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Abstracts

Invited Lectures

INV2

JAKi-MECHANISM OF ACTION: WHAT EXPLAINS THEIR EFFICACY IN SpA?

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Over the past ten years drugs targeting of the Janus kinases (JAKs) have entered the clinical armamentarium and first generation pan-JAK inhibitors (JAKi) are now used worldwide for the treatment of autoimmune diseases as well as malignancies. Studies on the mechanism of action of successful JAK inhibitors have revealed that, besides T and B cells, they act on innate immune cells and can promote tolerance. For this reason, JAKi are proving to be useful for a variety of immunological diseases ranging from hematological malignancies, rheumatoid arthritis, psoriatic arthritis, diabetic nephropathies, alopecia to rare inflammatory diseases.
More selective, second-generation JAKi are now being developed and some have already reached the late stages of clinical development for several of immune-mediated pathologies
I will review the most recent findings related to JAKis' mechanism of action, discuss their role in Spondyloarthritis and some of the newest diseases for which inhibition of the JAK-STAT pathway is proving to be a successful therapeutic approach or is being actively investigated.

INV3

THE STROMAL CODE IN SPA – LESSONS FROM OTHER JOINT TISSUES

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Joints, tendons, and ligaments are primarily involved in different inflammatory, metabolic and degenerative diseases. The connective tissues are an important structural part of these tissues and organs. Whereas chronic arthritis, including spondyloarthritis, have long been considered in the context of infiltrating immune cells, new paradigms highlight the role of tissue-resident inflammatory cells, of different types of fibroblasts and of the extra-cellular matrix molecules. To understand pathology, it is important to also understand the homeostatic role of the tissues involved. As part of the musculoskeletal system all these connective tissue sites undergoing substantial biomechanical stress. Hence insights into homeostatic and pathological mechanisms of different disease in the joint fits well to achieve a more comprehensive understanding of different joint diseases including SpA. New tools and concepts are available to achieve these goals and promise to also impact our conceptual understanding of SpA, which may lead to better diagnosis and management of the disease.

INV4

STROMAL CELLS: COMMANDERS OF JOINT INFLAMMATION, OR INNOCENT BYSTANDERS?

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In *The Structure of Scientific Revolutions* (1), Thomas Kuhn popularized the term "paradigm shift". Kuhn defined the stages of scientific progression, whereby periods of stable, incremental research are upheaved by disruptive observations. As a result, existing paradigms are thrown into disarray, forcing the scientific community to change their perspective and embrace new paradigms. The rheumatology research community has spent the last 30 years focusing on the immune system as the driver of inflammatory arthritides. Indeed, this paradigm has served the community well, resulting in effective immune-targeting therapeutics (2). Yet, inconvenient truths remain; a significant portion of patients do not respond to immunotherapies. Further, we have largely ignored the "other" cells that comprise musculoskeletal tissues, namely the stromal cells.
In the last few years, the advent of single cell technologies and advances in tissue sampling techniques have allowed us to characterize joint stromal cells with unprecedented resolution. We are now aware of anatomically distinct populations of stromal cells, which play specific roles in the pathogenesis of arthritis (3, 4). Such landmark studies have placed us in the midst of a paradigm shift, with growing acknowledgment that stromal cells are important players, and maybe even the instigators, of joint inflammation. The translational value of this knowledge remains in its infancy, but holds great potential in developing novel treatments for patients unresponsive to immune-targeting therapeutics (5, 6).
In this invited talk, the diversity of stromal cells in joint tissue will be discussed, ranging from tendon, bone and cartilage to the more commonly studied synovium. Phenotypic shifts in these cells, and the stimuli causing the shifts, will be examined. Key publicly available datasets will be explored to reveal how such data can be leveraged for novel research. Finally, the past attempts and future promises of targeting joint stromal cells for the treatment of arthritis will be explored.

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INV6

THE UPDATED ASAS CORE SET: WHAT ARE THE CONTROVERSIES AND REMAINING UNMET NEEDS?

