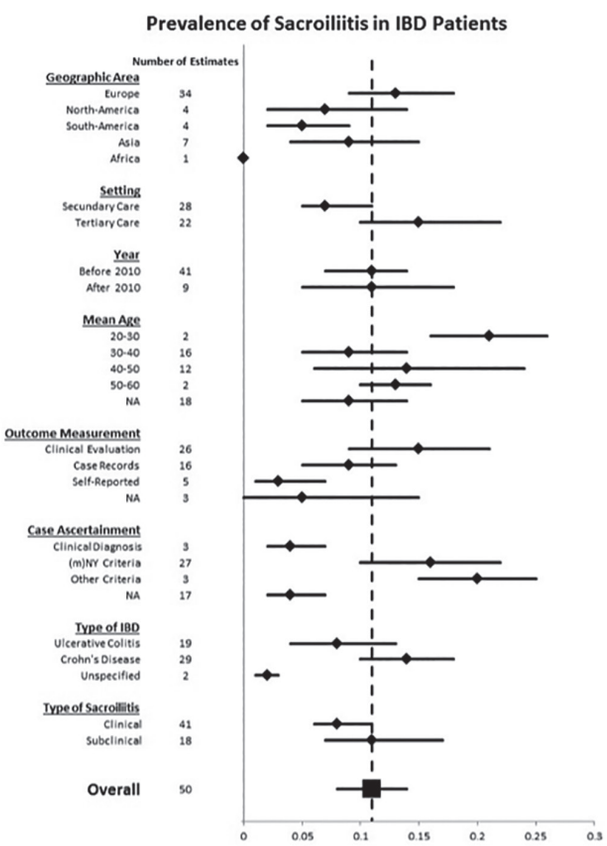
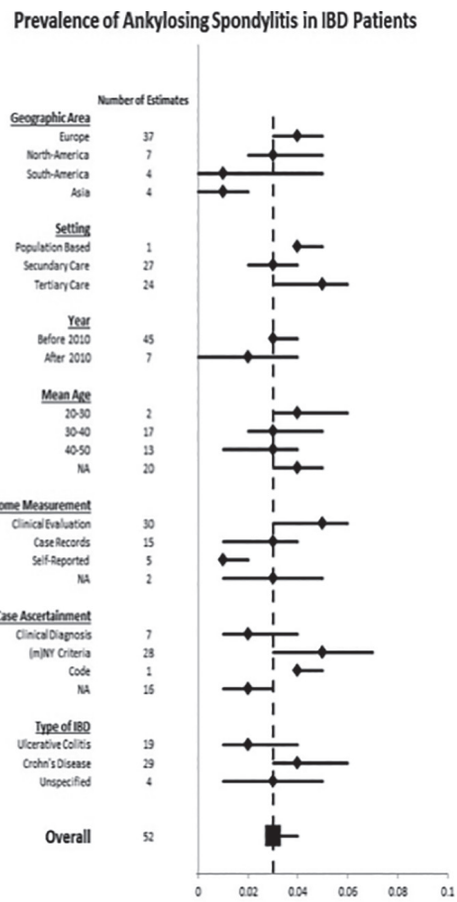
Background. Inflammatory Bowel Disease (IBD) is a chronic disease, comprising both Crohn's Disease (CD) and ulcerative colitis (UC). Various extra-intestinal manifestations can occur, among which spondyloarthritis (SpA). SpA can manifest with both axial and peripheral manifestations, but prevalence estimates 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 sacroiliitis was 0.11(95%CI 0.08-0.014), 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 extraintestinal manifestation in IBD. Peripheral arthritis is slightly more common with a pooled prevalence of 0.14 than axial manifestations as sacroiliitis (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.





P44

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

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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 a rheumatic condition before the invitation for the study.
The majority of patients was informed by their medical specialist (40.3%) or gained this knowledge by themselves (39.6%), only 1.4% was informed by their GP. 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.

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

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

	Psoriasis (n=552)	IBD (n=344)
% Awareness	43.1	41.9
% Informed by GP	13.5	1.4
% Informed by medical specialist	24.4	40.3
% Via surroundings	18.5	9.7
% Looked it up themselves	34.0	39.6
% Patient organization	8.4	2.8
% Other	1.3	6.3

P45

VALIDATION OF THE CONTEST QUESTIONNAIRE TO SCREEN FOR PSORIATIC ARTHRITIS IN PRIMARY CARE PSORIASIS PATIENTS

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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 suboptimal. 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-jt (including the PEST manikin). 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 (0.86). 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 I. Performance of the CONTEST questionnaires in the development study and in the SENSOR dataset

	AUC			Sensitivity			Specificity		
	Development	Sensor	Sensor selection*	Development	Sensor	Sensor selection*	Development	Sensor	Sensor selection*
CONTEST	0.69	0.69	0.60	0.86	0.53	0.64	0.35	0.75	0.5
CONTEST -w	0.74	0.67	0.60	0.86	0.30	0.36	0.48	0.87	0.73
CONTEST -jt	0.70	0.69	0.60	0.86	0.51	0.62	0.37	0.78	0.55
Pest	0.91	0.71	NA	0.92	0.68	NA	0.78	0.71	NA

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

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

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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 21(31.3%), 40(59.7%) and 21(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 positive 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

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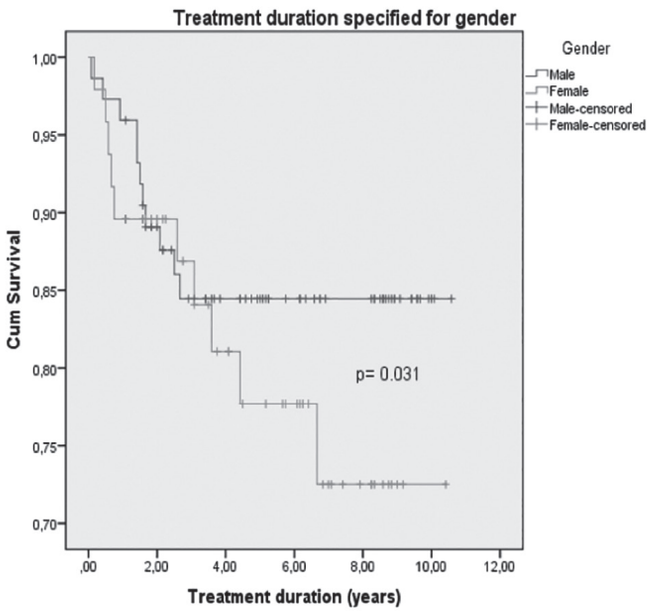
Introduction/Aim. Anti-TNF treatment is available for Ankylosing Spondylitis (AS) for many years now, but the data on long term follow up in daily practice are limited. To determine treatment survival and adverse events of anti-TNF treatment in AS patients in a large peripheral hospital in daily practice. 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 significant shorter treatment period compared to males (33.4 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%).



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

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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 (generic), 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, while 9% suffered from unspecified IBD, with a mean disease duration of 12.3 (SD9.3) years. 274 patients (79.4%) suffered from any kind of MSC (CD 85%, UC 74%).
With regard to HRQoL as measured with the IBDQ, patients suffering from MSC score significantly lower on all subscores compared with patients without MSC. Patients with CD score significantly lower on all subscores than patients with UC. These findings are confirmed when measuring HRQoL with the SF-36 (Figure 1) in both physical and psychosocial domains. Joint, tendon and lower back complaints all have equal influence on the HRQoL when compared with the scores of the general Dutch population.
Conclusions. IBD causes significant impact on HRQoL compared to the Dutch healthy population, where patients with CD report lower scores than patients with UC. This reduce in HRQoL might be explained by the presence of MSC.

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

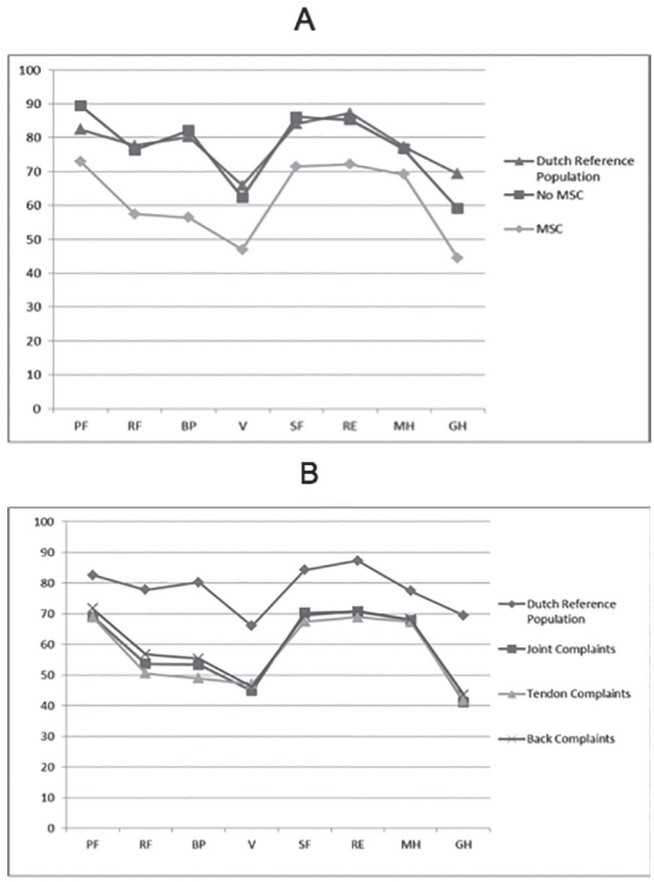

Fig. 1. SF-36 scores in IBD patients (**A**) with or without MSC & (**B**) with joint, tendon or lower back complaints.

P49

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

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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); iii) 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 axSpA, 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

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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 (GESPIC) were included in the current study. Spinal radiographs were scored according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) system 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 (for the presence of syndesmophytes at baseline, smoking status and NSAIDs intake) odds ratio (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

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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 (GESPIC) 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 -0.05-0.21), 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=0.61 (95%CI 0.50-0.71). 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.

P52

PATIENT REPORTED OUTCOMES IN SPONDYLOARTHROPATIES FROM REUMA.PT: TRANSITIONING FROM PAPER TO TOUCH SCREEN TECHNOLOGY

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Introduction. Patient reported outcomes PRO are a key element in the global evaluation of patients, especially those followed in a day hospital. The use of touchscreen computers is one of the new features in the day hospital of Instituto Português de Reumatologia.
Objectives. To evaluate the transition from paper to touchscreen computers technology of the PRO in use in Reuma.pt.
Methods. We considered a step up model of comparison with 2 months intervals one before the use of the touchscreen computers, one two months after the introduction of touchscreen computers and a third after an intermediate evaluation (comparison between interval 0 and 1) of the results.
A specific formation to physicians and nurses to be aware of missing data from non-total completion of the questionnaires was introduced between the first and second evaluation. The percentage of questionnaires totally completed by number of patients were obtained for every period and diagnosis.
Results. 370 day hospital appointments were evaluated according to diagnosis and interval and the percentage was obtained (Table I).

Table I. Results comparing questionnaires by diagnosis and intervals.

	Paper interval 0 (Sept –Nov 15)			Interval 1 (Nov 15- Jan 16)			Interval 2 (Jan – Mar 16)		
AS	**N**	**N Quest.**	**Pct.**	**N**	**N Quest.**	**Pct.**	**N**	**N Quest.**	**Pct.**
BASDAI	95	95	100,00%	92	87	94,57%	93	92	98,92%
BASFI	95	94	98,95%	92	89	96,74%	93	92	98,92%
EQ5D	95	91	95,79%	92	85	92,39%	93	88	94,62%
AsQol	95	88	92,63%	92	83	90,22%	93	85	91,40%
SF-36	95	80	84,21%	92	72	78,26%	93	77	82,80%
HADS	95	27	28,42%	92	87	94,57%	93	91	97,85%
FACIT	95	93	97,89%	92	91	98,91%	93	92	98,92%
Pso A									
BASDAI	32	29	90,63%	30	23	76,67%	28	28	100,00%
BASFI	32	29	90,63%	30	24	80,00%	28	28	100,00%
ASQol	32	30	93,75%	30	23	76,67%	28	28	100,00%
HAQ	32	27	84,38%	30	23	76,67%	28	27	96,43%
EQ5D	32	30	93,75%	30	30	100,00%	28	28	100,00%
SF-36	32	25	78,13%	30	23	76,67%	28	26	92,86%
HADS	32	3	9,38%	30	27	90,00%	28	28	100,00%
FACIT	32	28	87,50%	30	30	100,00%	28	27	96,43%

Only HADS had a significant (p<0.000) improvement for every disease, with the use of the touchscreen computers from interval 1 to 2.
Discussion. On our intermediate evaluation comparing paper to tablet we saw a lower percentage of questionnaires fully completed (although not statistical significant) and a formal awareness formation addressing the causes was made with all the physicians and nurses of the day hospital. The PRO from Reuma.pt was not developed for tablets and some issues regarding missing data associated with that was found.
Conclusion. The use of technology can contribute for better data in Reuma.pt and other national registries by saving time (medical and nurse) for clinical evaluation, by integrating patients in their evaluations and by cost reduction. Issues regarding the adaptability of software to tablet technology have to be addressed to insure an overall improvement.

P53

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

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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 antiTNF has not yet been assessed.
Objectives. Main objective: to evaluate the effect of antiTNF 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 antiTNF. 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 HD group showed immune response to HBV vaccination whereas only 14 patients (46.7%) in the SpA 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 mcg/mL.
Conclusions. In our study, immune response to HBV vaccination in patients with SpA treated with antiTNF 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

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The aim was to evaluate the risk of malignances 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, DAS-28 score, (BASDAI, 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<0.001) 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 1.1; 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 SYNDESMOPHYTE IN AXIAL SPONDYLOARTHRITIS: DATA FROM KOREAN COLLEGE OF RHEUMATOLOGY BIOLOGICS (KOBIO) REGISTRY COHORT

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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/m^2) 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±13.3. 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 QUIESCENT DISEASE ACCORDING TO THE RHEUMATOLOGIST'S OPINION DO NOT ACHIEVE MINIMAL DISEASE ACTIVITY

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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

CASPAR criteria and quiescent disease according to the treating rheumatologist, defined by the fact that the rheumatologist did not consider to modify the current treatment. Patients were systematically evaluated by an independent research physician on disease activity.
Results. 88 out of the 250 PsA patients did not fulfill MDA criteria (MDA-). There were no group differences in treatment use. A high TJC, VASpain and VASptglobal were most frequently contributing to the failure to achieve MDA (83%, 82% and 80%). However, also objective signs of disease activity were more prevalent in the MDA- group: SJC>1 35% versus 7% (p0.000), enthesitis>1 14% versus 3% (p0.002), PASI>1 43% versus 26% (p0.002). PRO scores on daily functioning (HAQ), quality of life (DLQI), daily activity impairment (WPAI/SF36-PCS) were significantly worse in the MDA- group.
Conclusion. One third of the PsA patients with quiescent disease according to the treating rheumatologist do not achieve MDA. These patients have a higher disease activity both on subjective and objective disease activity measurements. As this is associated with worse PROs, further research should evaluate if treatment adjustments may be beneficial for this patient group with residual disease activity.

P57

SUBCLINICAL ATHEROSCLEROSIS IN ANKYLOSING SPONDYLITIS – DOES IT REALLY EXIST AND WHICH ARE THE EFFECTS OF TREATMENTS? A SYSTEMATIC REVIEW

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Objectives. Accelerated atherosclerosis and increased cardiovascular morbidity and mortality have been associated with ankylosing spondylitis (AS). Noninvasive methods have been developed to evaluate vascular dysfunction which is correlated with future development of atherosclerosis. The objectives were to determinate 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 patent 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 blockers efficacy. Conversely it seems that endothelial dysfunction is present and reversible after treatment with TNF blockers, statins and spironolactone. These results are consistent to treat AS patients with early effective treatment to prevent the risk of CV morbidity and mortality.

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

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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 fullfilling 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 hypthesized with Spearman correlations from low (age: 0.10) to good (BASDAI: 0.70). ASAS HI scores showed a high internal consistency with a Cronbachs-α of 0.93. 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 I). 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 I. Discriminant ability of the ASAS HI stratified by disease activity.

	ASDAS status groups			
	Inactive (n=245)	**Moderate (n=283)**	**High (n=500)**	**Very high (n=289)**
ASAS HI (mean/SD)	2.9 ± 3.1	5.1 ± 3.5	7.3 ± 3.6	10.4 ± 3.5
BASFI (mean/SD)	0.9 ± 1.4	2.1 ± 1.9	3.7 ± 2.5	5.9 ± 2.5
BASDAI (mean/SD)	1.2 ± 0.9	2.7 ± 1.3	4.7 ± 1.7	7.0 ± 1.6

All values given as mean±SD.

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

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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.
Objectives. 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 (PASS) 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: 3.34±3.05) vs non-MDA Patients (7.13±5.21), 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.
Disclosure. This study has been funded by Pfizer.

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CORRELATION OF THREE ENTHESITES INDICES WITH DISEASE ACTIVITY AND FUNCTION IN BRAZILIAN PATIENTS WITH SPONDYLOARTHRITIDES

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Introduction. Although enthesitis are associated with higher disease activity, more disability and poorer quality of life in spondyloarthritis (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) fulfill 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.

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

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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 15-64%.
Conclusion. The prevalence of MDA found in these Brazilian sample is in accordance with data from other real life studies.

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LONG-TERM EFFICACY AND TOLERABILITY OF GOLIMUMAB IN ACTIVE NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: RESULTS OF THE OPEN-LABEL EXTENSION OF A RANDOMIZED, DOUBLE-BLIND STUDY

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Introduction. We report the results from an open-label extension (OLE) of a phase 3 study evaluating golimumab (GLM) for nonradiographic axial spondyloarthritis (nr-axSpA) (GO-AHEAD; NCT01453725)[1].
Methods. Patients completing the 16-week randomized, double-blind (DB), placebo (PBO) controlled study received open-label GLM 50 mg every 4 weeks (36-week efficacy period; 8-week safety follow-up).
Prespecified responder analyses for ASAS20, ASAS40, BASDAI50, and ASAS partial remission (PR) at weeks 16, 20, 24, 32, 40, and 52 used the OLE-treated population (GLM/GLM, n=93; PBO/GLM, n=96). In a post hoc analysis, the DB-treated population was used for GLM/GLM responder analyses (GLM/GLM, n=97). The incidence/severity of adverse events (AEs) were recorded.
Results. In total, 176/189 (93%) patients entering the OLE completed week 60 (GLM/GLM, 85/93 [91%]; PBO/GLM, 89/96 [93%]). The proportions of ASAS20, ASAS40, BASDAI50, and ASAS PR responders in the OLE were similar to those in the DB phase among patients who continued GLM (GLM/GLM group); consistent results were observed in the GLM/GLM group when using the DB-treated population (Figure A, B). Among patients who switched from PBO to GLM (PBO/GLM group), there were higher proportions of responders to GLM in the OLE than responders to PBO in the DB phase (Figure C). Treatment-emergent AEs occurred in 42% and 54% of GLM/GLM and PBO/GLM patients, respectively and serious AEs occurred in 2.2% and 3.1% of GLM/GLM and PBO/GLM patients, respectively.
Conclusions. In the GO-AHEAD OLE, improvements in disease activity were retained in patients who received GLM and who switched from PBO to GLM. Treatment with GLM in the OLE was generally well tolerated in patients with nr-axSpA.
Reference
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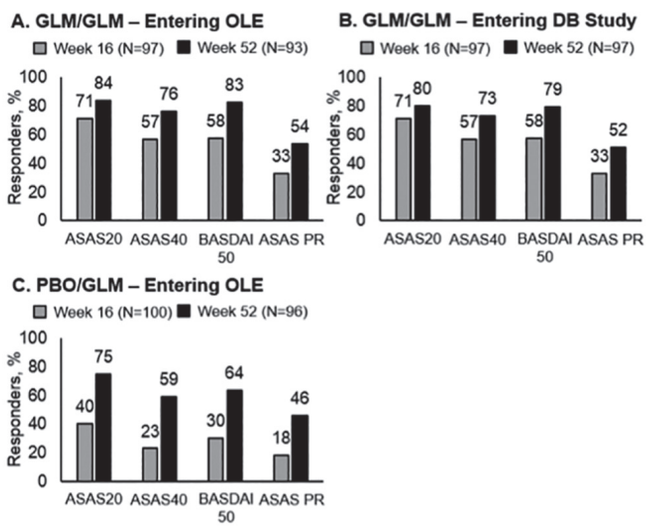

Figure. Proportions of Responders in the GO-AHEAD OLE.

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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?

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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 axial 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;10). 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.
Fulfilment of 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 PCS 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 over one year.

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

	n	Coefficient	Standard error	P-value
ΔPCS				
Univariable model				
ΔASDAS	86	-9.7	1.5	<0.001
Model for gender and ASAS classification				
Men fulfilling the clinical arm ΔASDAS	18	-11.8	4.0	0.010
Men fulfilling the imaging arm ΔASDAS	24	-15.8	2.7	<0.001
Women fulfilling the clinical arm ΔASDAS	32	-6.9	2.1	0.002
Women fulfilling the imaging arm ΔASDAS	12	-1.2	4.8	0.815
Abbreviations: Physical Component Summary (PCS), Ankylosing Spondylitis Disease Activity Score, CRP-based (ASDAS)				

Fulfilment of clinical or imaging arm and gender had a two-way interaction (p=0.10,R^2=38.6%). The effect of ΔASDAS on ΔPCS was most pronounced in men (imaging arm (-15.8;SE 2.7); clinical arm (-11.8;SE 4.0)) and to a lesser extent in women fulfilling clinical (-6.9;SE 2.1) but not the imaging arm (-1.2;SE 4.8).
Conclusions. Improvement in ASDAS is correlated to improvement in the physical component of HRQoL. The impact of this correlation largely depends on gender and arm of ASAS criteria.

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

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Aim. To describe illness perceptions and to explore the association between illness perceptions and disease activity in patients with early axial 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 that 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 1.0). Patients reported on average 4.2(SD 2.3) symptoms to be associated with axSpA (Tab. I). Pain, joint stiffness, fatigue, and sleeping problems were the most reported symptoms. All other dimensions showed a mean of approximately 3, except psychological attributions, risk factors, immunity and accident of the causal section, which had a mean of approximately 2. Patients with axSpA attributed their complaints mostly to heredity, chance or bad luck, or stress and worries.

Table I. Baseline characteristics of the Revised illness Perception Questionnaire (IPQ-R) and linear regression models of Ankylosing Spondylitis Disease Activity Score, CRP-based (ASDAS) and subscales of the IPQ-R at baseline adjusted for age and gender (n=119).

Baseline characteristics			Linear regression models with ASDAS (independent variable)		
Scale	**Range**	**Mean (SD)**	**Coefficient (β)**	**Standard error**	**p-value**
Illness identity (n=115)					
Identity	0-15	4.2 (2.3)	0.63	0.21	0.003*
Illness perceptions (n=119)					
Consequences	1-5	2.9 (0.8)	0.32	0.07	<0.001*
Timeline (acute/chronic)	1-5	3.7 (0.7)	0.01	0.06	0.863
Personal control	1-5	3.2 (0.6)	-0.10	0.06	0.086
Treatment control	1-5	3.4 (0.5)	-0.07	0.04	0.095
Illness coherence	1-5	3.3 (0.8)	-0.24	0.08	0.003*
Timeline (cyclical)	1-5	3.6 (0.8)	-0.04	0.07	0.634
Emotional representation	1-5	2.7 (0.8)	0.22	0.07	0.003*
Causal attributions(n=119)					
Psychological attributions	1-5	2.0 (0.8)	*Men* 0.22 *Women* 0.03	0.10 0.12	0.034* 0.796
Risk factors	1-5	2.2 (0.6)	0.08	0.05	0.133
Immunity	1-5	2.2 (0.7)	0.17	0.07	0.010*
Accident	1-5	1.8 (1.0)	0.07	0.09	0.405
Chance	1-5	3.3 (1.1)	0.12	0.10	0.248
** Statistically significant (p<0.05). Abbreviations: Ankylosing Spondylitis Disease Activity Score, CRP-based, ASDAS; standard deviation, SD.*					

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=0.010) 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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IS DISEASE ACTIVITY ASSOCIATED WITH WORK PRODUCTIVITY LOSS, PRESENTEEISM, AND ABSENTEEISM IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS? RESULTS FROM THE SPACE COHORT

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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 Spondyloathritis (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). Mean 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 univariable model (Table I), 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, absenteeism and stratified for its related effect modifiers at baseline among axial Spondyloarthritis patients who performed paid work in the SPondyloArthritis Caught Early (SPACE)-cohort (n=87).

	WPL		Presenteeism		Absenteeism	
	Coefficient (SE)	*p-value*	*Coefficient (SE)*	*p-value*	*Coefficient (SE)*	*p-value*
Univariable model (n=87)						
ASDAS	19.3 (2.6)	<0.001	16.9 (2.3)	<0.001	8.7 (2.1)	<0.001
Model for gender						
Men (n=46) ASDAS	14.3 (3.5)	<0.001	12.1 (2.8)	<0.001	4.4 (2.5)	0.086
Women (n=41) ASDAS	22.0 (3.7)	<0.001	19.3 (3.3)	<0.001	12.6 (3.5)	0.001
Model for duration of back complaints[1]						
<11 months (n=43) ASDAS	13.5 (4.3)	0.003	12.5 (3.9)	0.003	5.0 (3.9)	0.207
≥11 months (n=44) ASDAS	21.4 (2.9)	<0.001	18.3 (2.6)	<0.001	11.0 (2.3)	<0.001

[1] Continuous variables were split by their median. Abbreviations: Work Productivity Loss, WPL; Standard Error, SE; Ankylosing Spondylitis Disease Activity Score, CRP based, ASDAS

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.

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

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Aim. To explore the association between illness perceptions and Health-Related Quality of Life (HRQoL) in patients with short symptom duration of axial Spondyloarthritis (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 have 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 (Tab. I; β=-1.8 axSpA, β=-2.1 CBP) was associated with lower PCS. In male axSpA patients belief in severe consequences (β=-12.1), more negative emotions towards their complaints (β=-9.3), and stronger belief of psychological attributions as a cause (β=-8.8) were associated with lower PCS. Whereas in male CBP patients stronger belief in risk factors (β=-8.1) and immunity as a cause (β=-10.0) were associated with lower PCS. More illness coherence was associated with higher PCS in male axSpA (β=6.2) and all CBP patients(β=2.8). In women consequences (β=-6.3, axSpA) and strong emotional representations (β=-4.0, CBP) were statistically significant. No gender differences were found for risk factors (β=-6.0), immunity(β=-5.7) in axSpA and consequences(β=-7.9) in CBP patients.

Table I. Linear regression models of Physical Component Scale (PCS) of Health-Related Quality of Life (HRQoL) and subscales of the Revised Illness Perception Questionnaire (IPQ-R) at baseline adjusted for age and gender, and stratified in case of effect modification by gender (n=315).

Scale	Range	axSpA	Coefficient (SE)	p-value	CBP	Coefficient (SE)	p-value
Illness identity		(n=119)			(n=175)		
Identity	0-15		*-1.8 (0.6)*	*0.003*		*-2.1 (0.5)*	*<0.001*
Illness perceptions		(n=123)			(n=190)		
Consequences	1-5	Men	*-12.1 (2.7)*	*<0.001*		*-7.9 (1.1)*	*<0.001*
		Women	*-6.3 (1.9)*	*0.002*			
Timeline (acute/chronic)	1-5		-1.6 (2.2)	0.474		-2.3 (1.5)	0.122
Personal control	1-5		1.8 (2.3)	0.448		3.0 (1.6)	0.074
Treatment control	1-5		2.9 (3.0)	0.339		2.9 (2.2)	0.174
Illness coherence	1-5	Men	*6.2 (3.0)*	*0.048*			
		Women	-1.5 (1.6)	0.379		*2.8 (1.2)*	*0.019*
Timeline (cyclical)	1-5		1.2 (1.8)	0.503		-0.1 (1.3)	0.938
Emotional representation	1-5	Men	*-9.3 (3.0)*	*0.003*	Men	0.9 (2.4)	0.712
		Women	-1.5 (1.9)	0.419	Women	*-4.0 (1.2)*	*0.001*
Causal attributions		(n=123)			(n=191)		
Psychological attributions	1-5	Men	*-8.8 (3.0)*	*0.004*		-0.5 (1.4)	0.717
		Women	-0.3 (0.2)	0.874			
Risk factors	1-5		*-6.0 (2.6)*	*0.023*	Men	*-8.1 (3.0)*	*0.010*
					Women	3.1 (2.3)	0.170
Immunity	1-5		*-5.7 (2.0)*	*0.004*	Men	*-10.0 (2.2)*	*<0.001*
					Women	-2.5 (1.6)	0.114
Accident	1-5		*-3.8 (1.5)*	*0.016*		-1.1 (1.0)	0.279
Chance	1-5		-0.4 (1.4)	0.776		-1.8 (1.0)	0.069

Statistically significant results are printed in italics. Abbreviations: axial Spondyloarthritis, axSpA; chronic back pain, CBP; standard error, SE

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 SPONDYLOARTHRITIS – RESULTS FROM MULTI-NATIONAL ASAS-COMOSPA STUDY

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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 males, mean age 43 (SD 14), median disease duration 5 years (SD 9.5) 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.

Outcome	RDCI (β [95%CI])
BASFI[$]	0.36 [0.30-0.43]
BASDAI~	0.53 [0.45-0.61]
ASDAS^	0.17 [0.13-0.20]
PAatient's global assessment of disease activity^	0.45 [0.36-0.53]
EQ5D**	-0.03 [-0.04- -0.02]

*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
**Model also adjusted for BASFI, ASDAS.

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 APREMILAST IN PATIENTS WITH PSORIATIC ARTHRITIS: POOLED ANALYSIS OF PALACE 1-3

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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. Adebajo 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

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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 QUality of Life as Outcomes and its VAriation with DIsease States (QUO-VADIS) study.
Materials and Methods. Bionaïve 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 (30 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 (31.1) 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.

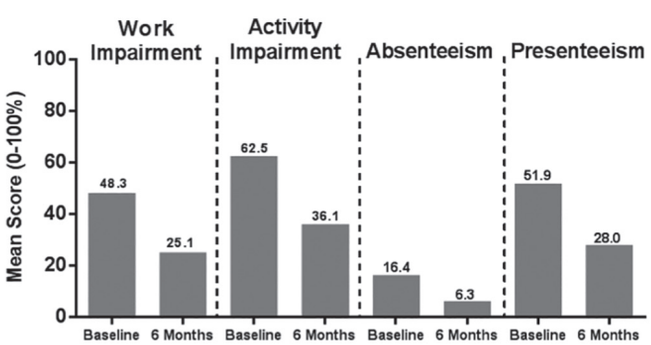

Figure. Mean WPAI-SpA at Baseline and 6 Months.

P70

CLINICAL AND QUALITY OF LIFE IMPROVEMENTS WITH GOLIMUMAB AND INFLIXIMAB IN A LARGE REAL-LIFE ANKYLOSING SPONDYLITIS (AS) POPULATION: RESULTS FROM THE QUO-VADIS STUDY

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Introduction/Aims. We assessed baseline parameters associated with health-related quality-of-life (HRQoL) improvement in AS patients with anti-TNF treatment (golimumab [GLM]; infliximab [IFX; originator]) in the QUality of Life as Outcomes and its VAriation with DIsease States (QUO-VADIS) study.
Methods. Bio-naïve AS patients (modified NY criteria) newly prescribed GLM or IFX were followed ~6 months in this prospective, observational study. Demographic and clinical characteristics, disease activity, and HRQoL were summarized. The Classification and Regression Trees (CART) analysis evaluated the association of baseline parameters with HRQoL change at 6 months, measured by ≥5-point improvement in Short-Form 36 (SF-36) Physical Component Summary (PCS) score. Clinical parameters included Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI), and AS Disease Activity Scores (ASDAS).
Results. 963 patients received ≥1 dose of medication (78% GLM; 22% IFX). Mean age was 42.7 years.
Mean symptom and diagnosis duration were 11.6 and 5.3 years, respectively; 63.8% of patients were HLA-B27 positive. Mean baseline BASDAI, ASDAS-CRP and BASFI scores were 6.21, 3.59 and 5.34, respectively. 41.4% and 49.3% of patients reported high and very high ASDAS disease activity. Clinical and HRQoL improvements were observed following 6 months of treatment (Figure). The CART analysis identified the following baseline parameters and cutoff values associated with SF-36 PCS response at 6 months: ASDAS (≥3.48), C-Reactive Protein (CRP) (≥8.55 mg/L), age (≤35.5 years), and BASFI (≥1.15); the algorithm had 57.5% sensitivity and 61% specificity with ROC-AUC of 0.61.
Conclusions. GLM or IFX treatment demonstrated clinical and HRQoL improvements over 6 months in a large, real-world population of AS patients. Higher ASDAS, elevated CRP, and younger age at baseline were associated with HRQoL improvements.

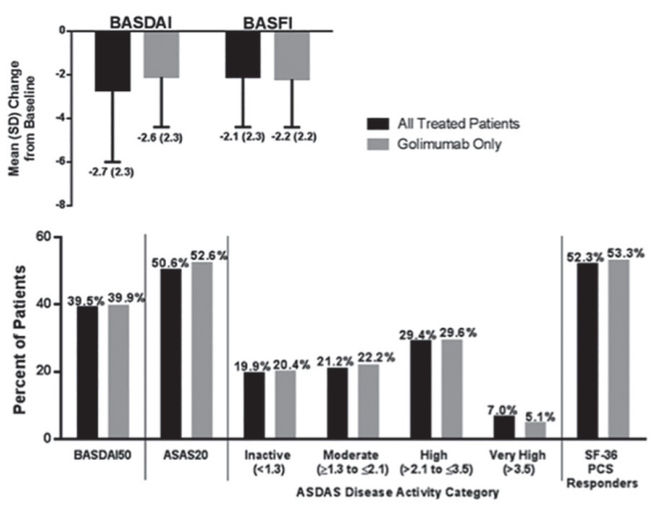

Figure. Improvement in Clinical and QoL Parameters Following 6 mounth of Treatment.

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DEVELOPMENT OF SPA-FEATURES IN PATIENTS WITH CHRONIC BACK PAIN OVER A ONE-YEAR COURSE

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Aim. To explore whether patients with suspicion of axial spondyloarthritis (axSpA) develop Spondyloarthritis (SpA)-features over time, and to study the effect of gaining features on diagnosis and classification.
Methods. 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.

	Number of features gained after one year					
Diagnosis	0	1	2	3	>3	**Total**
AxSpA baseline and FU	71	50	18	9	2	150
AxSpA only at FU	5	9	2	-	-	16
AxSpA only at baseline	11	8	2	1	-	22
No AxSpA baseline and FU	40	23	2	1	-	66
Total	127	90	24	11	2	254

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.

P72

DOES THE PRESENCE OF MULTIPLE SPA-FEATURES IN PATIENTS WITH CHRONIC BACK PAIN ALWAYS LEAD TO DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS?

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Aim. To investigate whether all patients with short duration chronic back pain (CBP) and multiple spondyloarthritis (SpA)-features are always diagnosed with axial spondyloarthritis (axSpA) by rheumatologists and to describe features of these patients.
Methods. The SPondyloArthritis Caught Early (SPACE)-cohort includes CBP patients (≥3 months, ≤2 years, onset <45 years). Baseline data were used for the analyses. Following a fixed protocol all patients underwent a full diagnostic work-up. Each center interpreted MRI-SI and X-SI on presence of sacroiliitis (yes/no) using global assessment as part of routine clinical practice. Total number of SpA-features was calculated excluding sacroiliac imaging and HLA-B27 status. The treating rheumatologist provided clinical diagnosis of patients and the ASAS-criteria for axSpA were used for classification.
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%, 83.2%, 68.0% respectively). Of the patients with 2 and 3 SpA-features with negative 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 with ≥4 SpA-features, 18/94 patients (19.1%) with negative imaging (of which 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.

Fig. 1. Diagnosis and classification of patients with 2, 3, and ≥4 SpA-features after medical history taking, physical examination, and measurement of acute phase reactants, followed by sacroiliac imaging and HLA-B27 testing.

Number of SpA-features	X-SI status	HLA-B27/MRI status	Rheumatologist SpA diagnosis yes	Rheumatologist SpA diagnosis no	ASAS axSpA classification yes	ASAS axSpA classification no
2 *n*=148	X-SI+ *n*=16	B27+/MRI+	14		14	
		B27+/MRI-	1		1	
		B27-/MRI+	1		1	
		B27-/MRI-				
	X-SI- *n*=132	B27+/MRI+	15		15	
		B27+/MRI-	15	20	35	
		B27-/MRI+	5	2	7	
		B27-/MRI-	11*	59		71
3 *n*=85 [1]	X-SI+ *n*=5	B27+/MRI+	3		3	
		B27+/MRI-	1		1	
		B27-/MRI+	1		1	
		B27-/MRI-				
	X-SI- *n*=78	B27+/MRI+	17*		18	
		B27+/MRI-	11*	9	21	
		B27-/MRI+	8		8	
		B27-/MRI-	8	21		29
≥ 4 [2] *n*=125	X-SI+ *n*=29	B27+/MRI+	15		15	
		B27+/MRI-				
		B27-/MRI+	8		8	
		B27-/MRI-	5		5	
	X-SI- *n*=94	B27+/MRI+	16		16	
		B27+/MRI-	21	4	25	
		B27-/MRI+	8		8	
		B27-/MRI-	28*	14		43

[1] 2 patients missing X-SI, not included in subanalyses. [2] 2 patients missing X-SI, not included in subanalyses. * 1 patient diagnosis not available. X-SI, radiograph of sacroiliac joints; HLA-B27, human leucocyte antigen B27; MRI-SI, magnetic resonance imaging of sacroiliac joints; Imaging according to global assessment (local reading). Diagnosis based on information after full diagnostic work-up: medical history, physical examination, imaging, and laboratory testing. ASAS axSpA criteria, Assessment of SpondyloArthritis international Society criteria for axial spondyloarthritis.

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

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Aim. This post-hoc analysis evaluated the performance of a modified MDA (mMDA) criteria (excluding psoriasis) in pSpA patients (pts) from the ABILITY-2 study.
Methods. The validity of mMDA was examined in pSpA pts from ABILITY-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 joints≤1); (2) (SJC, 76 joints≤1); (3) pt pain VAS≤15/100 mm; (4) PtGA VAS≤20/100 mm; (5) HAQ-DI≤ 0.5; and (6) tender entheseal points ≤1.
Enthesitis was assessed by Leeds Enthesitis Index (LEI) or SPARCC) Enthesitis Index. Proportion of pts achieving the 4 different versions of mMDA were evaluated (either 4 or 5 of 6 using LEI or SPARCC).
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 1-3 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

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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 occiput-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 daily 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.