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The Assessment of SpondyloArthritis international Society-Outcomes Measures in Rheumatology (ASAS-OMERACT) COS for ankylosing spondylitis was developed more than two decades ago and needed to be updated. An international working group representing different key stakeholders (rheumatologists and other health professional experts in axial spondyloarthritis (axSpA), patient representatives, pharmaceutical industry representatives, drug regulation officer, and methodologists) selected a preliminary core outcome set of domains and instruments following a predefined process (1, 2). These were later presented, discussed and voted at the annual ASAS meeting 2019 and 2022.
ASAS recently updated the COS for AS into the COS set for axSpA. The first component of the updated COS for axSpA (the domains "*what to measure*") was published in 2021 (3) and the second component (the instruments "*how to measure*") was published in 2022 (4). The updated COS set for axSpA includes seven instruments for the domains that are mandatory for all trials: ASDAS and NRS patient global assessment of disease activity; NRS total back pain; average NRS of duration and severity of morning stiffness; NRS fatigue; BASFI; and ASAS Health Index. There are 9 additional instruments considered mandatory for disease modifying drugs (DMARDs) trials: MRI activity SPARCC sacroiliac joints and SPARCC spine, uveitis,

IBD and psoriasis assessed as recommended by ASAS, 44 swollen joint count, MASES, dactylitis count, and mSASSS. The imaging outcomes are considered mandatory to be included in at least one trial for a drug tested for DMARD-properties. During this lecture the controversies encountered throughout the course of the updating process of the COS for axSpA and the remaining needs will be presented and discussed.

Acknowledgements. The COS for axSpA project received funding from ASAS.

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INV7

NOVEL BIOMARKER TECHNOLOGIES FOR AXSPA: LESSONS LEARNED FROM RA AND PSA

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Introduction. In the last 10 years, significant technological advances in multi-omic single-cell approaches have led to an exponential increase in the availability of high-quality data from disease tissues and have furthered our understanding of the pathological pathways and the key cell types/states that underpin them.
Methods/Results. We will review some of the recent novel data generated in RA and PsA and discuss the potential implications for axSpA. In particular, we will focus on our group's work in the single-cell RNA sequencing of immune cell transcriptomes and immune receptor repertoires in addition to time-of-flight mass cytometry data (CyTOF) in PsA and consider the work of the Accelerating Medicines Partnership in rheumatoid arthritis.
Conclusions. The next 10 years represent an unprecedented opportunity to understand the pathobiology of axSpA at high resolution using novel technologies. These new insights will likely test many existing dogmas. The key challenge will be our ability to utilise these novel data to develop new therapeutic approaches for patients.

INV10

DEVELOPMENTS IN AXIAL SPONDYLOARTHRITIS IN THE LAST DECADES – A PERSONAL VIEW

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Axial spondyloarthritis (axSpA) is a frequent chronic inflammatory rheumatic disease that affects mainly the axial skeleton, while patients with predominantly peripheral SpA suffer mainly from arthritis, enthesitis and dactylitis. The concept of spondyloarthritis also covers psoriasis, inflammatory bowel disease and anterior uveitis which are also referred to as extramusculoskeletal manifestations. The pathognomonic musculoskeletal findings of patients with axSpA are inflammatory, osteodestructive and osteoproliferative changes in the sacroiliac joints (SIJ) and in spinal structures, many of which are of entheseal nature. Inflammatory and structural changes in the axial skeleton are assessed by magnetic resonance imaging (MRI) and conventional radiography (CR). The value of the latter was first recognized in 1934, of MRI in 1984. The most severe outcome is total spinal ankylosis which radiographically presents as 'bamboo spine'; this has long been recognized as the clinically leading sign that led to the term ankylosing spondylitis (AS) which is now, based on the new classification criteria developed by ASAS in 2009, slowly being replaced by the term radiographic axSpA (r-axSpA) which is largely equivalent to AS. The ASAS criteria followed the concept of SpA recognized in 1974, the modified New York criteria (1984), the Amor criteria (1989) and the ESSG criteria (1990). For the first time, MRI and HLA B27 were part of the criteria. The association of AS with HLA B27 was first described in 1973, and two other genes, ERAP 1 and the IL-23R were added in 2007 as a result of a genome wide association study. The fact that the ERAP 1 gene coding for an enzyme that trims peptides in the endoplasmatic reticulum is only associated with AS in connection with HLA B27 can be regarded as an argument that CD8+ T cells are involved in the pathogenesis of AS.
The diagnosis axSpA covers different stages, variable courses and outcomes of *one* disease which is initially treated with non-steroidal anti-rheumatic drugs (NSAIDs). For classification purposes, non-radiographic (nr-axSpA) is differentiated from r-axSpA because of differences in the approval status of biologic disease modifying anti-rheumatic drugs (bDMARDs), e.g. the first TNF blocker approved in AS, infliximab, in 2003, is currently not approved for nr-axSpA. The treatment with bDMARDs such as the IL-17 inhibitors and with JAK inhibitors has made a big difference for patients with axSpA in the last decades, including the reduction of inflammation and the partial inhibition of new bone formation. The latter is a methodological problem because only retrospective data are available to date. This is in contrast to prospective studies with NSAIDs, the first one of which showed that giving NSAIDs continuously was superior to an on demand strategy (with a coxib in 70% of the cases).
The table below shows the historical development of positive findings and results in axSpA related scientific research related to major inventions in imaging and immunology. This table is most probably incomplete, and the selection presented highly subjective. However, it becomes clear that the progress in studies for a disease depends much on a major development in basic research. Several decades after the Roentgen technique had been used, MRI came into the game, and HLA B27 was of course only discovered after the HLA system had been recognized decades ago. Genom wide association studies could only be performed after the discovery of DNA sequencing about 60 years ago. Regarding therapy the revolution was only possible by the major invention of monoclonal antibody production almost 50 years ago. The last decades have been a revolution in that regard. Until about 20 years ago we had nothing but NSAIDs to treat relatively young patients whom we had to tell: these drugs and physiotherapy is about all we can do for you. Importantly, and has also been recognized that axSpA is a frequent disease – for example much more frequent than M.Crohn – a disease that also affects young people, more frequently females though. The sex ratio in axSpA has been much discussed recently. After times where it used to be 16:1 it became close to 1:1 – with males more frequently having r-axSpA and females nr-axSpA. However, recent data on the prevalence of MRI detected bone marrow edema in the population, in conjunction with the high prevalence of back pain and psoriasis (2-3% of the population), the fact that >95% of HLA B27+ subjects do not get the disease at all and the result of clinical studies with either low response rates on bDMARDs or high placebo response rates have raised doubt that the prevalence of axSpA in women is that high – a definite challenge for further research in axSpA.