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FLARE IN AXIAL SPONDYLOARTHRITIS – RESULTS OF CLINICAL REAL PRACTICE

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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 (ptn) with worsening of axSpA status according BASDAI and ASDAS-CRP, number of swollen joint, and MASES. The second step of the study was collection the rheumatologists' opinion about each ptn, 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, if not – Δ pain ≥3), 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 ptn's treatment? If «yes», then what parameter had maximal influence in treatment decision?
Results. Data from 661 ptn with axSpA fulfilling ASAS criteria for axSpA (2009) were analyzed totally. 86 patients had flare due their physician's decision (65 of them had ankylosing spondylitis fulfilling mNew-York criteria, 21 – nr-axSpA, fulfilled ASAS criteria for axSpA), mean age was 34.7±9.8 years (min – 19, max-64 years), 61,6% male, mean disease duration– 86,5±92,1 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 I. Occurrence of different axial spondyloarthritis' flare definitions (n=86 patients).

Activity measurement tool	Definition of flare	Occurrence, %
Pain (0-10)	Δ pain ≥ 2.0 and final level ≥ 4.0	50.0
	Δ pain ≥ 3.0	31.4
	If initial level of pain ≥ 4.0: Δ pain ≥ 2.0, if not: Δ pain ≥ 3.0	47.7
BASDAI	Δ BASDAI ≥ 2.0	17.4
	Δ BASDAI ≥ 2.0and final level ≥ 4.0	36.0
	Δ BASDAI ≥ 3.0	20.9
	Δ BASDAI ≥ 3.0 and final level ≥ 4.0	36.0
	If initial BASDAI ≥ 4.0: Δ pain ≥ 2.0, if not: Δ pain ≥ 3.0	34.9
ASDAS-CRP	Δ ASDAS ≥ 0.6	40.7
	Δ ASDAS ≥ 0.9	29.1
	Δ ASDAS ≥ 1.1	33.7
	Δ ASDAS ≥ 0.6 and final level ASDAS ≥ 1.3	72.1
Night pain	Δ pain ≥ 2.0 and final level ≥ 4.0	44.2
	Δ pain ≥ 3.0	29.1
	If initial pain ≥ 4.0: Δ pain ≥ 2.0, if not: Δ pain ≥ 3.0	39.5
Number of swollen joints	Δ ≥ 1.0	37.2
MASES	Δ pain ≥ 1.0	39.5

The most important definitions ASAS flare according the opinion of physicians are Δ ASDAS-CRP ≥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 mostly depended 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 ptn 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.

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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

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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 APR ≤4 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 (51.1%); DAS-28 (CRP) <2.6 (41.9%); SJC/TJC mean percent improvements (–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%). No new safety concerns were identified. Most AEs were mild/moderate; few discontinuations were due to AEs (0.7%) over Weeks >104 to ≤156.
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. Adebajo contributed as an original author.

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

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Introduction/Aim. The phase 3b LIBERATE (Evaluation in a Placebo-Controlled Study of Oral Apremilast and Etanercept in Plaque Psoriasis) study (NCT01690299) evaluated efficacy and safety of apremilast (APR) 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 Wk16; thereafter, pa-

tients switched to or continued APR30 (PBO/APR30, ETN50/APR30, APR30/APR30). The primary endpoint was achievement of a ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI-75) at Wk16 with APR30 vs. PBO; secondary endpoint was PASI-75 achievement at Wk16 with ETN50 vs. PBO. Nail (Nail Psoriasis Severity Index [NAPSI]) and scalp (Scalp Physician Global Assessment [ScPGA]) involvement were assessed at Wks16 and 52.
Results. At Wk16, PASI-75 achievement was significantly greater (p<0.0001) with APR30 (39.8%) or ETN50 (48.2%) vs. PBO (11.9%). This study was not designed for APR30 vs. ETN50 comparisons; Wk16 PASI-75 achievement was not significantly different between APR30 and ETN50 (p=0.2565, post hoc).
PASI-75 response (APR30/APR30: 50.6%; ETN50/APR30: 55.4%) was sustained with APR30 at Wk52.
At Wk16, mean percent improvement from baseline in NAPSI score and achievement of ScPGA 0 (clear) or 1 (minimal) were higher for APR30 and ETN50 vs. PBO. Continued improvement in nail and scalp psoriasis was observed at Wk52 in all groups. AEs were consistent with known safety profiles of APR and ETN.
Conclusions. APR30 demonstrated significant efficacy vs. PBO at Wk16, which was generally sustained at Wk52. Efficacy was maintained in ETN50 patients who switched to APR30.

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

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Introduction. In enteropathic spondyloarthritis (ES) the coexistence of gut and articular inflammation advocates an integrated approach of the patients in clinical practice, to achieve an optimal therapeutic management and defined clinical outcomes.
Methods. From January 2014 to January 2016, 225 patients affected by IBD were enrolled in a prospective study and evaluated at baseline, 6 and 12 months for gastrointestinal and articular activity and patient-reported outcomes on quality 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 articular symptoms and in 60 (24%) an active ES was diagnosed according to ASAS criteria. Peripheral arthritis was present in 31/60 (52%) whereas axial involvement was diagnosed in 29/60 (48%) patients. At baseline, the QoL in ES patients resulted significantly worse than IBD according to IBDQ (p<0.0001). PtGA (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-CRP 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 improvement 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 between gastroenterologist and rheumatologist.
Conclusion. Only an integrated clinical evaluation is able to improve significantly disease activities and QoL in patients with ES.

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

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Background. The potential influence of pain characteristics including the neuropathic 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 component in patients with axSpA (including non-radiographic axSpA and ankylosing 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. Patients 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 36.5±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.

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

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Introduction. The concept of axial spondyloarthropathy (SpA) recently recommended by the ASAS includes patients comprising the early and late stages of the disease. This concept also includes patients not meeting the criteria for ankylosing 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.

		BASDAI	BASFI	VAS spinal pain	ASQOL
STAI –I(state anxiety)	R	0.432	0.343	0.373	0.481
	P	<0.001	<0.001	<0.001	<0.001
STAI-II (trait anxiety)	R	0.375	0.342	0.234	0.420
	P	<0.001	<0.001	0.005	<0.001
Beck anxiety	r	0.430	0.375	0.326	0.508
	p	<0.001	<0.001	<0.001	<0.001
Beck depression	r	0.427	0.432	0.410	0.595
	p	<0.001	<0.001	<0.001	<0.001

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

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Aim. Axial spondyloarthritis (axSpA) comprises patients with axial psoriatic arthritis (axPsA) as well as other non-psoriatic forms of SpA. The aim of this study was to compare clinical features in patients with axPsA and non-psoriatic axSpA.
Methods. Patients with PsA (meeting the CASPAR criteria for PsA) with predominantly axial involvement (presence of IBP and/or sacroiliitis on imaging), and patients with axSpA (meeting the ASAS criteria for axSpA who never had psoriasis) were examined for clinical and laboratory parameters and specific tests by using standard forms.
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).

	axPsA (n=94)	Non-psoriatic axSpA (n=153)
Age	40.84 ± 10.35	38.60 ± 9.01
Male,%	45.7	53.6
HLA B27+,%[a]	25.0	53.2
Peripheral arthritis,%[a]	61.5	34.2
Symptom duration	8.41 ± 7.47	10.48 ± 8.69
VAS-pain	5.11 ± 2.79	4.68 ± 3.05
Patient global	4.91 ± 2.71	4.91 ± 2.87
Physician global	4.38 ± 2.30	4.08 ± 2.43
BASDAI	4.81 ± 2.52	4.34 ± 2.42
BASFI	2.96 ± 2.79	2.93 ± 2.57
Hospital depression score	6.82 ± 3.38	7.03 ± 4.16
Hospital anxiety score	6.96 ± 4.20	7.45 ± 4.39
SF36 Physical functions[b]	50.47 ± 28.34	58.90 ± 25.91
SF36 Physical role	41.58 ± 41.99	45.42 ± 42.57
SF36 Bodily pain	37.55 ± 25.62	43.06 ± 24.97
SF36 General health	39.14 ± 22.09	41.42 ± 20.76
SF36 Vitality	43.37 ± 21.51	45.37 ± 21.80
SF36 Social functions[b]	52.19 ± 30.33	61.14 ± 25.96
SF36 Emotional role	41.36 ± 43.30	46.05 ± 41.12
SF36 Mental health	54.15 ± 22.14	58.15 ± 20.36
CRP, mg/l	10.53 ± 14.08	11.43 ± 19.44

[a]<0.001, [b]<0.05, others not significant.

Conclusion. Axial SpA is an umbrella term of diseases that share clinical, genetic and pathological characteristics. Patients with axPsA share many similar clinical features with non-psoriatic axSpA however may have poorer physical functions and more frequent peripheral arthritis. Longitudinal data in the matched groups may provide vigorous data for the potential differences and similarities and natural course.

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

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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 (χ^2) 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 JSpADA (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 (χ^2:10.05) and ACR Pedi 90 (χ^2:10.12) 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 JSpADA 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.

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FOOD INTAKE, HEALTHY EATING INDEX AND DIETARY INFLAMMATORY INDEX IN PATIENTS WITH PSORIATIC ARTHRITIS

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Introduction. It is not well established if a healthy diet could potentially improve joint and skin disease activity in patients with psoriatic arthritis (PsA) and metabolic syndrome (MetS).
Aim. To analyze the food intake of patients with PsA, including the Dietary Inflammatory Index (DII) and Healthy Eating Index (HEI).
Patients and Methods. A total of 97 patients with PsA were included in this cross-sectional study.
Food intake was evaluated using a 3-day food-record. Nutrients were adjusted for energy using Willet and Stampfer's method, to then calculate the HEI and the DII. Level of significance was set as $p<0.05$.
Results. Patients with PsA had higher caloric consumption and inadequate intake of sodium, fibers, vitamin A, vitamin E, magnesium, zinc and copper when compared to Dietary Reference Intake. The HEI had low scores (63.24±10.25), suggesting that 95% of them would need a nutritional intervention or dietitian counseling. Similarly, DII scores were high (+2,48±0,90).
Conclusion. Patients with PsA had inadequate diet intake, with low vitamin and mineral intake, and a pro-inflammatory pattern that could hamper the MetS.

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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?

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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, C-reactive protein) and skin (PASI, BSA) and joint (DAS28-CRP, 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 (FMI) (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.

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

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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 (Work productivity and Daily activity). Depression risk (HAD-depression ≥7), anxiety risk (HAD-anxiety ≥10 and fatigue severity scale score ≥36 were assessed in patients with PsA.
Results. A total of forty patients with PsA (mean age 46.26±11.5 year) were included. Mean symptom duration was 7.49±10.33 years. Fatigue Severity Score was 3.48±1.27 years. HDO Depression Score was 6.46±4.09 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.

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FEET BIOMECHANICS IN PSA PATIENTS

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Introduction. The enthesis have been recognized as a central anatomical and functional pathogenic "target' organ in psoriatic arthritis (PsA). We aim to characterize biomechanical parameters of foot function in PsA patients in comparison with healthy controls (HC).
Patients and Methods. A cohort of patients with PsA (CASPAR criteria), less than five years disease duration, was assembled. Demographic and clinical data including disease activity assessment were collected and registered, as well as, joint involvement asymmetry, whenever present.
Patients gait was characterized using a six-segment model for feet biomechanics assessment based in the application of 25 spherical reflective markers placed, in both left and right shank and foot.
Plantar pressure measures and spacial and temporal parameters during gait were also registered.
Results. A total of 13 PsA patients and 14 HC were included in this pilot analysis. Ground reaction forces of PsA patients did not differ from HC although absolute values were higher in the former. We highlight the statistical results concerning the lateral forefoot segment revealing differences in eversion and inversion motion in opposite toe off ($p=0.015$), feet adjacent $p=0.001$), toe-off ($p=0.017$), eversion peak ($p=0.013$) and inversion peak ($p=0.015$) between both groups. Considering the mean values, the affected foot has lower values when compared with the healthiest foot. Significant differences in midfoot contact area in cm2, segment and foot percentage ($p=0.039$, $p=0.033$, $p=0.052$, respectively) and in first metatarsal contact area in segment percentage ($p=0.011$) were observed. Similarly the midfoot contact area showed higher values in the affected foot when compared with the healthy foot.
The analysis of spacial and temporal parameters denoted that patients have a longer double support than HC.
Conclusions. This work allowed comparing feet biomechanical features between PsA patients and HC, but, as important, between affected and non-affected feet in the same patient.

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DETERMINANTS OF QUALITY OF LIFE, HEALTHCARE SERVICES DEMAND AND LABOR-MARKET STATUS IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS PATIENTS

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Introduction. Ankylosing Spondylitis (AS) or radiographic axial spondyloarthritis, typically affects young people, leading to progressive deterioration of physical function and quality of life (QoL) with higher use of healthcare services. Work disability, measured by sick leave days and early retirement, is also higher in AS patients than in the general population, with a remarkable negative impact on productivity and social costs. The objectives of this study were to assess the gradient of AS severity for QoL, healthcare services demand and labour-market status, in a group of AS patients.
Materials and Methods. We collected cross-sectional data in patients, above 17 and under 65 years old (working active ages), concerning demographic characteristics, disease duration, time to diagnosis, BASDAI, BASFI, BASMI, SF-36, ASQoL, EQ-5D and the ASDAS. The number of appointments and emergency room visits during the year before and working status, were also collected. To measure the gradient of AS on QoL scores, healthcare use and working status, regression models, with application of stepwise procedure, were performed.
Results. A total of 133 patients were included (62.3% men and 37.1% women), with a mean age of 43.5±11.9 years (range 20–65 years). For SF-36 (51.5±18.7), ASQoL (7.3±5.2) and EQ5D (0.7±0.2), the BASDAI and BASFI scores matter

and all mean higher value associated with lower health. The effect of mSASSS seems to be modest. Regarding healthcare use only the BASFI is positively associated with the number of medical appointments. The ASDAS seems to be the only determinant for emergency rooms visits. In this group of patients, 3,96% referred sick leave days and 20,30% were retired. The probability of being employed is negatively associated to age and to BASMI. Time to diagnosis have no influence on these gradients.
Conclusions. BASDAI 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.

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PATTERNS OF CLINICAL ASSESSMENT OF GENERAL PRACTITIONERS WHEN FACING A PATIENT SUSPECTED FOR SPONDYLOARTHRITIS; A STUDY WITH UNANNOUNCED STANDARDIZED PATIENTS IN DAILY PRACTICE

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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. GP (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 education versus the control group.
Results. Thirty-eight GP-residents (mean age 27.9 yrs, 32% male) and 30 GPs (mean age 52.5 yrs, 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.

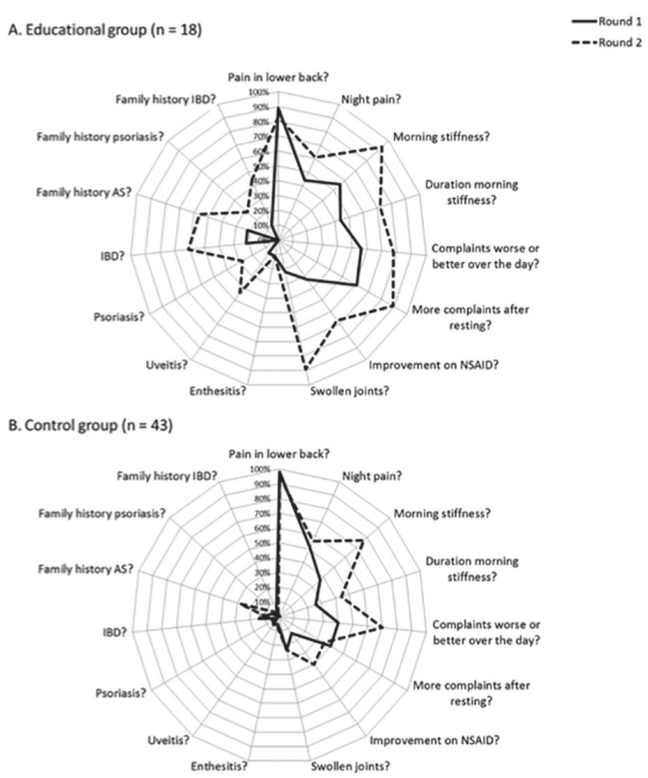

Figure. History taking pattern of GP (residents) facing a patient with axial SpA in round 1 and 2.

Controls also tended to ask more questions regarding the inflammatory character of the complaint and family history of SpA in round 2, but not the other subgroups. Peripheral SpA case: in round 2, GP residents who received the educational intervention asked more questions regarding extra-articular complaints and family history of SpA. However, the observed gain was less evident as compared to the axial SpA case.
Conclusion. Targeted education can help GPs to improve their history taking and hence pattern recognition of patients suspected for SpA.

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

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Aim. To assess whether presence of spondyloarthritis (SpA) manifestations (ankylosing spondylitis (AS), psoriasis, uveitis, reactive arthritis, inflammatory bowel disease (IBD)) in first- and second-degree relatives of patients with chronic back pain (CBP) is associated with higher risk for axial spondyloarthritis (axSpA).
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, IBD, 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%), IBD 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, IBD, 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).

	HLA-B27 positivity	
	OR (95% CI)	*P*- value
Any FH	2.7 (1.6-4.5)	<0.0001
AS	5.0 (2.6-9.7)	<0.0001
Psoriasis	1.1 (0.6-2.1)	0.774
Uveitis	25.2 (3.2-196.9)	0.002
IBD	0.8 (0.3-1.9)	0.640
Reactive arthritis	1.9 (0.3-15.6)	0.531
	ASAS axSpA criteria	
	OR (95% CI)	*P*- value
Any FH	2.1 (1.3-3.5)	0.003
AS	2.9 (1.5-5.5)	0.001
Psoriasis	1.1 (0.6-2.1)	0.795
Uveitis	12.4 (2.7-57.3)	0.001
IBD	1.1 (0.5-2.5)	0.864
Reactive arthritis	0.7 (0.07-6.5)	0.730

HLA-B27: human leukocyte antigen B27; any FH: any family history manifestation in first-and second-degree relatives; AS: ankylosing spondylitis; IBD: 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.

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ETHNICITY AND DISEASE SEVERITY IN ANKYLOSING SPONDYLITIS

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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 Hispanic) 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 62.5[IQR 35.7, 79.4] vs. 27.8 [12.6, 52.3] 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 3.5[1.7, 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 [7.0, 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 9.5 [±4.3] and median 38.2 [46.0, 55.2], respectively) compared to whites (7.3 [±4.1] and 6.4 [0, 32.6]) and Hispanics (7.3 [±4.1] and 8.1 [0, 35.9], $p=0.004$, 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 with AS have more severe disease compared to either whites or Hispanics.

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COMPARISON OF THE IMAGING AND CLINICAL ARMS OF ASAS AXIAL SPONDYLOARTHRITIS CLASSIFICATION CRITERIA IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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Aim. The ASAS classification criteria have provided new insights in the classification of axial spondyloarthropathy (axSpA). Based on the clinical and imaging data patients are classified 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 subgroup of patients who had been treated with TNF inhibitors (TNFi) and responses at 3 months was analyzed.
Results. There were a total of 71 nr-axSpA patients (34 imaging and 37 clinical). Median age and disease durations were 34.9 (18-64) and 7 (1-34) years respectively. 52.1% of the group were males and 80.3% were B27 positive. Patients were stratified by classification and patients in the imaging arm categorized into B27+ (n=20) and B27- (n=14) subsets. Comparison of three groups (imaging B27+ *vs* imaging B27- *vs* clinical arms) revealed no difference with respect to age, sex distribution, disease duration, extra-articular 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.

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FUNCTIONAL INTERACTION OF THE ANKYLOSING SPONDYLITIS ASSOCIATED ENDOPLASMATIC RETICULUM AMINOPEPTIDASE 2 (ERAP2) WITH THE HLA-B*27 PEPTIDOME IN HUMAN CELLS

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Introduction. The final steps of the antigen processing pathway of Major Histocompatibility 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 pathogenetic mechanism of this disease.

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EPIGENETIC AND EXPRESSION ANALYSIS OF ANKYLOSING SPONDYLITIS ASSOCIATION LOCI POINT TO KEY CELL TYPES DRIVING DISEASE

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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 AS 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 pleiotrophy 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 in 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 $CD8^+$ T cells. Epigenetic analyses also showed evidence that AS-associated signals operate in gut cell types including in mucosa from the small intestine, sigmoid colon and rectum. These findings particularly relate to pleiotropic loci also associated with IBD, psoriasis, and PSC.
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.

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IDENTIFICATION OF DIFFERENTIALLY METHYLATED GENES IN PURIFIED DISEASE RELEVANT BLOOD CELL POPULATIONS IN PATIENTS WITH SPONDYLOARTHRITIS

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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 53.2±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 monitoring 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 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.

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ERAP1 DIFFERENTIALLY SHAPES THE TWO MAJOR SUBPEPTIDOMES OF HLA-B*51:01: IMPLICATIONS FOR THE PATHOGENESIS OF BEÇHET'S DISEASE

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Introduction. HLA-B*51:01 is the main risk factor for Beçhet's disease. ERAP1, 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 Beçhet's disease.
Objectives. To characterize the endogenous HLA-B*51:01 peptidome and its implications for the functional and pathogenic interaction of ERAP1 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 ERAP1 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 Pro2 showed a preference for ERAP1-susceptible P1, while ligands with Ala2 showed a strong preference for Asp1, which is very resistant to ERAP1. The Pro2 subpeptidome showed higher affinity for B*51:01 than the Ala2 subpeptidome.
Conclusions. ERAP1 does not trim peptidic bonds involving Proline. This feature is crucial, since ligands with Pro2 cannot be destroyed by ERAP1, while ligands with Ala2 can be destroyed by over-trimming when the P1 residue is susceptible to this enzyme, favoring peptides with ERAP1-resistant P1 residues. We propose a mechanism in which ERAP1 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 peptidome. The correct balance between both subpeptidomes may be crucial for Behçet's disease susceptibility.

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FUNCTIONAL INTERACTION OF ERAP1 WITH HLA-B*27 SUBTYPE-BOUND-PEPTIDOME

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Introduction. Ankylosing spondylitis (AS) is strongly associated with HLA-B*27. Genome wide association studies revealed that the Endoplasmic Reticulum Aminopeptidase (ERAP) 1 is a significant risk factor for this disease in HLA-B27$^+$ individuals. Thus, ERAP1 polymorphism may affect AS susceptibility by altering peptide-dependent features of HLA-B27.
Objectives. 1) To characterize the alterations, and their mechanism, induced in the HLA-B*27:04 and B*27:05 peptidomes expressed in live cells by natural ERAP1 polymorphisms predisposing to AS, 2) to analyze the relationship between the peptidomes from subtypes differentially associated with AS and their ERAP1 dependency.
Methods. HLA–B*27–bound peptides were isolated from human lymphoid cell lines expressing the same or distinct ERAP1 variants and characterized by mass spectrometry. The relative amount of each shared peptide, in any given cell line pair, was estimated from the respective ion peak intensities.
ERAP1 values ranging 0 to 100 were assigned to N-terminal flanking and P1 residues based on their susceptibility to ERAP1 trimming.
Results. 1) AS-associated ERAP1 polymorphisms generated in HLA-B*27:04 an optimized peptidome with more ERAP1-resistant N-flanking and P1 residues, shorter length and higher affinity and thermostability, 2) AS-associated ERAP1 polymorphisms generated in HLA-B*27:05 a peptidome with higher molecular weight, more ERAP1-resistant P1 residues, differential use of internal residues and higher affinity, 3) peptidomes from AS-associated subtypes showed higher dependency on ERAP1 compared to non-associated ones.
Conclusions. 1) The mechanism of ERAP1/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 ERAP1 variants, 2) the lower discrimination of non-AS-associated subtypes for peptides differing in the susceptibility of their P1 residues to ERAP1 is similar to the effect of low-activity variants on the HLA-B*27:05 and B*27:04 peptidomes and suggests that non-AS-associated subtypes are less influenced by ERAP1 polymorphism than AS-associated ones.

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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)

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Introduction. Susceptibility to spondyloarthritis (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-

tients 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.

All patients (both with and without axSpA)			
	DESIR	Controls	OR
HLAB27+/HLA-B*40:01+	19 (3.3%)	36 (0.4%)	19.0 (95% CI: 10.7-33.6)
HLAB27+/HLA-B*40:01-	319 (54.8%)	832 (8.2%)	13.7 (95% CI: 11.5-16.6)
HLAB27-/HLA-B*40:01+	11 (1.9%)	936 (9.2%)	0.4 (95% CI: 0.2-0.8)
HLAB27-/HLA-B*40:01-	233 (40.0%)	8373 (82.3%)	1
Total	582 (100%)	10177 (100%)	
	SPACE	Controls	OR
HLAB27+/HLA-B*40:01+	13 (4.8%)	22 (0.4%)	18.0 (95% CI: 8.9-36.3)
HLAB27+/HLA-B*40:01-	85 (31.3%)	381 (6.8%)	6.8 (95% CI: 5.1-9.0)
HLAB27-/HLA-B*40:01+	25 (9.2%)	654 (11.7%)	1.2 (95% CI: 0.8-1.8)
HLAB27-/HLA-B*40:01-	149 (54.8%)	4527 (81.1%)	1
Total	272 (100%)	5584 (100%)	
AS patients only			
	AS (DESIR)	Controls	OR
HLAB27+/HLA-B*40:01+	8 (6.3%)	36 (0.4%)	19.0 (95% CI: 10.7-33.6)
HLAB27+/HLA-B*40:01-	88 (69.8%)	832 (8.2%)	13.7 (95% CI: 11.5-16.6)
HLAB27-/HLA-B*4001+	1 (0.8%)	936 (9.2%)	0.4 (95% CI: 0.2-0.8)
HLAB27-/HLA-B*4001-	29 (23.0%)	8373 (82.3%)	1
Total	126 (100%)	10177 (100%)	
	AS (SPACE)	Controls	OR
HLAB27+/HLA-B*4001+	2 (8.3%)	22 (0.4%)	68.6 (95% CI: 13.1-358.7)
HLAB27+/HLA-B*4001-	14 (58.3%)	381 (6.8%)	27.7 (95% CI: 10.6-72.6)
HLAB27-/HLA-B*4001+	2 (8.3%)	654 (11.7%)	2.3 (95% CI: 0.5-11.5)
HLAB27-/HLA-B*4001-	6 (25)	4527 (81.1%)	1
Total	24 (100%)	5584 (100%)	

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

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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 cells in response to Gram-positive and Gram-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 on 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 20±12.94months (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 (7772.07±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 ± 42.73±39.05, p=0.56) and on neutrophils (2072.85±1414.27 vs 5061.93±3363.33, p=0.56).
Conclusions. 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.

P99

INCREASED LYMPHOCYTE GM-CSF PRODUCTION IS A HALLMARK OF SPONDYLOARTHRITIS

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Background. Immunological, genetic and therapeutic studies have implicated the "type 17" inflammatory axis in SpA. GM-CSF is emerging as a cytokine that marks out a potentially pathogenic subset within this inflammatory axis. Inhibition of this cytokine pathway is currently in clinical trials for rheumatoid arthritis. However, it is not clear whether GM-CSF-producing T cells are part of the "type 17" axis or function independently. We sought to investigate GM-CSF production by SpA blood and joint leucocytes.
Methods. Blood, synovial fluid and synovial tissue from patients with SpA was studied ex-vivo. Age and sex matched healthy controls, and RA inflammatory disease controls were also studied. GM-CSF production by different cell types was characterised using multi-colour flow cytometry (FACS) and time-of-flight cytometry (CyTOF).
Results. CyTOF analysis revealed ex-vivo GM-CSF production from multiple lymphoid cell lineages, with CD4 cells representing the largest group of GM-CSF-producers. In FACS the percentage of CD4 cells producing GM-CSF was significantly increased in SpA PBMCs ex-vivo compared to healthy controls (mean 7.73 % vs 4.96% n=38, p<0.005). In addition, there was an expansion of GM-CSF+CD8 cells in SpA and an expansion of IL-17A/GM-CSF double positive CD4, CD8, γδ and NK cells in AS compared to RA and healthy controls. The mean percentage of GM-CSF-positive CD4 cells from *ex-vivo* synovial fluid mononuclear cells (SFMCs) was 32.2% and significantly higher compared to matched PBMCs (n=5, p=0.005). Phenotypic and transcriptional characterisation of GM-CSF-producing CD4 T cells showed overlap with both classical Th1 and Th17 phenotypes.
Conclusion. Increased numbers of CD4 and CD8 T cell produce GM-CSF in the blood and joint in SpA. GM-CSF may be a key pathogenic cytokine in SpA and can potentially be targeted therapeutically.
Acknowledgement. Funded by Wellcome Trust (HA-M), and Oxford NIHR Biomedical Research Unit (PB).

P100

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

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Background. Polymorphisms of position 97 (P97) of HLA-B have recently been associated with Ankylosing Spondylitis (AS)1. Mutation of Asparagine (N) at P97 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 T2 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 expression. 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.
Conclusions. 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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P101

MOLECULAR SIZE PROFILE OF SURFACTANT PROTEIN-D IN SPONDYLOARTHRITIS

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Introduction. Surfactant protein-D (SP-D), an innate immune defence molecule with immune modulatory 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 have anti-inflammatory properties, while low Mw (LMw) variants lacks this capacity.
Aim. To investigate HMw and LMw variants of SP-D in serum among spondyloarthritis (SpA) patients and controls according to the Met11Thr gene polymorphism.
Materials and Methods. 34 SpA patients and 57 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. Integration of the area under 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 size molecular variants. SpA related disease mechanisms may disrupt the multimeric state of SP-D.

P102

GENETIC ASSOCIATION OF ANKYLOSING SPONDYLITIS WITH *TBX21* INFLUENCES T-BET AND PRO-INFLAMMATORY CYTOKINE EXPRESSION IN HUMANS AND SKG MICE AS A MODEL OF SPONDYLOARTHRITIS

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Introduction/Aim. *TBX21* encodes the transcription factor T-bet and is genome-wide significant associated with AS. T-bet is implicated in innate and adaptive immunity. However, the role of T-bet in AS pathogenesis is unclear.
Methods. We assessed T-bet in PBMCs from 172 AS cases and 83 healthy controls carrying either risk or protective alleles of the peak AS-associated *TBX21* SNP, rs11657479. The role of T-bet in disease pathogenesis in the SKG mouse model of spondyloarthropathy was examined, along with the impact of *Tbx21* on the gut microbiome and response of T-bet+ cells to bacterial stimuli.
Results. AS patients had higher T-bet expression than healthy individuals, driven predominantly by NK and CD8+ T cells, with expression levels in CD8+ T cells completely distinguishing AS cases from healthy controls. T-bet expression was increased in AS cases carrying risk compared with protective alleles of rs11657479. In curdlan-treated SKG mice, T-bet expression increased early after disease initiation and persisted throughout the disease course. There was marked reduction in gut and peripheral joint inflammation, and fewer IFN-γ- and IL-17-producing CD8+ T cells, in Tbx21-/- compared with wild-type SKG mice. *Tbx21* influenced the intestinal microbial composition with decreased abundance of inflammatory species such as *Bacteroidaceae, Prevotellaceae, Rikenellaceae, Lachnospiraceae* observed in *Tbx21*-/- compared with *Tbx21*+/+ SKG mice. In AS cases, T-bet+ cells displayed a memory phenotype and secreted IL-17 and IFN-γ following TLR agonist challenge.
Conclusion. AS-associated variants in *TBX21* influence T-bet expression and numbers of IL-17 and IFN-γ secreting NK and CD8+ T cells. T-bet is a major component of inflammatory pathways of spondyloarthropathy in humans and mice and may contribute to inflammation by influencing the gut microbiome and/or through influences on immune cell function.

P103

TISSUE DEFICIENCY OF THE ATYPICAL CHEMOKINE RECEPTOR D6 IS ASSOCIATED WITH THE SELECTIVE INCREASE OF GUT-DERIVED PRO-INFLAMMATORY CXCR1-HIGHLY6HIGHTL1A+IL-23+CCR7+ CELLS IN THE PERIPHERAL BLOOD, SYNOVIAL FLUIDS AND BONE MARROW OF AS PATIENTS

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Background. Gut derived innate lymphoid cells of type 3 (ILC)3 are increased in number 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 D6 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 of pro-inflammatory monocytes in the peripheral blood and in secondary lymphoid tissues. The role of D6 and of in 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 CX3CR1highLy6highTL1A+CCR7+ 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 CX3CR1highLy6highTL1A+CCR7+ cells in the gut, synovial tissues and BM of AS patients and controls. Isolated peripheral CX3CR1highLy6highTL1A+CCR7+ 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 CX3CR1highLy6highTL1A+ in the gut and in peripheral blood. D6 down-regulation was accompanied by a complex macrophage signature. Tissue resident CX3CR1highLy6low macrophages were expanded in the ileum of AS patients compared to controls. A significant increase in the frequency of pro-inflammatory CX3CR1highLy6high 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 CXCR1lowLy6High and intestinal derived CXCR1highLy6highCCR7+TL1A+IL-23+ monocytes, the latest being also expanded in AS synovial fluids and synovial tissues and bone marrow. Expansion of gut derived CXCR1highLy6highCCR7+TL1A+IL-23+ monocytes was accompanied by increased TL1A serum levels. Isolated pro-inflammatory CXCR1highLy6highTL1A+ 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 CXCR1highLy6highTL1A+IL-23+CCR7+ monocytes. We also demonstrate for the first time the increased serum levels of TL1A in AS patients and the ability of CXCR1highLy6highTL1A+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

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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 and ligaments 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 determinator 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, enthesitis and pathological new bone formation, are driven by biomechanical strain. Whereas unloading of diseased TNFARE mice stopped disease progression completely, voluntary running significantly increases 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 (un)loaded 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 determinator 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

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Introduction/Aim. Ankylosing Spondylitis (AS) is characterized by chronic joint inflammation which, 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 study 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. Mean serum PFN in AS patients with elevated CRP was 2811±538 ug/ml, and in those with normal CRP was 4488±680 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?

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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 spondyloarthritis. Cell-specific deletion of A20 in the myeloid compartment ($A20^{myeloid\text{-}ko}$) 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 spondyloarthritis.
Methods. To explore the role of these S100-DAMPs as upstream ligands of TLR4 in the $A20^{myeloid\text{-}ko}$ mice, we crossed the $A20^{myeloid\text{-}ko}$ strain onto an $S100A9^{ko}$ strain which functionally 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 $A20^{myeloid\text{-}ko}$ $S100A9^{ko}$ compared to $A20^{myeloid\text{-}ko}$ $S100A9^{wt}$. Although histology of the ankle was similar, inflammation in the knee was less pronounced in the absence of S100A8/A9.
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-on. High systemic levels of S100A8/S100A9 in SpA patients might thus be caused by engulfment of neutrophils and monocytes into peripheral tissues in the acute stage, releasing high levels of S100A8/S100A9 that spill over into the circulation.
Conclusion. While increasing evidence supports a role for S100A8/S100A9 as useful biomarkers for disease activity, their role as drivers of disease in spondyloarthritis however may be limited.

P107

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

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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 *IL23R*, *IL12B*, *STAT3*, and *CARD9*, all associated with IL-23 signalling. In mouse studies, IL-23 increases the pathogenicity of Th_{17} by upregulating GM-CSF, and GM-CSF is essential for inflammation in mouse EAE. We investigate whether GM-CSF is important in PsA, and the relationship between GM-CSF and IL-23.
Materials and Methods. PBMC, naïve T cells or synovial fluid MC [SFMC] from patients with PsA or healthy donors [HD], were stimulated with anti-CD3/CD28 ± cytokines and supernatants analysed. Cells were also activated with PMA/ionomycin, and levels of CCR6, CD161 & IL-23R plus IL-17A, IFN-γ and GM-CSF analysed by FACS.
Results/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 Th_{17}-associated chemokine receptor. Whilst IL-23 upregulates GM-CSF release by Th_{17} 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 Th_{17}-expanding conditions.
Conclusions. IL-23 and Th_{17} cells are therapeutic targets in PsA, and mouse models of inflammation suggest that pathogenic Th_{17} 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 Th_{17}. 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.

P108

A20 INHIBITION OF STAT1 EXPRESSION IN MYELOID CELLS: A NOVEL ENDOGENOUS REGULATORY MECHANISM PREVENTING DEVELOPMENT OF ENTHESITIS

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Introduction. A20 is an important endogenous regulator of inflammation. SNP's in A20 have been associated with various immune-mediated inflammatory diseases, and cell-specific deletion of A20 results in diverse inflammatory phenotypes. Our goal was to delineate the underlying mechanisms of joint inflammation in myeloid-specific A20-deficient mice ($A20^{myelKO}$ mice).
Methods. Bone marrow-derived monocytes/macrophages were derived from $A20^{myelKO}$ 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 A20 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 $A20^{myelKO}$ 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 $A20^{myelKO}$ mice. A20 negatively modulated STAT1- (CXCL9, CXCL10, MX1, USP18), but not STAT3-dependent (BCL2L1, MCL1, VEGF) target gene transcription in myeloid cells by suppressing STAT1 but not STAT3 expression. A20 suppressed STAT1 expression, both in unstimulated conditions and after IFN-γ or IL-6 stimulation.
Consequently, JAK-STAT inhibition *in vivo* resulted in significant reduction of enthesitis, both clinically and histopathologically.
Conclusions. Our data reveal an important and novel interplay between myeloid cells and tissue resident cells at entheseal sites that is regulated by A20. In the absence of A20, STAT1 but not STAT3 expression is enhanced leading to STAT1-dependent inflammation. A20 therefore acts as a novel endogenous regulator of STAT1 that prevents onset of joint inflammation.

P109

INVARIANT NATURAL KILLER T CELLS DOMINATE TREGS IN CONTROLLING ARTHRITIS IN $TNF^{\Delta ARE}$ MICE

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A better understanding of immunoregulatory networks may significantly contribute to our ability to optimize treatment modalities 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 $TNF^{\Delta ARE}$ 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 Tregs, there was a significantly increased cytokine release induced by α-GalCer (a prototypical iNKT ligand), along with a more robust expansion of iNKT cells 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 $TNF^{\Delta ARE}$ DEREG mice and iNKT deficient ($J\alpha18^{-/-}$) $TNF^{\Delta ARE}$ DEREG mice by clinical scoring, histopathology and micro-CT analyses of hind paws. Lack of iNKT cells in $J\alpha18^{-/-}$ $TNF^{\Delta ARE}$ mice was found to result in a substantial increased disease progression as compared to $TNF^{\Delta ARE}$ mice. Rather unexpectedly, Treg depletion did not cause worsening of arthritis in both $TNF^{\Delta ARE}$ as well as $J\alpha18^{-/-}$ $TNF^{\Delta ARE}$ mice. We found that Treg frequencies in lymphoid organs of $TNF^{\Delta ARE}$ mice were increased.
Moreover, Tregs were functionally blunted in the joint-draining lymph nodes but not in spleens of $TNF^{\Delta ARE}$ mice. Finally, in contrast to the marked difference in joint phenotype, we observed a comparable exacerbated gut pathology in $TNF^{\Delta ARE}$ 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 Treg cells are particularly prone to site specific functional modulation under conditions of high TNF load.