INV 10. Table. The historical development of major scientific discoveries in medicine which later influenced axSpA related research in relation to some advances in the field of AS – the period between 1895-1986.

Topic	Date of discovery or first publication	Name	Nobel prize
Röntgen (X-rays)	1895	K. Roentgen	1905
HLA-system	1958	J. Dausset	1980
Determination of base sequences in nucleic acids	1967	F. Sanger	1980
HLA B27	1973	D. Brewerton, L. Schlossstein	
Magnetic resonance imaging (MRI)	1973	P. Lauterbur & P. Mansfield	2003
Concept of spondyloarthritis (SpA)	1974	J.M. Moll & V. Wright	
Monoclonal antibodies	1975	G. Koehler & C.Milstein	1984
Inflammatory back pain	1977	A. Calin	
Gut inflammation in SpA	1985	H. Mielants, E.Veys	
Polymerase chain reaction (PCR)	1986	K. Banks Mullis & W. Smith	1993

INV12

INVESTIGATING THE MICROBIOTA IN GUT AND JOINT DISEASE USING TRANSGENIC AND GERM-FREE MOUSE TECHNOLOGY

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Arthritis is the most common extra-intestinal complication in IBD. Conversely, spondyloarthritis (SpA) patients are at risk for developing IBD and often display subclinical gut inflammation. These observations suggest a shared disease etiology between IBD and SpA, commonly termed 'the gut-joint-axis'. The clinical association between gut and joint inflammation is further supported by the success of common therapeutic strategies, including anti-TNF and anti-IL23 therapies. Moreover, both IBD and SpA are characterized by distinct changes in microbiota composition and community structure, termed dysbiosis. In contrast, other arguments support a functional disconnect between gut and joint inflammation and indicate independent tissue intrinsic disease mechanisms.
Using two independent transgenic mouse models of gut and joint disease, either TNF or IL-1b driven, we investigated the role of the microbiota and intestinal inflammation on arthritis development, by rederiving both transgenic lines in germ-free condition. In both transgenic arthritis models, joint pathology develops independent of the intestinal microbiota or gut inflammation, as genetically susceptible mice develop full-blown articular inflammation under germ-free conditions. In contrast, TNF-induced gut inflammation is fully rescued in germ-free conditions, despite systemic joint pathology. Together, using two independent transgenic mouse arthritis models, we demonstrate that in a specific genetic contexts joint inflammation can be induced by sterile factors only, and can develop independent of the gut microbiota and gut inflammation.