P110

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

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Introduction. Radiological structural changes in the sacroiliac joint (SIJ) over time in non-radiographic axial spondyloarthrits (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 after 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 or 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.

P111

QUANTIFICATION OF SACROILIAC JOINT INFLAMMATION USING DIFFUSION-WEIGHTED IMAGING IN YOUNG PEOPLE: BIOLOGICAL VALIDATION IN ENTHESITIS-RELATED ARTHRITIS

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Introduction. Early treatment in enthesitis-related arthritis (ERA) may have a disease-modifying effect with consequently good outcomes. Although clinical evaluation is helpful in assessing disease activity of peripheral joints in ERA, clinical assessment of sacroiliitis is somewhat unreliable and blood inflammatory markers may be normal in active disease. The aim of this study was to *biologically validate* a quantitative magnetic resonance imaging tool for measuring sacroiliac joint (SIJ) inflammation and adolescents and young adults (AYA) with ERA.
Materials and Methods. 22 AYA with axial ERA aged between 12 and 24 years underwent routine MRI and diffusion weighted imaging (DWI) before and after TNF inhibition (TNFi). SIJ normalized ADC (nADC) was measured on each scan. Therapeutic clinical response was defined as an improvement of ≥30% physician global assessment and radiological response defined as ≥2.5-point drop in Spondyloarthritis Research Consortium of Canada (SPARCC) score. We compared nADC changes in responders and non-responders using the Mann-Whitney-Wilcoxon test.
Results. For both radiological and clinical definitions of response, reductions in nADC after treatment were greater in responders than in non-responders (for radiological response: p=0.055; for clinical response: p=0.089). nADC could predict radiological response with a high level of sensitivity and specificity, and was a moderately sensitive and specific predictor of clinical response (the area under the receiver operating characteristic curves were 0.82 for radiological response and 0.78 for clinical response).

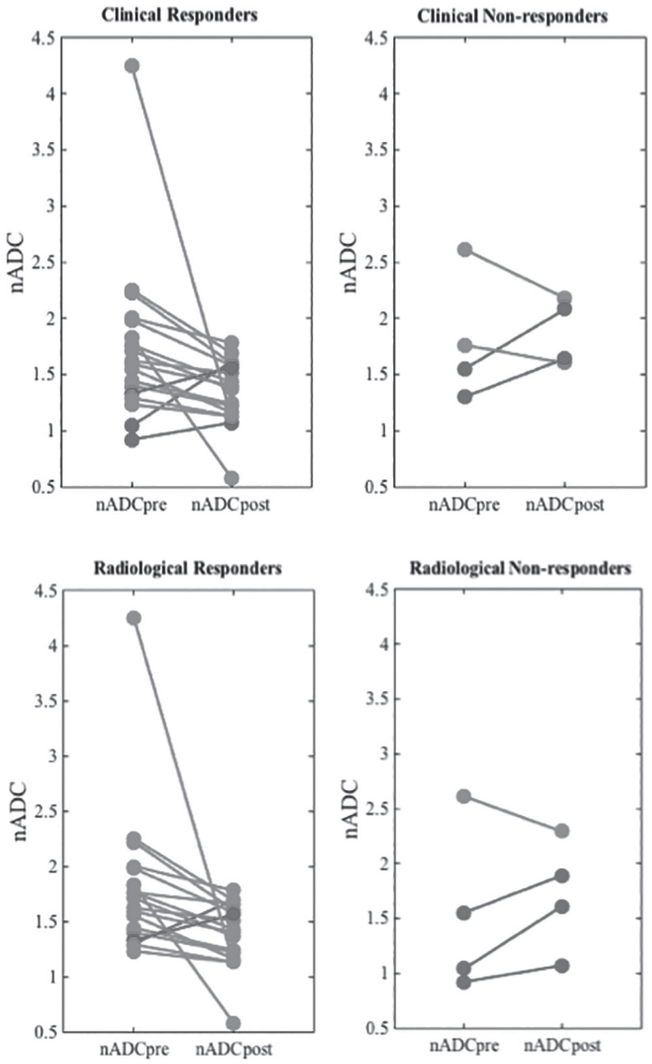

Fig. 1. Response plots showing the change in nADC after treatment, classified by clinical response and radiological response. Patients whose nADC reduced after treatment are shown in green, whilst patients whose nADC increased are shown in red.

Discussion and Conclusion. DWI measurements reflect response to TNFi treatment in ERA patients with sacroiliitis, as defined using both clinical and radiological criteria. DWI measurements are derived from pixel values in the image itself, and are therefore intrinsically more objective than visual scoring. nADC could be used as a biomarker for sacroiliitis in the clinic and in clinical trials to aid in stratifying treatment and quantifying response to treatment.

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P112

THE NATURAL HISTORY OF SACROILIITIS IN YOUNG PEOPLE WITH ENTHESITIS-RELATED ARTHRITIS ON BIOLOGIC THERAPY

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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.

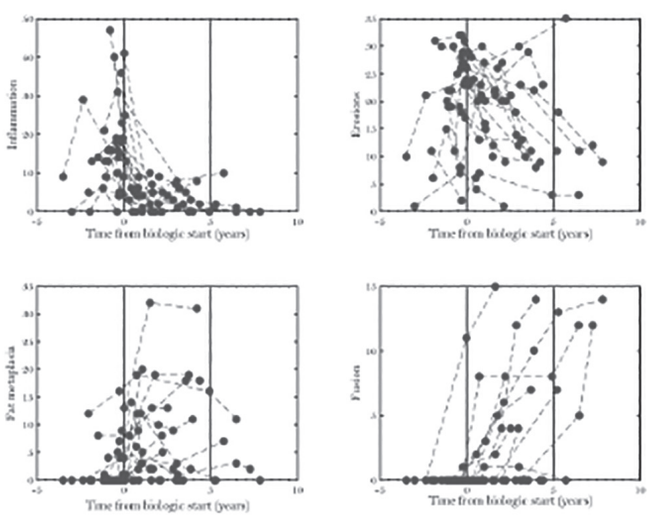

Fig. 1. Scatterplots showing inflammation, erosions, fat metaplasia and fusion over time from biologic start. Biologic therapy was started at time 0. Repeated data from individual patients are joined by dotted lines.

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 SACROILIITIS THAN VISUAL SCORING IN YOUNG PEOPLE WITH ENTHESITIS-RELATED ARTHRITIS

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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).

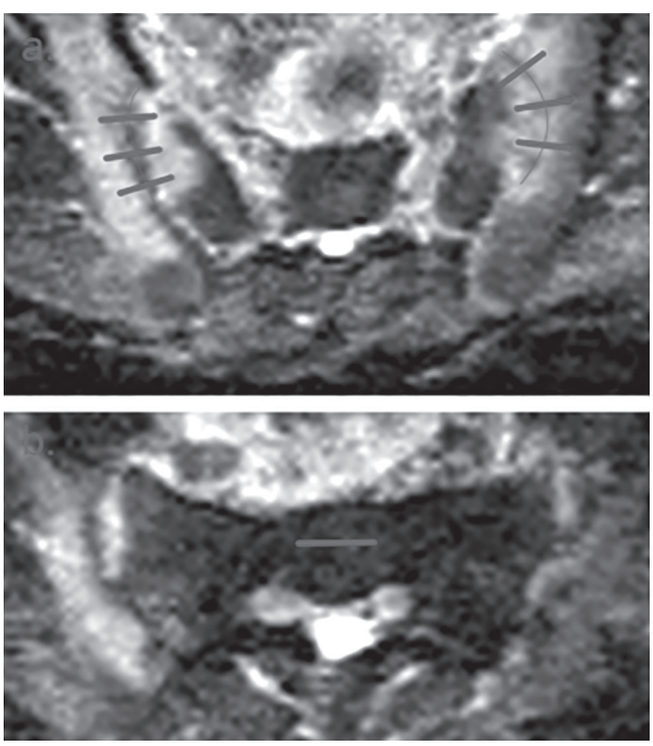

Fig. 1. Placement of regions-of-interest (ROIs) on ADC maps.
(a) Three linear ROIs are placed on both sacroiliac joints (thick red lines). The joint itself is shown as a thin red line.
(b) A further ROI is placed on interforaminal sacral bone.

Results. Bland Altman 95% limits of agreement were ± 82 x 10^{-6}mm^2/s (**9.9% of the mean**) for quantitative ADC measurements, and ± 6.4 (**31% of the mean**) for visual STIR scoring. Intraclass correlation coefficients were 0.988 for ADC, and 0.986 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.

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P114

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

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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%. Positive and negative predictive values were 16.2% and 94.1% respectively. For synovitis the Youden point was 25 and the AUC 0.74, sensitivity 100% and specificity 48.8%; LR+: 1.81 (95%CI 1.35-2.43). For PASE questionnaire the AUC for detecting enthesopathy was 0.62 and Youden 25. Sensitivity was 82.1% and specificity 41.7%; LR+ 1.39 (1.06-1.84) and OR 3.07 (1.06-8.85). Synovitis predictor variables: CRP p=0.0003 and ESR p=0.0041.
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

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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. We examined the presence of bone spurs in vertebral bodies (VB) and radiographic changes of facet joints in L and T spine and costovertebral joints (CVJ).
Results. Of the 1,170 enrolled patients. 920 were men (79%) and 85 % were HLA B27 positive. Incidences of past history of peripheral arthritis and uveitis were 29.0 % and 30.6 %, respectively.

Mean age was 33.0±10.0 years and mean disease duration was 10.5±9.5 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 already at least one bone spur, 28.2% had at least one lesion in facet joints. 32.8% had already 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.

P116

BACK PAIN IS RELATED TO MRI-LESIONS IN PATIENTS INCLUDED IN THE SPACE COHORT

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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, buttock). Average MRI-scores from two sets of two readers (for axSpA and degenerative lesions separately) were used.
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/syndesmophytes 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 buttock pain were investigated by logistic regression analysis. Associations between axSpA/degenerative MRI-spine lesions and thoracic/lumbar pain were investigated by generalized estimating equations.
Results. 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 (35.9%), lumbar spine (82.5%) or buttock(s) (57.8%). 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 buttock pain.
Modic type 1 lesions in patients >35 years (OR 5.19, p=0.001), HIZ in females not fulfilling ASAS-criteria (OR 5.09, p=0.001) and herniation in various subgroups (OR ranged 2.07–4.66) were associated with pain.
Conclusions. 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 buttock pain.

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THE CHARACTERISTICS OF ANDERSSON LESIONS (SPONDYLODISCITIS) BASED ON WHOLE SPINE MAGNETIC RESONANCE IMAGING IN ANKYLOSING SPONDYLITIS

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Introduction/Aim. Andresson 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 discovertebral unit (DVU) including the central, peripheral, and diffuse disc types of Andersson lesion was assessed. We compared the number of DVUs with Andersson lesion with clinical and radiographic indicies 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 DVUs with Andesson 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 of 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.

P118

CURRENT SMOKING, ITS INTENSITY AND DURATION, IS ASSOCIATED WITH FAT METAPLASIA ON MRI IN PATIENTS WITH SPONDYLOARTHRITIS

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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 STIR scans using the SPARCC SIJ and 23-DVU Spine scores while structural lesions were assessed on T1W scans using the SPARCC SSS score for SIJ fat, erosion, backfill, ankylosis, and the FASSS 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), SIJ ankylosis (p=0.01), and spinal inflammation (SPARCC 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 SIJ 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 SIJ 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?

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Introduction/Aim. The majority of patients with AS develop new bone in the spine although disease may remain isolated in the SIJ. A new hypothesis has proposed that MRI can identify a "progressive phenotype" in early SpA characterized by the appearance of fat metaplasia in the SIJ. We aimed to determine whether MRI lesions in the SIJ 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 backfill and ankylosis were associated with no damage (OR[95%CI]=0.83[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 SIJ 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 SIJ 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

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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 (SIJ) 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. SIJ 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, sacroiliitis (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 associated spondyloarthritis in patients 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

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Objective. To assess the prevalence of inflammatory and structural lesions on MRI of the sacroiliac joints (SIJ) 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 SIJ 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 SIJ. Bone marrow edema (BME) of the SIJ was quantified using the Spondyloarthritis Research Consortium of Canada (SPARCC) scoring system. Besides BME of the SIJ, all MRIs were also scored for other inflammatory lesions such as enthesitis and capsulitis. Structural MRI lesions of the SIJ 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 SIJ 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 SIJ. Therefore, almost 86% 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 SIJ 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.

Inflammatory lesions of the SIJ, n (%)	ASAS MRI + (n=21)		ASAS MRI – (n=39)	
	Unilateral	Bilateral	Unilateral	Bilateral
BME	16 (76.2)	5 (23.8)	1 (2.6)	0
Capsulitis	7 (33.3)	0	0	0
Retroarticular enthesitis	5 (23.8)	1 (4.8)	1 (2.6)	0
Chronic lesions of the SIJ, n (%)				
Sclerosis	1 (4.8)	2 (9.5)	0	0
Fat metaplasia	2 (9.5)	4 (19.0)	1 (2.6)	0
Erosions	3 (14.3)	8 (38.1)	4 (10.3)	0
Ankylosis	2 (9.5)	0	0	0
Pelvic enthesitis, n (%)				
Symphysis	1 (4.8)	1 (2.6)		
Ischial tuberosity	2 (9.5)	0	1 (2.6)	2 (5.4)
Posterior superior iliac spine	3 (14.3)	0	0	0
Greater trochanter	0	1 (4.8)	0	2 (5.4)
Gluteus posterior	1 (4.8)	0	0	0
Hip, n (%)				
Joint effusion/ BME	4 (19.0)/ 1 (4.8)	0	4 (10.3)/ 1 (2.6)	1 (4.8)/0
Bony changes of the cortex	1 (4.8)	1 (4.8)	2 (5.4)	0

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

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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 FASSS 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 (12.3) 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 normalised 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 normalised CRP, in the presence of definite SIJ erosion, and in the absence of SIJ ankylosis.

	Adjusted R^2	Significant independent variables	OR [95%CI]	p-value
Basic Model (age, sex, ASDAS, current smoker, duration of follow up)	0.12	age	0.95 [0.92-0.98]	<0.0001
		Baseline ASDAS	0.65 [0.47-0.90]	0.009
		Current smoking	0.33 [0.14-0.80]	0.014
Basic Model plus post-treatment CRP<6	0.17	Post-treatment CRP<6	10.30 [1.28-82.62]	0.028
Basic model plus SSS erosion ≥2	0.38	Baseline ASDAS	0.34 [0.14-0.84]	0.019
		SSS erosion ≥2	8.86 [1.57-50.0]	0.013
Basic model plus SSS ankylosis	0.39	Baseline ASDAS	0.34 [0.13-0.92]	0.033
		SSS ankylosis	0.86 [0.76-0.98]	0.019

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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

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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-tumor necrosis factor alpha (anti-TNF-α), 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 AS Spine Score (FASSS) for fat metaplasia in the spine. 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 FASSS 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 18.4 (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 0.56, p=0.002), baseline CRP (HR 0.99, p=0.03) and early post-treatment attainment of ASDAS<1.3 (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=2.2[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 remission of MRI inflammation may also be a factor but this requires further study with larger sample size.

Table. Multivariable Cox Regression.

Variable	Hazard ratio	p-value	95% CI
Age	0.82	0.47	0.48-1.41
Gender	1.01	0.29	0.99-1.03
Baseline CRP	0.99	0.035	0.98-1.00
CRP<6 post-treatment*	0.46	0.008	0.26-0.82
ASDAS<1.3 post-treatment*	0.54	0.027	0.32-0.93

*Within first year of treatment.

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CAN STRUCTURAL PROGRESSION ON MRI OF SACROILIAC JOINTS IN PATIENTS WITH SPONDYLOARTHRITIS BE RELIABLY DETECTED AND WHAT TYPE OF CALIBRATION IS NECESSARY TO ACHIEVE THIS?

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Introduction/Aims. Assessment of structural lesions of the SIJ 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 SIJ reviewed either a web-based training module (n=3) or DICOM-based reference MRI scans (n=2). Both calibration methods used the SPARCC SIJ Structural Score (SSS). Baseline and 2-year T1W scans from 30 patients with axial SpA blinded to time point and STIR scan were assessed. Interobserver reliability for status and change scores was calculated by ICC and comparisons made with prespecified expert readers (n=3).
Results. Mean (SD) reduction in SSS erosion score was significantly greater for expert readers (-1.62 (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 (-0.07 (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 SIJ 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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ASSOCIATIONS BETWEEN SPONDYLOARTHRITIS FEATURES AND MRI FINDINGS: A CROSS-SECTIONAL ANALYSIS OF 1020 PATIENTS WITH PERSISTENT LOW BACK PAIN

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Introduction/Aim. The objectives were in a low back pain (LBP) cohort including an unknown proportion of patients with spondyloarthritis, to: 1) estimate the prevalence of clinical features and MRI findings included in Assessment of SpondyloArthritis international Society (ASAS) criteria, and 2) explore the associations between clinical features and MRI findings.
Methods. Patients aged 18-40 years with persistent LBP referred to an outpatient spine clinic were included. Information on clinical features (incl. HLA-B27 and CRP) and MRI findings of the spine and sacroiliac joints (SIJ) were collected.
Results. Of 1,020 included patients, 537(53%) had minimum 1 clinical feature included in the ASAS criteria. Three clinical features were common; inflammatory back pain, good response to NSAID and family disposition. The prevalence of these features ranged from 15%-17%. MRI sacroiliitis, according to ASAS definition, was present in 217(21%) patients. Of those, 91(42%) had bone marrow edema (BME) at the minimum requirement according to ASAS (*low BME score*). HLA-B27, peripheral arthritis, good response to NSAID, and preceding infection were independently positively associated with SIJ MRI findings (ORs of 1.9-9.0). The remaining 8 clinical features did not associate positively with MRI-findings. Importantly, only age associated independently with *low BME score* at the SIJ (OR 1.1 per year).
Conclusion. In this population, 53% had minimum one clinical feature and 21% had sacroiliitis according to ASAS; furthermore, the associations between the clinical and imaging domains were inconsistent. The results indicate a need for further investigation of the importance of these findings in spondyloarthritis, including investigation of the minimum requirements for defining MRI sacroiliitis.
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SUBCLINICAL UNGUEAL DYSTROPHY IN PATIENTS WITH PSORIASIS WITHOUT JOINT INVOLVEMENT: IS THERE ANY ROLE FOR NAIL ULTRASOUND?

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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, enthesitis 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 enthesitis, 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 no nail dystrophy. However, patients with CNI (67.4%) had higher number of tender and swollen joints. The presence of nail power-Doppler (N-PwD) 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-PwD (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 SPONDYLOARTHRITIS

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Aim. Mechanisms underlying the striking association of spondyloarthritis (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 on their intracellular distribution. We have previously observed that high expression levels of HLA-B in HeLa cells induces cytoplasmic vesicles formation containing HLA-B molecules and that the density of vesicles was more important for HLA-B27 subtypes associated with SpA than for the non-associated HLA-B*2706 and HLA-B*0702 alleles. Here, we further examined the nature and composition of theses vesicles and the putative differences between associated and non-associated HLA-B alleles.
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 and live-cell imaging.
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-B*2706 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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PREVALANCE OF HIP ARTHRITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TNF INHIBITORS

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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 differenced in hip arthritis in AS.
Materials and Methods. 241 AS patients (162 men, age: 48.6±11years (mean±SD), 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.
Definite hip involvement was detected in 85/241(35%) patients, 10/241(4%) had underwent bilateral THR and 6/241(2.5%) unilateral THR. No gender difference was observed (females:25/85(30%) vs. 54/156(35%). The patients with hip arthritis had significantly higher BASDAI-score (6.1±1.7 vs. 5.4± 1.9, p=0.026), ASDAS-CRP (3.9± 0.8 vs. 3.4±0.9, p<0.0001), CRP [12.4(4.2-32) vs. 7(2.5-21) median-IQR, p=0.001], ESR [26(8-39) vs. 14(7-30), p=0.006], compared to those without. Additionally, the aforementioned patients had higher BASFI-score (6.2±1.9vs. 4.8±2.3, p<0.0001), BASMI-score (5±2.3vs. 3.3±1.9, p<0.0001) and reduced intermalleolar distance (88±23 vs. 104±19 cm, p<0.0001).
AS patients with hip arthritis had also higher mSASSS-score [13.5 (2- 38.5) vs. 3(0-14), p<0.0001] and increased percentage of presence of syndesmophytes (52/84,62% vs.58/153, 38%, p=0.001) and peripheral arthritis (48/83,58% vs. 66/155, 42%, p=0.001). According to multivariate logistic regression analysis, independent risk factors for hip arthritis in AS are: ASDAS-CRP (OR:1.8, CI: 1.2-2.8), presence of syndesmophytes (OR: 2.4, CI: 1.2-5) and intermalleolar distance (OR: 0.97, CI: 0.95-0.9).
Conclusions. AS patients with hip arthritis have higher disease burden, functional impairment and severe spinal changes.

P129

RADIOGRAPHIC PROGRESSION OF HIP ARTHRITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TNF INHIBITORS

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Introduction. Current evidence suggests that anti-TNF treatment may not inhibit radiographic progression in the spine; whether it affects the progression of hip joint space narrowing in AS patients with hip arthritis is not known.
Aim: 1. Estimate the impact of long-term anti-TNF treatment on radiographic progression of hip arthritis in AS; 2. Add a hip joint space scoring method, used in osteoarthritis, to the BASRI-score.
Materials and Methods. 205 AS patients (136 men, age: 49±11years) under anti-TNF treatment were included in this retrospective study. Anteroposterior X-rays of pelvis and lateral x-rays of cervical and lumbar spine were scored blindly, by 2 independent readers at 3 time points: at baseline (*i.e.* prior anti-TNF treatment initiation), 2.6±0.7 and 7.2±2.4 years after anti-TNF treatment initiation. Both hips were scored using: a) the BASRI-hip scoring system, b) mean joint space width (MeanJSW) estimated by measurement of 3 distinct points of inter bone distance, (2mm inner of the external end of the acetabulum, vertical line through femoral head center, head-neck center line) (Figure 1). Spine X-rays were scored by the mSASSS. 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.
Results. After 7.2±2.4 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. 1.13±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. 1.12±0.9 vs. 1.14±0.98, p=0.001), 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. 4.17±0.8 vs. 4.17±0.7), both 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.

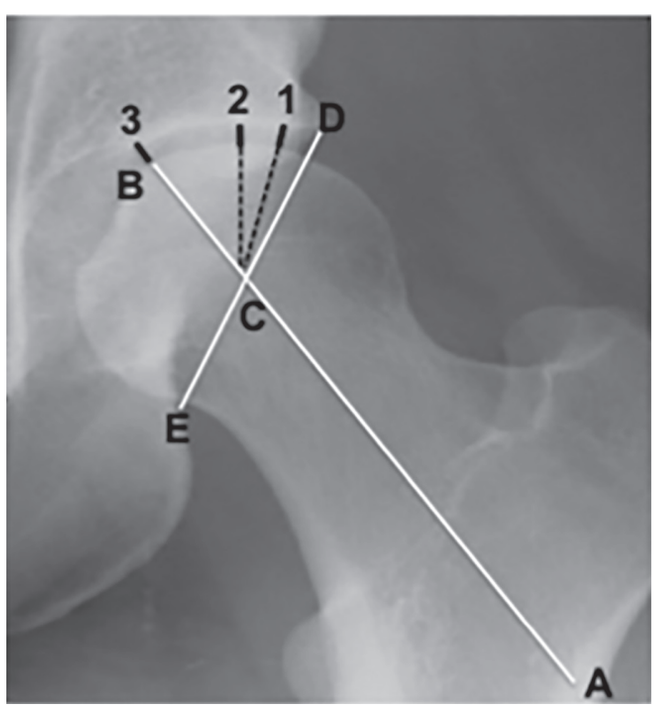

Figure 1.

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DYSBIOSIS AND ZONULIN UP-REGULATION ALTER GUT EPITHELIAL AND VASCULAR BARRIERS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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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 was 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 assayed 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 the 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+sCD14 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.

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MICROSCOPIC GUT INFLAMMATION IN SPA IS A PROGNOSTIC FACTOR FOR INITIATION AND RESPONSE TO ANTI-TNFα THERAPY

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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-α initiation and response to anti-TNF-α therapy.
Patients and Methods. 126 newly diagnosed axial and peripheral SpA patients from the Ghent Inflammatory Arthritis and spoNdylitis cohort (GIANT) were included. All patients underwent an ileocolonoscopy at baseline to assess the presence of microscopic bowel inflammation. The rate of anti-TNF-α initiation was assessed performing survival analysis. Response to anti-TNF-α 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-α therapy.
Microscopic gut inflammation at baseline, present in 47 (37.3%) patients, was significantly linked to the rate at which anti-TNF-α therapy was started (log rank p=0.025). Other baseline factors associated with anti-TNF-α initiation were BASDAI, BASFI, past or present enthesitis and BASMI. However, the association between gut inflammation and anti-TNF-α initiation remained significant after adjustment for these factors. ASDAS response to anti-TNF-α was assessed in 35 axial SpA patients of which 15 had microscopic gut inflammation. Significantly more patients with gut inflammation showed a clinically important ASDAS improvement (≧1.1 as defined by ASAS) under anti-TNF-α therapy (p=0.034), and this association remained significant after correction for age, sex or CRP.
Conclusions. Mucosal 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-TNFα therapy.

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ACTIVE TUBERCULOSIS, FACTORS ASSOCIATED WITH LATENT TUBERCULOSIS AND TUBERCULIN SKIN TEST CONVERSIONS DURING ANTI-TUMOUR NECROSIS FACTOR THERAPY IN PATIENTS WITH SPONDYLOARTHRITIS IN A MEXICAN COHORT

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Background. The Anti Tumour Necrosis Factor (aTNF) therapy in spondyloarthritis (SpA) had changed the prognosis of these conditions. Unfortunately, aTNF therapy is associated a high-risk rate of infections, especially active tuberculosis (TB). The use of tuberculin skin test (TST) to detect and to treat latent tuberculosis (LTBI) before to initiate aTNF therapy had reduced the progression to TB. However, multiple factors compromise the sensitivity and specificity of the test to distinguish between remote and recent disease. These factors are also associated with TST conversions (TSTc) and progression of LTBI to TB differing between populations.
Objectives. To determine the frequency of TB, LTBI, TSTc and associated factors during aTNF therapy in patients with SpA from a Mexican cohort.
Methods. 74 patients from a Mexican cohort from 2011-2016 were examined. Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA) cases fulfilled Amor and CASPAR criteria respectively. LTBI (TST induration ≥ 5 mm recorded to 48 hours) diagnosis occurred before and TB occurred after to start aTNF therapy. TSTc happened in the second TST. Demographic factors, comorbidities and pharmacologic treatments were examined for patients under aTNF therapy. Univariable and multivariable analyses were used it.
Results. Of 74 patients, 71 had AS and 3 had PsA; of them 78.4% were men. The mean age [standard deviation (SD)] was 44.8 (11.5) years. The mean of time at onset of SpA [standard deviation (SD)] was 9.7 (7) years. A total of 3 patients among who screened TST negative developed extrapulmonary TB. LTBI was detected in 35 (47.3%) patients and was more associated with smoking (OR 31.7, 95% CI 5.9-170.5, p=<0.005). TSTc were presented in 22 (29.7%) cases and were more associated with patients living in rural areas (OR 2.4, 95% CI 1.9-5.25, p=<0.005).
Conclusion. Patients with SpA in this Mexican cohort have a high prevalence of TB, LTBI and TSTc. Smoking and living in rural areas were factors associated with LTBI and TSTc respectively.

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ANTI TNF TREATMENT OF REACTIVE ARTHRITIS – A MONOCENTRIC EXPERIENCE

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Reactive arthritis (ReA) is still a current problem, its treatment is not standardized, with the possibility of a chronic evolution.
Aim. To evaluate efficacy and safety of anti TNF agents in the treatment of patients with ReA followed in a single center.
Methods. retrospective analysis of patients with ReA, treated with TNF blockers, from July 2007 to December 2013 in an University Hospital in France.
Results. of 31 cases of ReA, 15 (48%) received at least one dose of anti TNF, male (n=13), mean age 35 years, 66% HLA-B27. Infection was found in 9/15 patients (4 Chlamydia). Anti TNF agents were introduced with a median delay of 116 days after onset of rheumatic symptoms: etanercept (ETN) 9 cases, infliximab (IFX) and adalimumab (ADA) (3 cases each). The clinical improvement was rapid, all patients developed response to anti TNF which could be stopped in 5 cases: 3 IFX after a mean of 4.6 infusions, 2 ETN after 4 and 10 months. Eight patients developed chronic spondyloarthritis, and one psoriatic arthritis, with a mean follow-up of 4.8 years, and requiring anti TNF continuation. Treatment was well tolerated, (mean exposition duration of 34 months/patient), neither serious infection nor reactivation of the triggering infection was recorded. Compared to ReA patients not treated with anti TNF over the same period, we found no differences regarding age, arthritis distribution, type of initial infection, biologic data (CRP, HLA-B27, evidence of infectious agent). In the same way, there were no differences between the patients who could stop anti TNF due to remission, and those for whom continuation was necessary, except a shorter median delay of initiation of the TNF blocker: 44 days versus 173 days respectively.
Conclusion. Anti TNF therapy for ReA is associated with symptomatic efficacy and good tolerance with the possibility, in one third of the cases of short lasting treatment leading to remission, associated to the precocity of anti TNF initiation.

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RESPONSE TO TREATMENT WITH NONSTEROIDAL ANTI-INFLAMATORY DRUGS IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND NON-RADIOLOGICAL AXIAL SPONDYLO-ARTHRITIS

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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 nonsteroidal 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±1,6 лет. 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 (67,6%)).
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%)). The median BASDAI was in patients with AS 4,0±0,1, in twelve months 2,4±0,1 (-40,0%, p<0,001), nr-axSpA - 3,4±0,2/0,15±0,04 (-95,5%, p<0,001).
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

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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. 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.
Methods. CAPTURE was a retrospective observational study of 141 consenting patients from 11 NHS centres. Patient eligibility: documented diagnosis of PsA (according to Classification of Psoriatic Arthritis criteria), first TNFi initiated ('baseline') ≥3years previously, aged ≥18years. Data were collected from medical records, including baseline disease characteristics, TNFi received during the 'study period' (baseline to date of data collection), and non-TNFi therapies prescribed for PsA pre-/post-baseline. (Denominator is stated where data unavailable for some patients).
Results. Study period (range): 3.4-5.5years. Pre-baseline, methotrexate (alone or in combination) was the most frequently received recent csDMARD: 103/141 (73.0%) patients. csDMARDs were co-prescribed in 102/137 (74.5%) patients receiving first TNFi, 26/46 (56.6%) receiving second TNFi, and 11/16 (68.8%) receiving third TNFi. With first TNFi, methotrexate was the most frequently co-prescribed csDMARD: 77/102 (75.5%), then leflunomide (25/102, 24.5%), then sulfasalazine (23/102, 22.5%) (not mutually exclusive). Following TNFi permanent discontinuation, 25/30 (83.3%) patients were prescribed csDMARDs, 7/30 (23.3%) non-steroidal anti-inflammatory drugs, and 5/30 (16.7%) other biologic agents (not mutually exclusive).
Conclusions. The use of concomitant csDMARDs in patients with PsA managed on TNFi (despite little evidence to support combination therapy[1]), 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.
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SECUKINUMAB IMPROVES MINIMAL DISEASE ACTIVITY RESPONSE RATES IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: DATA FROM PHASE 3 FUTURE-2 STUDY

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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-naïve 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-naïve 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 for both secukinumab doses.
Proportion of patients achieving MDA with secukinumab at Week-16 was higher in anti–TNF-naïve patients with low versus longer disease duration, and higher in the anti–TNF-naïve cohort than the anti–TNF-IR cohort at all times (Figure).

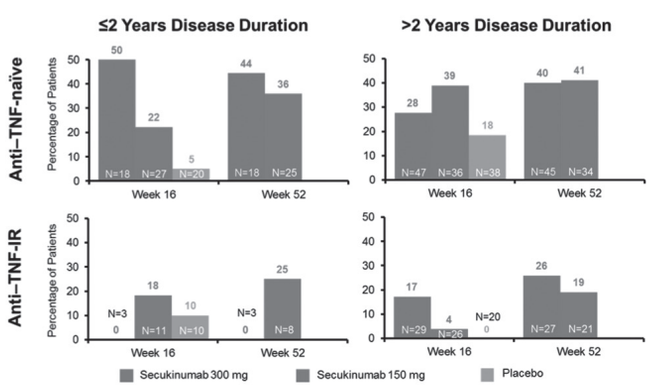

Figure. MDA by Anti-TNF Status and Disease Duration (≤2 and >2 Years).

Conclusions. Secukinumab patients had higher MDA response rates versus placebo at Week-16, with response rates sustained through Week-52. Response rates were consistent with those previously reported with anti-TNF therapies in comparable patient populations.

Disclosures:
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LC: Grant/research support from: Abbvie, Pfizer, Janssen, Consultant for: Abbvie, Celgene, Pfizer, UCB, MSD, Boehringer Ingelheim, Novartis, and Lilly
BK: Grant/research support from: Abbvie, Novartis and Roche, Consultant for: Abbott, BMS, Chugai, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: Abbott, BMS, Chugai, MSD, Novartis, Pfizer, Roche and UCB
LM: Consultant for: Novartis through employment at RTI Health Solutions, Employee of: RTI Health Solutions
SM: Shareholder of: Novartis, Employee of: Novartis
CK: Shareholder of: Novartis, Employee of: Novartis
KG: Shareholder of: Novartis, Employee of: Novartis
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IS IT POSSIBLE TO INTERRUPT ANTI-TNF THERAPY USING A TAPERING STRATEGY IN PATIENTS WITH ANKYLOSING SPONDYLITIS ACHIEVING CLINICAL RESPONSE?

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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) or relative frequency values for baseline characteristics of these patients at the beginning of anti-TNF therapy were: age 44 (25-52) years old, 80% males, disease duration 8 (0.8-21) years, 80% HLA-B27+ and 60% had peripheral arthritis. Characteristics when interrupting treatment were: time receiving anti-TNF therapy 5.0 (2.0-6.3) years, time on a tapering strategy 2.0 (1.5-3.0) years, last administered dose of anti-TNF (% of standard dose) 22% (18.5-35), BASDAI 1.0 (0-2.1), patient´s VAS 0 (0-20), physician´s VAS 0 (0-15), CRP 0.9 (0.8-2.6) mg/L. After 12 months of follow up, 70% of patients who interrupted anti-TNF therapy had a flare. 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.

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IS THE PATTERN OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS STARTING BIOLOGICAL THERAPY CHANGING OVERTIME? RESULTS FROM REGISPONSERBIO?

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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 overtime.
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.

Table I. Characteristics at baseline visit of all patients included in REGISPONSERBIO.

	Total N= 258	Prevalent cases n=174 (67%)	Incident cases n= 84 (33%)	p value
Age (year)	48 ± 12	48 ± 11	48 ± 13	0.8
Male	201 (78)	144 (83)	57 (69)	0.01
Disease duration (year)	13 ± 11	15 ± 11	8.6 ± 11	<0.001
BMI	27 ± 4	27 ± 4	27 ± 4	0.7
Smoking habit				0.8
Non smoker	102 (41)	70 (42)	32 (40)	
Ex-smoker	70 (28)	49 (29)	21 (26)	
Smoker	76 (31)	49 (29)	27 (34)	
Working disability	42 (16)	28 (17)	14 (19)	0.7
SpA subgroup				
AS	191 (74)	135 (78)	56 (67)	0.06
nr-axSpA	18 (7)	6 (3)	12 (14)	0.001
PsA	12 (5)	9 (5)	3 (4)	0.6
SpA related to IBD	20 (8)	13 (8)	7 (8)	0.8
HLA-B27 positive	205 (80)	145 (84)	60 (71)	0.06
Extra-articular manifestations				
Uveitis	62 (24)	43 (26)	19 (23)	0.6
Psoriasis	18 (7)	13 (8)	5 (6)	0.6
IBD	24 (9)	15 (9)	9 (11)	0.7
Disease activity at biological start				
VSG (mmHg)	25 ± 21	26 ± 22	22 ± 19	0.1
BASDAI (0-10)	5.5 ± 2.0	5.4 ± 1.8	5.6 ± 2.4	0.5
VAS patient dis. activity (0-10)	6.3 ± 2.2	6.2 ± 2.0	6.5 ± 2.5	0.3
EVA dolor axial nocturno (0-10)	5.8 ± 2.7	5.7 ± 2.5	6.1 ± 2.6	0.2
BASFI	5.1 ± 2.3	4.9 ± 2.2	5.4 ± 2.5	0.1
Previous biological therapy	-	66 (38)	-	-
NSAID concomitant	153 (59)	89 (53)	64 (77)	<0.001
DMARD concomitant	56 (22)	37 (22)	19 (23)	0.8
Disease dur. at the beginning therapy	9.7 ± 10	10.2 ± 10	8.6 ± 11	0.3

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.

P139

IMPACT OF AEROBIC FITNESS ON AXIAL SPONDYLOARTHRITIS ACTIVITY: A META-ANALYSIS OF CONTROLLED STUDIES

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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) in axial spondyloarthritis.
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 ratio, disease duration. Aerobic fitness provides in the intervention group (148 patients) a positive impact on the BASDAI (weighted mean difference WMD: - 0.52 [95% CI -0.9; -0.13]) (heterogeneity index I2: 10.3%, p=0.35). When compared to a control group (152 Patients) aerobic exercise does not provide a more positive impact on the BASDAI (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; 0.1]) (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.

P140

CERTOLIZUMAB PEGOL FOR THE TREATMENT OF AXIAL SPONDYLOARTHRITIS: 4-YEAR OUTCOMES FROM THE RAPID-AXSPA TRIAL

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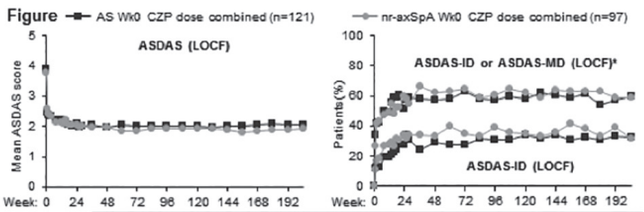
Introduction/Aim. RAPID-axSpA (NCT01087762) investigated efficacy and safety of certolizumab pegol (CZP) in patients with axial spondyloarthritis (axSpA), including ankylosing spondylitis (AS) and non-radiographic (nr)-axSpA patients. Here we report 4-year efficacy and safety data.
Patients and Methods. 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 case 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.