INV14

FIBROBLAST SUBSETS IN SPONDYLOARTHRITIS

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The synovium is a thin mesenchymal membrane encapsulating the joint space and is the major site of pathology in rheumatoid arthritis. Synovial fibroblasts comprise a key cell type in the hyperplastic pannus that invades and destroys cartilage and bone via their production of matrix degrading enzymes. However, they are also major contributors to inflammation by providing an amplificatory loop that drives the production of cytokines such as IL6. Emerging data now suggests that they also play a role in dictating stromal memory (the tendency for arthritis to flare at the same set of joints) [3] and mediating chronic pain via the production of nerve growth factors.
Until now, it has remained unclear if all these functions are mediated by one, or several different subsets of fibroblasts as functional subclasses of fibroblasts have proven difficult to define, characterize and study in health and disease. In contrast the identification of leucocyte subsets with non-overlapping effector functions provided a molecular framework for the development of targeted therapies that have demonstrated spectacular success in immune-mediated inflammatory diseases.
In this lecture I will explain the interrelationships between synovial fibroblast subsets in the lining and sub-lining layers of the synovium and observe how selective deletion of these subsets or changes in their biology alter the balance between persistent inflammation and tissue damage during the development of arthritis. Next I will describe the functional relationships between alterations in fibroblast subsets and disease outcome during the development of inflammatory arthritis. Finally, I will speculate that distinct subsets of synovial fibroblasts are responsible for tissue inflammation, damage, memory, and pain with relevance to spondyloarthritis.

INV17

NEW APPROACHES TO TREATING PSORIATIC ARTHRITIS – BREAKING THE THERAPEUTIC CEILING?

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Psoriatic arthritis (PsA) is clinically heterogeneous comprising pathology affecting numerous discrete tissue compartments including the synovium, enthesis, skin, intestine, eye, adipose tissue, vascular bed and brain. Whereas much progress has been made in the last decade in terms of novel therapeutics, targeting *e.g.* TNF, IL-17 family members, IL-12, IL-23, and Janus Kinases, there are now emerging discrepancies in the magnitude of benefit achieved by different modes of action across distinct tissues. This is most evident in the gastrointestinal mucosa but is also qualitatively and quantitatively significant in other tissues. The key challenges in the coming years will require a necessarily detailed molecular phenotype of the PsA clinical spectrum as new targets are selected to optimise the therapeutic benefit and thereby deliver higher hurdle responses in a larger proportion of patients. This presentation will test the hypothesis that it is the host tissue that defines the pivotal pathogenetic effector pathway and thereby the optimal choice of therapeutics for phenotypically varied clinical presentations. This approach will improve early clinical trial success and in the longer term, should deliver robust remission in a higher number of patients by facilitating a novel approach to treat-to-target strategy.

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INV18

COMMON PITFALLS IN THE ANALYSIS AND INTERPRETATION Of axSpA RCTs

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Introduction. A series of landmark RCTs performed in the past two decades revolutionized the treatment of patients with axSpA. These trials proved that biological DMARDs are effective, first in patients with (advanced) radiographic axSpA (r-axSpA), and later also in patients with non-radiographic axSpA (nr-axSpA). It is hard to overstate the significance of having highly effect drugs at our disposal to treat the full spectrum of axSpA. This success was largely made possible by the development of the ASAS classification criteria for axSpA that classify both r-axSpA and nr-axSpA. There are important methodological challenges imposed by trials performed in a broader phenotypical spectrum of axSpA. Decisions on inclusion criteria, definition of active disease and outcome assessment can influence the analysis and interpretation of the trials' results.
Methods. In this lecture we will review the evidence behind the methods used to conduct clinical trials in the full spectrum of patients with axial SpA.
Results. Findings on MRI of the sacroiliac joints are used to classify patients with axSpA, but these are not as specific as initially thought. New definitions for active and structural lesions have been proposed. Both the definition of active disease and the outcome measure used to assess response can influence the magnitude of the contrast between active treatment and placebo. Currently, testing the effects on drugs on structural damage in the context of an RCT is unfeasible, but new imaging modalities can change that in the near future.
Conclusions. Recent advancements in the definition of imaging findings, innovative imaging modalities and progress in clinical outcomes assessment promise to further enhance our ability to study the effects of current and new drugs in patients with axSpA.