Figure



Table

	Combined CZP 200mg Q2W + 400mg Q4W								
	axSpA (n=218)			AS (n=121)			nr-axSpA (n=97)		
	Wk24 (NRI)	Wk204 (NRI)	Wk204 [a] (OC)	Wk24 (NRI)	Wk204 (NRI)	Wk204 [c] (OC)	Wk24 (NRI)	Wk204 (NRI)	Wk204 [e] (OC)
ASAS20 (%)	68.3	54.1	83.7	68.6	56.2	85.3	68.0	51.5	81.7
ASAS40 (%)	51.8	44.0	68.1	52.9	44.6	68.0	50.5	43.3	68.3
ASAS PR (%)	30.3	23.4	36.5 [b]	28.1	21.5	32.5 [d]	33.0	25.8	41.7
Mean [f]	BL	Wk24 (LOCF)	Wk204 (LOCF)	BL	Wk24 (LOCF)	Wk204 (LOCF)	BL	Wk24 (LOCF)	Wk204 (LOCF)
ASDAS	3.8	2.1	2.0	3.9	2.1	2.0	3.8	2.0	1.9
ASDAS-ID (%)	-	30.3	32.1	-	27.3	32.2	-	34.0	32.0
ASDAS-ID or ASDAS-MD (%)	-	55.1	59.2	-	51.3	59.5	-	59.8	58.8
BASDAI	6.4	3.3	3.0	6.4	3.4	3.0	6.6	3.3	2.9
BASFI	5.3	3.0	2.7	5.6	3.3	3.0	5.0	2.6	2.2
BASMI-linear	3.8	3.2	3.1	4.2	3.6	3.6	3.2	2.6	2.5
MASES	3.5	1.6	1.2	3.0	1.1	0.9	4.0	2.3	1.6

*Percentage of patients achieving either an ASDAS-ID or an ASDAS-MD response. [a] n=135; [b] n=137; [c] n=75; [d] n=77; [e] n=60; [f] Unless otherwise noted. ASAS PR: ASAS Partial Remission; ASDAS-ID: ASDAS Inactive Disease (<1.3); ASDAS-MD: ASDAS Moderate Disease activity (<2.1); BL: baseline; LOCF: last observation carried forward; MASES: Maastricht Ankylosing Spondylitis Enthesitis; NRI: non-responder imputation; OC: observed case.

P141

CERTOLIZUMAB PEGOL FOR THE TREATMENT OF PSORIATIC ARTHRITIS: 4-YEAR OUTCOMES FROM THE RAPID-PSA TRIAL

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Introduction/Aim. RAPID-PsA (NCT01087788) investigated the efficacy and safety of certolizumab pegol (CZP) in patients with psoriatic arthritis (PsA). Here we report efficacy and safety data over 4 years.
Patients and Methods. RAPID-PsA was double-blind and placebo-controlled to Week (Wk) 24, dose-blind to Wk48 and open-label thereafter. Patients had active PsA and failed ≥1 DMARD. Patients randomized to CZP (200mg Q2W/400mg Q4W) continued assigned dose in the open-label period.
Efficacy data are presented for all patients originally randomized to CZP as observed case and with imputation (NRI for categorical measures, LOCF for continuous). Safety set contained all patients treated with ≥1 CZP dose to Wk216.
Results. 273/409 patients were randomized to CZP, of whom 67% completed to Wk216. In the open-label period, 6.2% of patients withdrew through adverse events (AEs), 1.8% through loss of efficacy. ACR responses were sustained with both CZP dose regimen from Wk24 to Wk216 (Table A). In those 166 CZP pts (60.8%) with ≥3% BSA skin involvement at baseline, PASI75/90/100 responses were maintained to Wk216 (Table A). Improvements in patient-reported outcomes were also maintained through Wk216 (Table B). Patients had further improvements from Wk24 to Wk216 in high-threshold outcomes (ACR70, minimal disease activity and PASI100) when observed case or conservative imputation methods (NRI) were used (Table A). The safety set (N=393) had 1321 patient-years (PY) CZP exposure with an AE rate/100PY of 258.0. No new safety signals

were identified from Wk96 to Wk216, and no additional deaths were reported.
Conclusion. CZP efficacy was maintained in PsA patients over 4 years, with no new safety signals identified. Additional improvements in high-threshold outcomes were seen from Wk24 to Wk216.

Table: A) Clinical outcomes to Week 216 of the RAPID-PsA trial

	CZP 200 mg Q2W (n=138)			CZP 400 mg Q4W (n=135)			CZP dose-combined (n=273)		
	Wk24 (NRI)	Wk216 (NRI)	Wk216 (OC)	Wk24 (NRI)	Wk216 (NRI)	Wk216 (OC)	Wk24 (NRI)	Wk216 (NRI)	Wk216 (OC)
Outcome, %									
ACR20	63.8	54.3	76.5 [a]	56.3	54.8	85.1 [b]	60.1	54.6	80.5 [c]
ACR50	44.9	42.0	59.2 [a]	41.5	44.4	69.0 [b]	43.2	43.2	63.8 [c]
ACR70	28.3	34.8	49.0 [a]	24.4	34.8	54.0 [b]	26.4	34.8	51.4 [c]
MDA	34.8	37.7	53.1 [a]	34.8	40.7	63.2 [b]	34.8	39.2	57.8 [c]
PASI75 [d]	62.2	60.0	81.8 [e]	60.5	42.1	76.2 [f]	61.4	51.8	79.6 [g]
PASI90 [d]	46.7	44.4	60.6 [e]	35.5	35.5	64.3 [f]	41.6	40.4	62.0 [g]
PASI100 [d]	30.0	32.2	43.9 [e]	13.2	23.7	42.9 [f]	22.3	28.3	43.5 [g]

B) Patient-reported outcomes to Week 216 of the RAPID-PsA trial

	CZP 200 mg Q2W (n=138)			CZP 400 mg Q4W (n=135)			CZP dose-combined (n=273)		
	BL	Wk24 (LOCF)	Wk216 (LOCF)	BL	Wk24 (LOCF)	Wk216 (LOCF)	BL	Wk24 (LOCF)	Wk216 (LOCF)
Outcome, mean									
HAQ-DI	1.3	0.8	0.8	1.3	0.9	0.8	1.3	0.8	0.8
Pain	59.7	31.1	29.1	61.1	32.7	27.3	60.4	31.9	28.3
PGADA	60.2	31.1	28.3	60.2	32.5	27.0	60.2	31.7	27.7

All patients received CZP loading dose of 400mg at Weeks 0, 2 and 4. [a] n=98; [b] n=87; [c] n=185; [d] PASI response rates reported in patients with ≥3% body surface area skin involvement at baseline (CZP 200mg Q2W, n=90; CZP 400 mg Q4W, n=76); [e] n=66; [f] n=42; [g] n=108. BL: baseline; LOCF: last observation carried forward; MDA: minimal disease activity; NRI: non-responder imputation; OC: observed case; PGADA: patient's global assessment of disease activity.

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ENTEROPATHIC SPONDYLOARTHRITIS: TREATMENT AND OUTCOME IN A 2-YEAR PROSPECTIVE STUDY

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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 continuatively referred to a combined gastro-rheumatologic outpatient clinic for 2 years.
Methods. 127 ESpA patients [F:M=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-rx 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 ($p<0.01$). HCQ was prevalent at T6/12/18/24 compared with T0 in peripheral-ESpA ($p<0.001$). In all ESpA CRP, DAS, ASDAS, and BASDAI were lower at T12 than T0 ($p=0.05$). In particular, CRP and HAQ were reduced at T18 ($p<0.05$) while CRP, BASDAI, and BASFI were lower at T24 than T0 ($p<0.01$). In ax-ESpA, DAS 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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EFFICACY OF GOLIMUMAB FOR NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS (NR-AXSPA): SUBGROUP ANALYSIS BY BASELINE MRI AND C-REACTIVE PROTEIN STATUS

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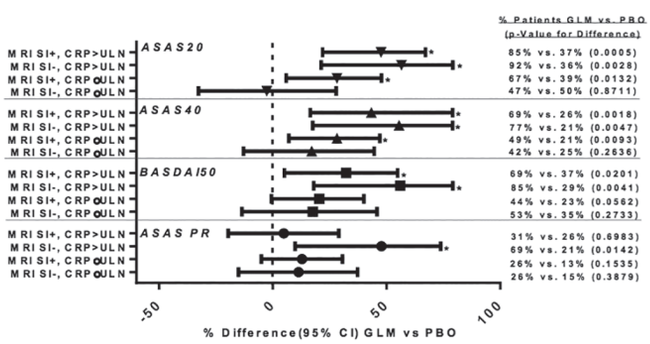
Introduction/Aims. Efficacy of golimumab (GLM) for nr-axSpA was demonstrated in a randomized, double-blind (DB), placebo (PBO)-controlled, phase 3 study (GO-AHEAD; NCT01453725) (1). In a subgroup analysis, we now investigate the effects of GLM based on presence or absence of objective inflammation (sacroiliitis on MRI and/or C-reactive protein [CRP] > upper limit of normal [ULN]) at baseline.
Methods. Patients with nr-axSpA (ASAS criteria, centrally read SI joint X-rays/MRIs, disease duration ≤5 years, chronic back pain ≥3 years, high disease activity, and inadequate response or intolerance to NSAIDs) were randomized (with ASAS-defined MRI sacroiliitis by single central reader [yes, SI+; no, SI–] and CRP level [≤ULN or >ULN] as stratification factors) to GLM 50 mg SC or PBO Q4W for 16 weeks. The primary endpoint was ASAS20 response at week 16. Estimated between-group differences in response at week 16 on ASAS20, ASAS40, BASDAI50, and ASAS partial remission (PR) were compared for four patient subgroups (MRI SI+ & CRP >ULN; MRI SI– & CRP >ULN; MRI SI+ & CRP ≤ULN; MRI SI– & CRP ≤ULN) by Miettinen-Nurminen methods; no multiplicity control was used.
Results. In total, 197 patients were treated (GLM=97; PBO=100). Treatment-group differences in ASAS20, ASAS40, BASDAI50, and ASAS PR response were greater in patients with baseline objective inflammation (Figure). Results should be interpreted with caution, given the small subgroups and absence of multiplicity control.
Conclusions. In the GO-AHEAD trial, responses to GLM (vs PBO) were greater in patients with objective inflammation (particularly with CRP >ULN) at baseline. No GLM treatment benefit was observed in pts with MRI SI– & CRP ≤ULN.
Reference
1. Sieper J *et al.*: *Arthritis Rheum* 2015; 67(10): 2702-12.



** p<0.05 for % Difference GLM vs. PBO*

Figure. Subgroup Analysis of Response by MRI SI Status and CRP Level at Baseline.

P144

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, DOUBLE-BLIND STUDY

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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) Index and Health State (0–10cm VAS), and Work Productivity and Activity Impairment (WPAI) at weeks 16 and 52 and the Patient's Global Disease Assessment (PGDA; 0–10cm VAS) 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 (GLM/GLM) and -26.5 (27.2) (PBO/GLM).
Conclusions. 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 PBO in the DB phase had notable improvement in QoL and work productivity.
Reference

1. SIEPER J *et al*.: *Arthritis Rheum* 2015; 67(10): 2702-12.

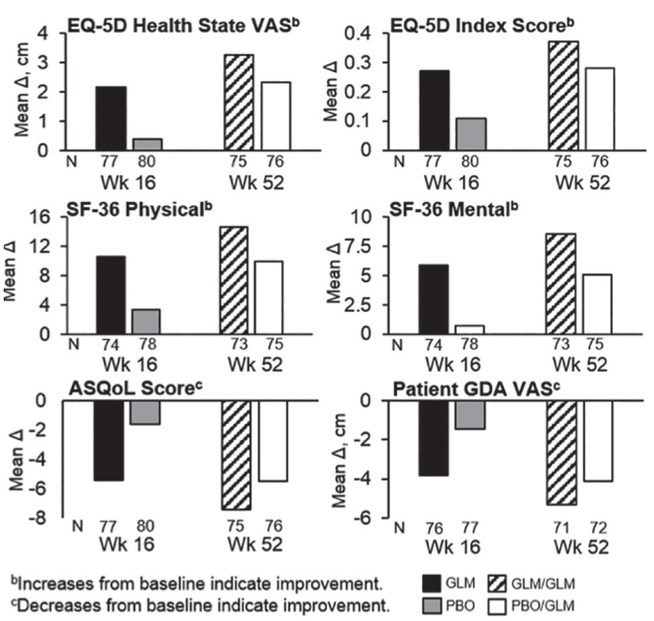

Figure. Mean Change From Baseline in QoL Scales.

P145

EFFECT OF SECUKINUMAB ON SPINAL RADIOGRAPHIC CHANGES THROUGH 2 YEARS IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS OF THE PHASE 3 STUDY, MEASURE-1

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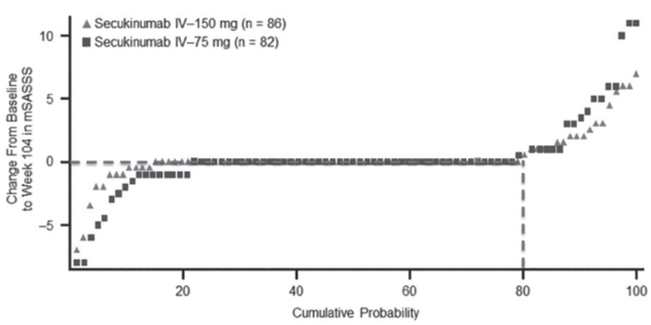
Introduction. Inhibition of radiographic spinal changes represents a main goal of therapy in active ankylosing spondylitis (AS). Here, we report effects of secukinumab on radiographic progression up to 104 weeks in MEASURE-1 trial (NCT01358175).
Materials and Methods. 371 patients with active AS were 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 10.22±16.62; 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

1. BAETEN *et al*.: *Arthritis Rheumatol* 2014; 66 (11 Suppl.): S360.

Disclosure of Interest:
BJ: Grant/research support from: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, Consultant for: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, Speakers bureau: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi- Aventis and UCB
BX: Grant/research support from: AbbVie, Merck, Pfizer, UCB, Novartis, and Chugai, Consultant for: AbbVie, Merck, Pfizer, UCB, Novartis, and Chugai, Speakers bureau: AbbVie, Merck, Pfizer, UCB, Novartis, and Chugai
DA: Grant/research support from: AbbVie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Consultant for: AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer, UCB
BD: Grant/research support from: Boehringer Ingelheim, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, Boehringer Ingelheim, BMS, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, UCB
SJ: Grant/research support from: AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB, Consultant for: AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB

EP: Consultant for: AbbVie, BMS, Merck, Novartis, Pfizer, Roche, UCB
TZ: Shareholder of: Novartis, Employee of: Novartis
MR: Shareholder of: Novartis, Employee of: Novartis
RH: Shareholder of: Novartis, Employee of: Novartis
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The study was sponsored by Novartis Pharma AG. Academic advisors and Novartis personnel designed the study. Novartis conducted the data analyses. All authors had access to the data and vouch for the completeness and accuracy of the data and analyses.

P146

SECUKINUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS: COMPARATIVE EFFECTIVENESS RESULTS VERSUS ADALIMUMAB UP TO 48 WEEKS USING A MATCHING-ADJUSTED INDIRECT COMPARISON

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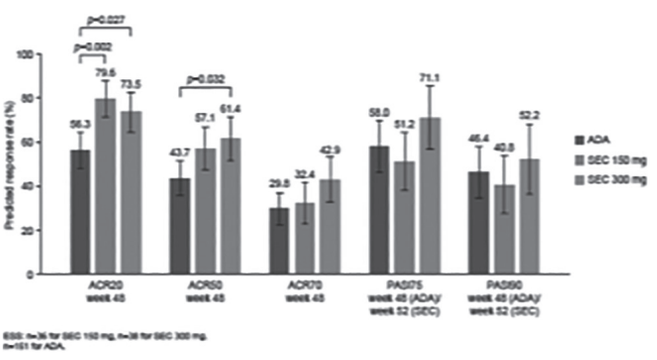
[1]University of Glasgow, Glasgow, UK; [2]University of Queensland, Brisbane, Australia; [3]Swedish Medical Center and University of Washington, Seattle, WA, USA; [4]University of Bristol, Bristol, UK; [5]Mapi Group, Munich, Germany; [6]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [7]Novartis 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, body weight, sex, race, methotrexate-use, presence of psoriasis (≥3% body surface area), mean PASI score, dactylitis, enthesitis, mean HAQ-DI and previous biologic therapy. FUTURE2 weighted outcomes (ESS: n=36/n=38 for SEC 150/300 mg) were compared with ADEPT (n=151). ACR was assessed at week 48 and PASI at week 48 for ADA and week 52 for SEC.
Results. SEC had higher mean ACR20/50/70 responses than ADA, with statistical significance for SEC 150/300 mg at ACR20 and for SEC 300 mg at ACR50. Findings were consistent across sensitivity analyses. PASI 75/90 response rates were numerically better for SEC 300 mg than ADA.
Conclusions. SEC was associated with numerically higher response rates for joint and skin outcomes with statistically significant higher responses versus ADA for ACR endpoints at week 48 after adjusting for several patient baseline characteristics. We recommend these findings are confirmed in a head-to-head trial.

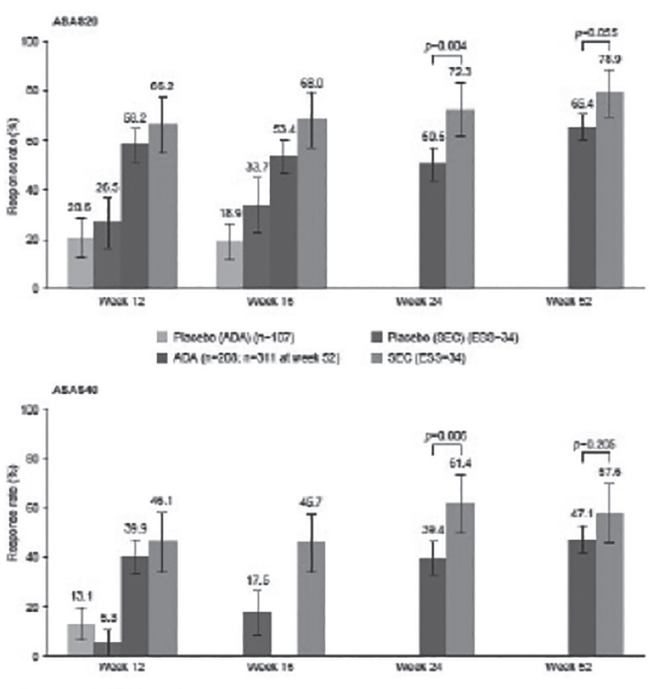


P147

SECUKINUMAB FOR THE TREATMENT OF ANKYLOSING SPONDYLITIS: COMPARATIVE EFFECTIVENESS RESULTS VERSUS ADALIMUMAB USING A MATCHING-ADJUSTED INDIRECT COMPARISON

Maksymowych W.[1], Strand V.[2], Baeten D.[3], Nash P.[4], Thom H.[5], Hunger M.[6], Gandhi K.[7], Richards H.[7], Jugl S.[8]
[1]University of Alberta, Edmonton, AB, Canada; [2]Stanford University, Palo Alto, CA, USA; [3]Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; [4]University of Queensland, Brisbane, Australia; [5]University of Bristol, Bristol, UK; [6]Mapi Group, Munich, Germany; [7]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [8]Novartis Pharma AG, Basel, Switzerland

Background. In the absence of direct comparison or a continuous common placebo arm, matching-adjusted indirect comparison (MAIC) is a recently developed method for comparative effectiveness research, simulating head-to-head comparison.
Objectives. To assess the relative efficacy of secukinumab 150 mg (SEC) versus adalimumab (ADA) in adults with active ankylosing spondylitis (AS).
Methods. MAIC adjusts for differences in patient baseline characteristics, reducing the effective sample size (ESS) for one trial, but matching this with the population of another trial. Patient-level data from the SEC arm in MEASURE2 (n=72) was 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 treatment led to statistically significant higher ASAS20/40 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.