INV19

PEPTIDE BASED RNA THERAPEUTICS IN ARTHRITIS

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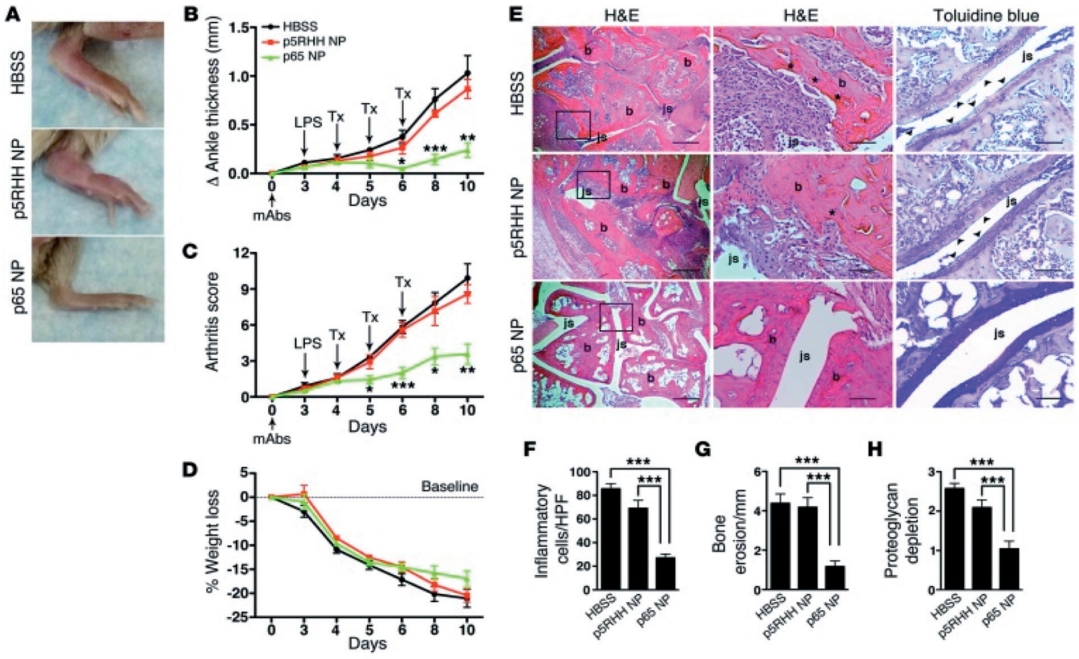
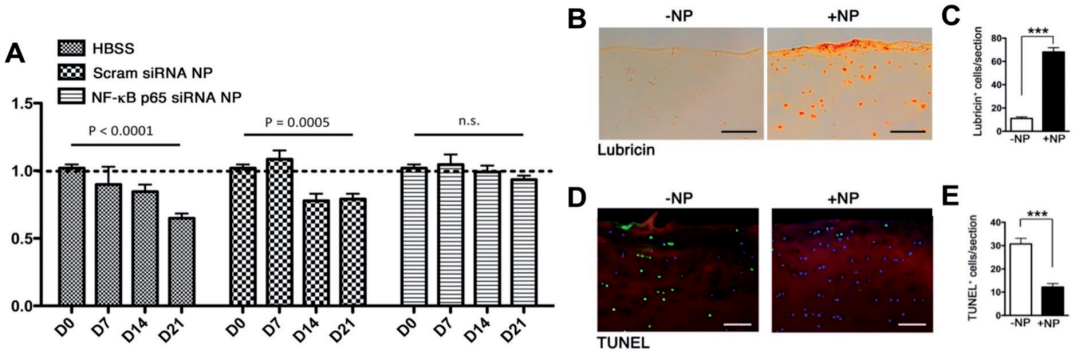
Introduction. Following the initial description of endogenous RNA silencing machinery, the possibility that exogenously synthesized siRNA might serve the same purpose to inhibit RNA translation by engaging the RISC complex was demonstrated. However, despite years of work by academic and industry scientists, the general problem of safe and efficacious delivery of therapeutic nucleotides continues to plague the field and limit its promise. Much has been discovered about the nature of the RNA molecule itself regarding modifications that stabilize and improve efficiency, but the search for a broadly applicable nonviral delivery platform remains the key to clinical adoption and utility. Indeed, the delivery problem now encompasses not only siRNA but all therapeutic nucleotides including miRNA, lncRNA, mRNA, and DNA, among other formats. What would be optimal is a single delivery platform that could accommodate all forms, lengths, and sequences of nucleotides in a one-pot scalable production process allowing ready multiplexing of therapeutic nucleotides directed at well-defined sets of molecular and/or cellular targets. These entities could silence (siRNA), overexpress (mRNA), or edit genes (CRISPR/Cas9) as desired, or perform these functions simultaneously, and repeatedly as needed. Traditional transfection agents including cationic lipids and polymers manifest high efficiency but can elicit cytotoxicity. While cell penetrating peptide-based siRNA transfection agents exhibit improved cytotoxicity profiles, they do not have the efficiency of existing lipidic agents due to endosomal trapping. Accordingly, we have designed a highly effective peptide(p5RHH)-nucleotide nanoplex delivery technology that is agnostic to the nucleotide cargo selected, including mRNA up to 4-5 kb range. This delivery technology protects nucleotides from serum degradation with circulation T1/2 ≈159 minutes, enables cytoplasmic delivery through endosomal escape because of its pH sensing capability, and exhibits a preferable safety profile without alteration of systemic innate or adaptive immunoresponsiveness, or cardiac toxicity. The simple and rapid benchtop formulation methods have been successfully adopted in many labs working in collaboration on various disease substrates beyond the liver such as cancer, atherosclerosis, necrotizing enterocolitis, and arthritis. Here, we present the applications of this technology enabled RNA therapeutics for rheumatoid arthritis and posttraumatic osteoarthritis (PTOA).
Methods. Rheumatoid arthritis (CAIA) mouse model was generated on 6 to 8 weeks old male DBA/1J mice (Taconic) with i.p. injection 1.5 mg of the 5-clone antibody cocktail on day 0 and 50 μg of LPS on day 3. Three-day consecutive treatment of *i.v.* injection with p5RHH-p65 siRNA nanoparticles (1 mg/kg) (inhibiting canonical NF-κB signaling) was started on Day 4. Treatment evaluations for osteoarthritis have been evaluated by using either mechanical joint injury in mice or human cartilage explants. Mechanical joint injury in mice was generated by using 10 to 12 weeks old male C57BL/6J mice. Under anesthesia, mice were subjected to cyclic axial compressive loads applied to the right knee joint, with loads transmitted through natural joint articulations. Compressive loads were applied at 6 Newtons (N) for 0.34 sec with a rise and fall time each of 0.17 sec and a baseline hold time of 10 sec between cycles for 60 cycles. The uninjured left knees were used as controls. The treatment with p5RHH-p65 siRNA nanoparticles coated with albumin was performed via intra-articular injection at dose of 0.1 μg siRNA per injection on day 0, 1, 2 post injury. The p5RHH-control siRNA nanoparticles or HBSS injections were served as control. The de-identified cartilage tissues were utilized to investigate the effects of p5RHH-p65 siRNA in suppressing IL-β induced p65 activity as well as subsequent chondrocytes apoptosis and cartilage homeostasis preservation. The de-identified cartilage tissues were also applied in studying the articular cartilage delivery of mRNA (WNT16) by



INV 19. Fig. 1. p5RHH-p65 siRNA nanoparticle treatment supresses inflammation in CAIA mouse model.



INV 19. Fig. 2. p5RHH-p65 siRNA nanoparticle treatment attenuates acute pain after joint injury (**A**) and p5RHH-WNT16 mRNA nanoparticle treatment upregulates lubricin expression and suppresses chondrocyte apoptosis (**B**-**E**).

using p5RHH-based technology for maintaining cartilage homeostasis. Human samples collection and animal studies were conducted under approved Washington University in St. Louis IRB and IACUC protocols, respectively.
Results. Treatment of p5RHH-p65 siRNA nanoparticle stabilized ankle swelling and significantly suppressed arthritis score, an effect that persisted until at least day 10 (Fig. 1A-C) without causing additional body weight lost (Fig. 1D). Moreover, p5RHH-p65 siRNA nanoparticles treatment significantly attenuated the influx of leukocytes to the inflamed paws, protected against bone erosion, and preserved cartilage integrity (Fig. 1E-H). In the mechanical joint injury mouse model, by using a Small animal ALGOmeter, it has been demonstrated that the mice treated with p5RHH-p65 siRNA nanoparticles maintained pain threshold while mice treated with HBSS or p5RHH-scrambled siRNA nanoparticles exhibited significantly pain threshold reduction (Fig. 2A). Articular cartilage, an avascular tissue, is poorly accessible even when drugs are intra-articularly administered. As demonstrated in the Figure 2B-E, cartilage discs from human osteoarthritis knee joints treated with p5RHH-WNT16 mRNA nanoparticles showed significantly upregulation of lubricin (Fig. 2 B-C) and suppression of chondrocyte apoptosis (Fig. 2 D-E).
Conclusions. The p5RHH-based nucleotide delivery technology homes p65 siRNA to the inflamed joins after systemic injection and suppresses inflammation. With intra-articular administration, this delivery technology demonstrated targeting NF-κB, not only to mitigate cartilage degeneration and synovial inflammation but also functional outcomes (pain sensitivity) of the inflammatory processes in PTOA. Moreover, p5RHH-based nucleotide delivery is also capable of deeply penetrating cartilage resulting efficient WNT16 mRNA expression and maintaining cartilage homeostasis.

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INV20

FAMILY STUDIES IN AXIAL SPONDYLOARTHRITIS: WHAT HAVE WE LEARNT?