P148

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 DOSING (MEASURE-2)

Marzo-Ortega H.[1], Legerton C.W.[2], Sieper J.[3], Kivitz A.[4], Blanco R.[5], Cohen M.[6], Martin R.[7], Readie A.[7], Richards H.[8], Porter B.[7]
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Introduction. Secukinumab improved signs and symptoms of ankylosing spondylitis (AS) over 52 weeks in the MEASURE-2 study (NCT01649375)[1]. 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 150 or 75mg or placebo. Details of the study design have been published elsewhere[1].
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 hsCRP, ASAS5/6, BASDAI, SF-36 PCS and ASAS partial remission were sustained through Week 104 with secukinumab. In TNF-inhibitor-naïve (TNFi-naïve) subjects, ASAS20/40 response rates at Week 104 (observed data) were 76.9/56.4% and 80.0/60.0% with secukinumab 150mg and 75mg, respectively; corresponding rates in TNF-inhibitor-inadequate responder (IR) subjects were 85.0/50.0% and 68.8/43.8%. Exposure-adjusted incidence rates for serious infections/infestations, IBD, malignant/unspecified tumours and MACE with secukinumab were 1.2, 1.4, 0.5 and 0.7 per 100 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 TNFi-naïve and TNFi-IR patients. Safety profile was consistent with previous reports.
Reference
1. BAETEN *et al*.: *N Engl J Med* 2015; 373: 2534-48.

Disclosure of Interest:
M-OH: Grant/research support from: Janssen and Pfizer, Consultant for: Abbvie, Celgene, Janssen, Novartis and UCB, Speakers bureau: Abbvie, Celgene, Janssen and UCB
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KA: Consultant for: AbbVie, Pfizer, Genentech, UCB and Celgene, Speakers bureau: Celgene, Pfizer, and Genentech
BR: None declared
CM: Consultant for: Abbvie, Amgen, BMS, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi and UCB, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi and UCB
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P149

REDUCTION IN SPINAL RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS PATIENTS RECEIVING PROLONGED TREATMENT WITH TNF INHIBITORS

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[1]Rheumatology and Clinical Immunology, UMCG, Groningen; [2]Rheumatology, MCL, Leeuwarden; [3]Rheumatology, MUMC, Maastricht; [4]Laboratory Medicine, UMCG, Groningen; [5]Radiology, UMCG, Groningen; [6]Radiology, MCL, Leeuwarden; [7]Epidemiology, UMCG, Groningen, The Netherlands

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 naïve 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, 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 2.3 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], Bos R.[2], Bootsma H.[1], Brouwer E.[1], Spoorenberg A.[1,2]
[1]Rheumatology and Clinical Immunology, University Medical Center Groningen; [2]Rheumatology, 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 damage over 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?

Kelsall J.[1], Choquette D.[2], Arendse R.[3], Rahman P.[4], Zummer M.[2], Avina-Zubieta J.A.[5], Rampakakis E.[6], Psaradellis E.[6], Maslova K.[7], Osborne B.[7], Nantel F.[7], Lehman A.J.[7], Tkaczyk C.[7]
[1]Private practice, Vancouver; [2]Montreal University; [3]Polmed Research, Saskatoon; [4]St Clare's Mercy Hospital, St-John's; [5]Arthritis Research Canada, Richmond; [6]JSS, Montreal; [7]Janssen, Toronto, Canada

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 sampled t-test and the 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 vs. 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%,19.7%, 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. The mean enthesitis count at baseline and 12 months was 4.4 vs. 2.6 (p=0.061) among AS patients and 5.0 vs. 3.8 (p=0.006) in PsA patients, respectively, and for dactylitis in AS: 1.36 vs. 0.79 (p≤0.001); PsA: 1.06 vs. 0.76 (p≤0.001) at baseline and 6 months, respectively.
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.

P152

MINIMAL DISEASE ACTIVITY AMONG PSORIATIC ARTHRITIS PATIENTS IN A REAL-LIFE REGISTRY

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[1]Montreal university, Montreal; [2]St Clare's Mercy Hospital, St-John's; [3]CHUL de Quebec, Quebec; [4]Private practice; Scarborough; [5]Arthritis Research Canada, Richmond; [6]Polmed Research Inc, Saskatoon; [7]JSS, Montreal; [8]Janssen, Toronto, Canada

Background. Minimal disease activity (MDA) is defined as the fulfillment of ≥5 of the following criteria: TJC28≤1, SJC28≤1, PASI≤1, pain (VAS) ≤15 mm, PtGA (VAS) ≤20 mm, HAQ≤0.5, and tender entheseal points ≤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 4/6 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 PtGA 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%, PtGA: 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, PtGA 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.

P153

DRUG SURVIVAL FOR ANTI-TNF TREATMENTS IN A UK COHORT OF AXIAL SPONDYLOARTHRITIS PATIENTS

Yahya F.[1,2], Cavill C.[1], Berry-Jenkins J.[1], Boyle C.[1], Bond D.[1], Sengupta, R.[1,3]
[1]Royal National Hospital for Rheumatic Diseases, Bath, UK; [2]University Malaya, Kuala Lumpur, Malaysia; [3]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.
Conclusion. There was no difference in drug survival times among the different anti-TNF drugs in this AxSpA cohort. In keeping with previous published data, switching to a second or third anti-TNF results in poorer drug survival.
Appendix:

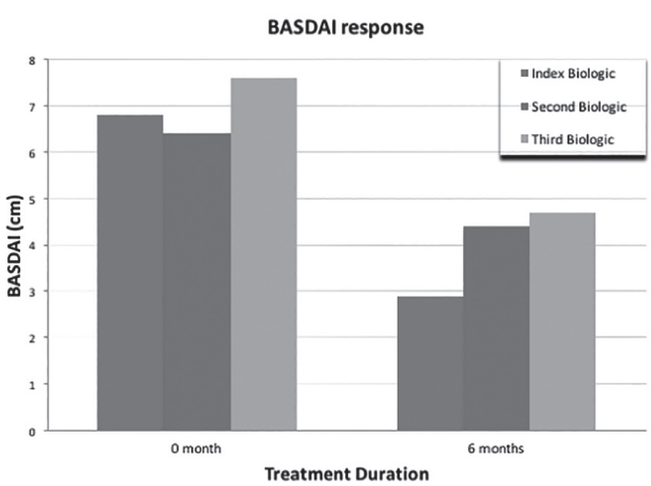

Fig. 1. BASDAI response 6 months after starting anti-TNF.

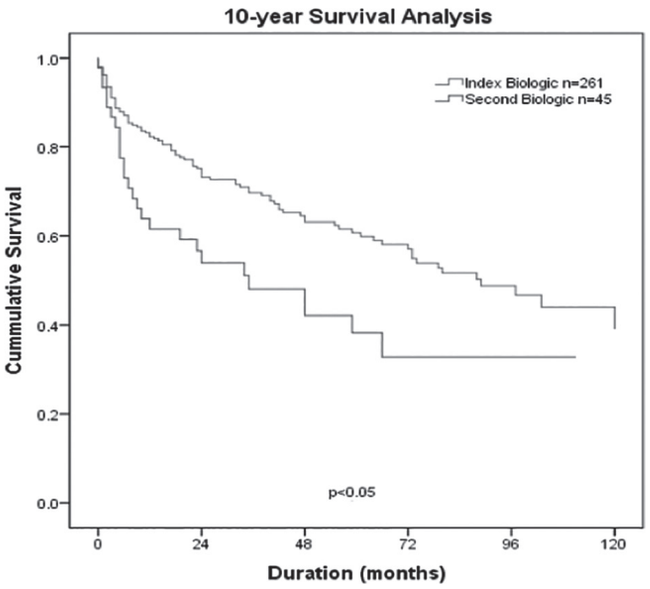

Fig. 2. Survival analysis for index and second-line anti-TNF.

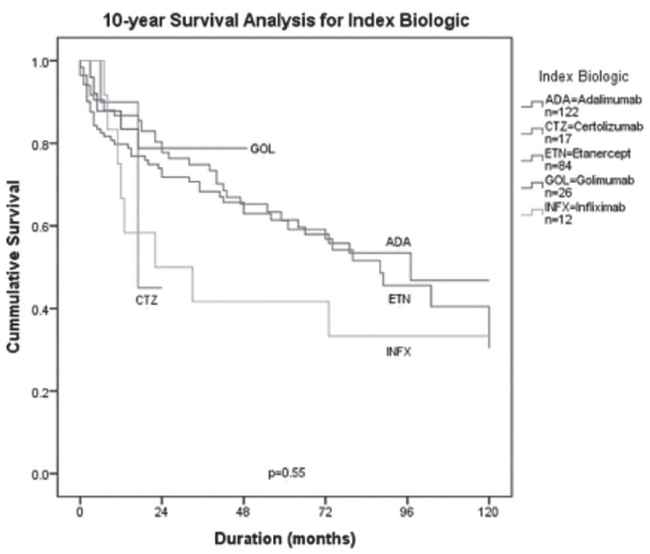

Fig. 3. Survival analysis for the different index anti-TNF.

P154

IMPACT OF METHOTREXATE DOSE ON ADALIMUMAB EFFICACY IN PSORIATIC ARTHRITIS: A SUBANALYSIS OF ADEPT

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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 PBO subgroups. 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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DRUG SURVIVAL OF TNF-INHIBITORS THERAPY IN DIFFERENT KINDS OF JUVENILE SPONDYLOARTHRITIS: SINGLE CENTER EXPERIENCE

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Background. Juvenile spondyloarthritis (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 of 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±3.7 years (range 3.58-17.9); mean disease duration was 50,4 months (range 2-163). 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 (185 patient-year 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 4.49-11.72), inefficacy -i10.73% (95%CI 7.19-15.71), 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, $p<0.05$). Due to inefficacy Infliximab was cancelled more often than adalimumab (16.9% vs 6.85%, $p<0.05$). Etanercept was rare withdrawn due to organization problem in compare to infliximab and adalimumab (6.3% vs 16.98% and 13.7%, $p<0.05$). 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. The average survival rate of etanercept and adalimumab was higher in ERA vs JAS and JPsA (84% vs 68% and 67% respectively), but for infliximab it was similar in all JSpA subtypes.
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.

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CLINICAL AND FUNCTIONAL EFFICIENCY OF HIP ARTHROPLASTY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Aim. To evaluate the results of the hip joints replacement in patients with SpA under the dynamic supervision of a rheumatologist and orthopaedist within the first year after the operation.
Materials and Methods. As part of special program for rheumatology patients hip endoprosthesis was done in 12 patients (mean age - 44,2±15,3 years) with SpA, 8 of them with ankylosing spondylitis (AS) and 4 with psoriatic arthritis (PsA). Duration of the disease - 13,3±7,9 years, positive for HLA B27 in 9 (75%) patients. High activity for ASDAS was at 58.3% of the patients. Took NSAIDs at the time of the operation - 11 (91.6%) patients, sulfasalazine 5 (41.6%), methotrexate- 2 (16.7%). 1 (8.3%) patient received etanercept,1 (8.3%) patient - infliximab. Dynamic observation of rheumatologist and orthopedist was carried out before, just after surgery, after 6 and 12 months, with the assessment of VAS, BASDAI, ASDAS, BASFI.
Results. The reduction of pain intensity on the VAS was observed in the first month after the surgery (47,3±18,6 mm), initially it was 74,0±24,1 mm, 42.5±9 after 6 months (p<0.05), after 12 months - up to 22,5±9,9 mm (p<0.05). ASDAS significantly (p<0.05) reduced from 2,94±2,01 to 1,68±1,35 - in 6 months and 1,26±0,88 - 12 months after operation; BASDAI: from 6,24±3,91 to 2,75±2,20 - 6 months, 2,65±1,53 at 1 year follow-up. BASFI index before surgery - 5,48±3,29, 6 months - 2,78±2,31, 1 year - 2,32±1,60 points. No complications after surgery were registered.
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.

P157

INFLUENCE OF SULFASALAZINE COMEDICATION IN SWITCHING AND RESPONSE TO ANTI-TUMORAL NECROSIS FACTOR IN ANKYLOSING SPONDYLITIS

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Introduction/Aim. Recently, comedication with methotrexate or use of any DMARD was associated to better anti-TNF retention in spondyloarthritis (SpA). However, data on the possible relevance 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 AS patients under 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 (59%) were prescribed only one anti-TNF, 48 (41%) switched to second anti-TNF (58% failure and 42% side effects) and 13 (11%) to third anti-TNF (62% failure and 38% 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=0.01) than patients who switched anti-TNF. The analysis of predictors of switch at baseline revealed that non-switchers were more often treated with sulfasalazine (SSZ) (63.8% vs. 41.7%, p=0.02), particularly the group with pure axial disease (70.8% vs. 27.3%, p=0.03). At the end of the study patients with SSZ concomitant with anti-TNF achieved lower disease activity (ASDAS-CRP, 1.5±0.9 vs. 1.9±0.9, p=0.009) and remission (ASDAS-CRP<1.3, 47.7% vs. 25.0%, p=0.041) than those without SSZ.
Conclusion. This study provides relevant evidence that SSZ comedication improves AS anti-TNF response and reduces anti-TNF switch in patients with pure axial disease.

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LATENT TUBERCULOSIS SCREENING AND TREATMENT IN ANKYLOSING SPONDYLITIS PATIENTS UNDER ANTI-TNF THERAPY IN ENDEMIC AREA

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Introduction/Aim. In the last decade anti-TNF agents have emerged as an important treatment for rheumatic diseases, particularly for ankylosing spondylitis (AS). Screening and treatment of latent tuberculosis infection (LTBI) is essential before the use of these drugs. However, current recommendations for this screening and treatment and their efficacy are still not well established in endemic regions. The purpose of the present study is to evaluate, in an endemic area, the efficacy of LTBI screening and treatment in AS patients under anti-TNF.
Methods. One hundred and ten AS patients eligible for anti-TNF agents were initially screened for LTBI by tuberculin skin test (TST), chest X-ray and history of contact. Patients were regularly followed at 1-3 months interval.
Results. LTBI screening was positive in 48 (43.6%) patients. TST positivity accounted for majority of LTBI diagnosis (46; 95.2%): 39 (81.2%) solely positive TST, 6 (12.5%) with positive TST and history of contact, 1 (2.1%) with positive TST and abnormal chest X-ray and 2 (4.2%) with isolated history of contact. These patients received at least 1 month isoniazid before starting anti-TNF treatment and all of them completed 6 months of isoniazid treatment. Two patients developed TB in spite of LTBI treatment: one was a medical doctor with proven exposure to TB after 8 months receiving adalimumab, and the other became symptomatic right after the second dose of adalimumab, and probably had active TB that was misdiagnosed as LTBI. Sixty-seven (60.9%) patients were treated with one anti-TNF, 33 (30%) with two and 10 (9.1%) with three (86 infliximab, 49 adalimumab and 75 etanercept). Thirty-three (30%) patients were under prednisone, mean dose 10.6 mg/day. No difference was observed in TST positivity rate in this group comparing with the patients without this drug (48.5% vs. 39%, p=0.40). TST was repeated in 9/64 (14%) patients initially screened negative in case of prolonged discontinuation and reintroduction of biologic treatment (n=2) or clinical tuberculosis (TB) suspicion (n=7). In the latter group, TST conversion was observed in 3 patients diagnosed with active pulmonary TB. Median duration of anti-TNF treatment (2 adalimumab e 1 infliximab) in these three patients before the diagnosis of TB was 1.8 (0.6 - 3.5) years.
Conclusion. Our study provides evidence that TBLI screening and treatment is also efficient for endemic areas. In addition, we report that new exposure accounts for nearly all cases of TB infection and further demonstrate that symptom guided TST repetition is very effective for TB diagnosis during anti-TNF therapy in high TB incidence region.

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ANTI-TNF THERAPY IN AXIAL SPONDYLOARTHRITIS: PREDICTION OF THERAPEUTIC RESPONSES USING IMMUNOLOGICAL SIGNATURES

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Introduction/Aim. The introduction of anti-TNF therapy has proven effective to reduce inflammation and clinical symptoms in several chronic inflammatory diseases. However, TNF-blockers are effective only in a subpopulation of patients and it is currently not possible to predict responsiveness of patients to anti-TNF treatment. To address this issue, we have asked whether the analysis of the immune functions of patients will allow us to define biomarkers that can predict therapeutic responses to TNF blockers.
The goals of this project were to define (i) the impact of anti-TNF therapy on immune responses to microbial challenges and stimuli targeting specific immune pathways in axial spondyloarthritis (axSpA) patients and (ii) to identify immunological correlates associated with therapeutic responses to TNF blockers before the initiation of therapy.
Methods. We have used whole-blood, syringe-based “TruCulture” assays to assess innate or adaptive immune responses to stimuli targeting specific signaling pathways or mimicking infections in patients. We have investigated immune responses to 20 different stimuli in a pilot study involving 12 axSpA patients before and 3 months after initiation of anti-TNF therapy. Validation of our findings in a replication cohort is ongoing.

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

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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-biological 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.
Disclosures. This study was funded by Merck Sharp & Dohme The Netherlands, a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA

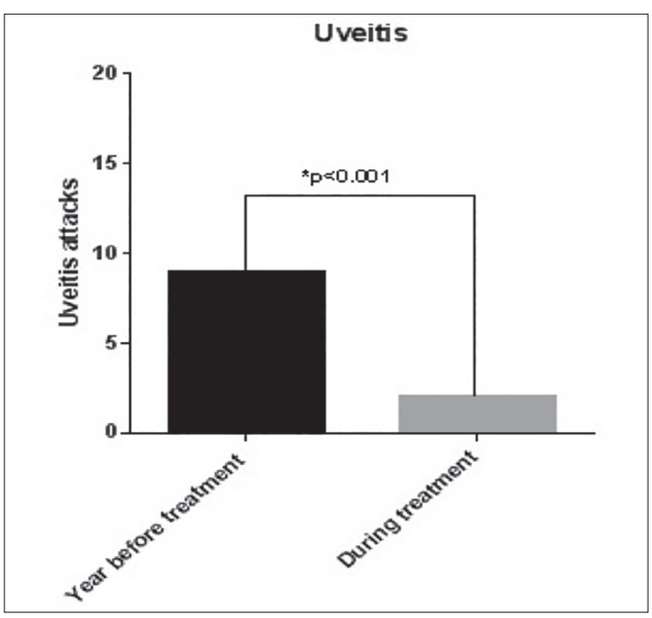

Figure 1.

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SMOKING RELATED WITH DISEASE RESPONSE AND AGE AT DIAGNOSIS IN ANKYLOSING SPONDYLITIS

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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.

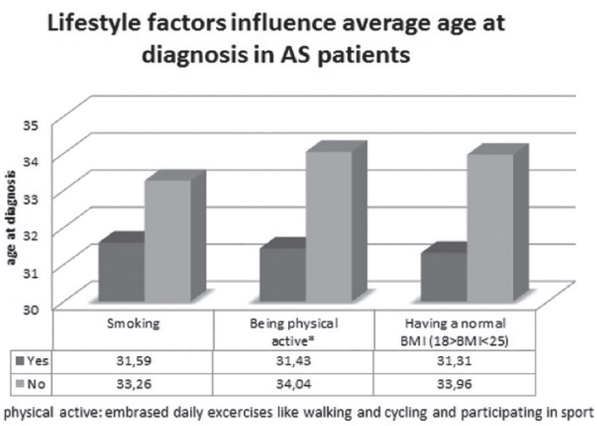

Fig. 1. Lifestyle related factors influencing the age at diagnosis in AS patients.

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DEVELOPMENT OF RECOMMENDATIONS ON THE CONTENT, ORGANISATION AND POSITIONING OF EXERCISE THERAPY FOR AXIAL SPONDYLOARTHRITIS IN THE NETHERLANDS

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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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