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Introduction. Spondyloarthritis (SpA) is characterized by a high familial aggregation, highlighting the existence of a strong genetic background in this disease. In the last decades, family-based studies have contributed to a better understanding of the genetic background of SpA.
Results. Family studies have first been used to determine and quantify genetic influence in SpA, and in particular in ankylosing spondylitis (AS), the prototypical phenotype of SpA. They helped to estimate disease heritability to 90% and to determine that the most likely model of transmission is oligogenic with multiplicative effects. Phenotypic studies of multiplex SpA families also reinforce the unified concept of SpA with the coexistence of different SpA phenotypes within families.
Historically, identification of genetic factors of susceptibility mainly relies on family-based linkage analyses. Several whole genome linkage analyses using sib-pairs or multiplex families were performed in the 1990s in ankylosing spondylitis (AS) or in SpA as a whole. Unfortunately, there were no consistent results and family-based studies have been progressively dropped in favor of case-control designs. Case-control genome-wide association studies have been successful in AS with the identification of 48 associated loci. However, all these loci, including HLA-B27, explain less than 30% of the disease heritability.
Several hypotheses have been proposed to explain this missing heritability, including rare variants involvement. This "common disease – rare variants hypothesis" combined to the development of next-generation sequencing led to a renewed interest in family-based designs. Indeed, variant filtering process is easier in families because of the possibility to analyse the cosegregation of variants with the disease in families. Moreover, family-based approaches are more robust to population stratification than case-control designs.
There is an increasing number of studies combining family-based design and NGS in SpA. All of them identified rare variants in genes not previously identified through GWAS approaches. However, to date, almost all the studies failed to confirm their results in an independent cohort, highlighting the challenge of replication of association with rare variants.
Conclusions. Recent gain of interest in the role of rare variants in complex diseases might lead family-based approaches to return to the front stage.

INV22

FROM GWAS TO FUNCTION: USING FUNCTIONAL GENOMICS TO IDENTIFY THE MECHANISMS UNDERLYING ANKYLOSING SPONDYLITIS

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Introduction. Ankylosing Spondylitis (AS) is a highly heritable disease with >100 genomic loci incriminated as demonstrated by a recent Genome Wide Association Study (GWAS). Most AS genetic associations are not in protein-coding sequences but lie in intergenic regions where their direct relationship with specific genes is difficult to assess. Among these, RUNX3, a transcription factor (TF) involved in diverse immunological processes, is robustly (10^{-15}) associated. We have extensively characterised the likely causal single nucleotide polymorphisms (SNPs) at the *RUNX3* locus with a functional genomics approach to elucidate the association with AS.
Methods. We used an array of functional genomics technique including Chromatin Immunoprecipitation, Assay for Transposase-Accessible Chromatin (ATAC) sequencing, Chromosome conformation capture (3C) techniques, Chromatin Hidden Markov Model (ChromHMM) analysis and 10X Chromium single-cell (sc) sequencing.
Results. 1. We have demonstrated that the association between AS and SNP *rs4648889* can be explained by allele-specific effects on TF recruitment (including IRF4, IRF5 and the NuRD complex) that alter gene expression, specifically in $CD8^+$ T-cells, and having a crucial role in $CD8^+$ T-cells function.
2. We have recently shown a clear chromatin looping event between the region encompassing SNP *rs4648889*, the RUNX3 promoter and other SNPs nearby confirming the functional role of this genetic variant and a possible super-enhancer behaviour of this genomic element.
3. Four different clusters were identified in $CD8^+$ T-cells obtained from AS peripheral blood via 10x sc-seq based on the expression of *RUNX3*. Specifically, cluster 1 showed a strong co-expression for RUNX3, IKZF3, CHD4 and EOMES. Further analysis will be required to better characterize this subpopulation.
Conclusions. The AS-associated *RUNX3* genomic locus has a plausible functional role in AS, probably by regulating gene transcription and DNA looping. These observations are critically important in defining dysregulated pathways and potential therapeutic drug targets.

INV23

WHAT DOES MOLECULAR IMAGING TELL US ABOUT TISSUE REPARATION IN AXSPA?

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Introduction. Psoriatic arthritis (PsA) is characterized by substantial mesenchymal tissue activation in the context of inflammation leading to structural damage. Measuring mesenchymal tissue activation in humans in vivo is challenging but may represent a possibility to detect regions at risk for structural damage. Recently, theranostic ligands have been developed that selectively bind Fibroblast Activation Protein (FAP) and allow recognition of activated mesenchymal cells in vivo. Accumulation of such FAP-based tracers can be visualized by positron-emission tomography (PET) (1).
Methods. 120 SpA patients and 100 healthy controls without musculoskeletal disease received full-body PET-CT investigation using a ^{68}Ga-labelled FAP inhibitor (68Ga-FAPI-04) tracer, specifically binding FAP. Tracer uptake was quantified in peripheral and axial joints and correlated to various composite scores of SpA. MRI scans were performed in parallel to assess inflammation and structural lesions. Follow-up ^{68}Ga-FAPI-04 PET-CT scans were obtained in a subset of patients treated with anti-inflammatory drugs (follow-up between 3-6 months) to assess joint damage over time. In addition, FAP related tissue responses in synovial biopsy samples were evaluated on a molecular level by single-cell RNA-sequencing.

Results. ^{68}Ga-FAPI-04 accumulated at synovial and enthesial sites in patients with SpA compared to healthy controls (p<0.0001). Active pain in peripheral as well as axial joints as measured on a visual analogue scale highly correlated with an increased ^{68}Ga-FAPI-04 uptake (peripheral pain: R=0.718, p<0.0001; back pain: R=0.875, p<0.0001). Increased ^{68}Ga-FAPI-04 uptake at baseline was associated with progression of joint damage 3-6 months later as assessed by SPARCC score (R=0.758, p<0.0001). Treatment with cytokine inhibitors partially reduced FAP expression which was associated with arrest of joint damage in MRI. In contrast, persistent FAP expression was associated with a rapid progression of joint damage in MRI. Molecular analysis of biopsy samples from FAP+ lesions revealed transdifferentiation within the mesenchymal compartment with a strong shift of interactions between FAP+ fibroblasts and immune cells such as T cells, innate lymphoid cells, eosinophils and macrophages.
Conclusions. Our study presents the first in-human evidence that fibroblast activation correlates with disease progression and joint damage in patients with SpA. FAP related imaging might therefore improve the risk assessment of rapidly emerging joint damage in SpA and open new options of treat-to-target strategies in SpA.

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INV24

TRIALS AND TRIBULATION OF CT IN axSpA: IS THERE A FINAL VERDICT?

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Computed Tomography (CT) was not routinely used in axial Spondyloarthritis (axSpA) because it was insensitive to active inflammation and exposed the patient to high ionising radiation. Historical attempts to reduce radiation exposure, *e.g.*, by establishing a limited acquisition protocol, did not prove helpful for clinical practice. Still, radiography was considered the clinical standard for bone erosion, sclerosis and ankylosis, while magnetic resonance imaging (MRI) could detect active bone marrow inflammation.
However, evidence accumulated that radiography is inferior to cross-sectional imaging for depicting structural changes (1); additionally, structural changes are essential factors for the differential diagnosis (2) as active inflammation of the bone marrow can also be seen in other conditions, especially mechanical stress. In parallel, developments in CT techniques such as dual-energy CT or the new photon-counting detectors, in principle, allow the detection of bone marrow oedema (3). Other advances in acquisition and reconstruction will reduce the radiation dose to the level of conventional radiography or even below. Given its high spatial resolution and undisputed accuracy for bone lesions, especially erosion, CT was recently used in several studies to compare imaging modalities, follow-up structural changes during therapy or investigate the pathophysiology of joint dysmorphism and other anatomical variations. Therefore, rheumatologists and radiologists alike must reconsider its value for the diagnostic process, therapy control and scientific studies.
This talk summarises the recent literature and applications of CT in axSpA, focusing on the sacroiliac joints. It will critically discuss the recent technical developments and give an outlook on the near future. Finally, the presenter will conclude on whether and how to use CT for axSpA patients, if it is already suited for clinical routine or reserved for imaging and clinical studies.

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Oral Presentations

O1

ASAS-EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF AXIAL SPONDYLOARTHRITIS: 2022 UPDATE

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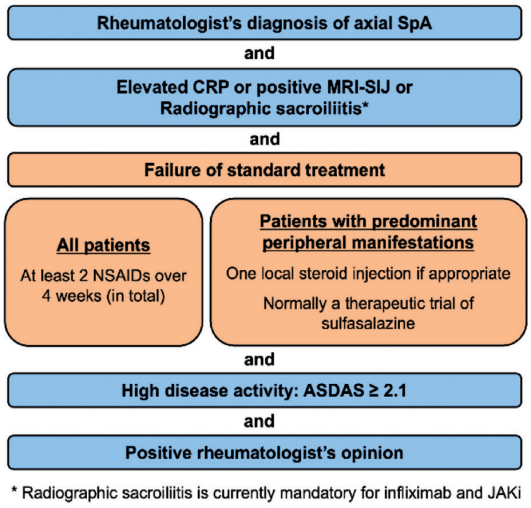
Objectives. To update the ASAS-EULAR recommendations for the management of axial spondyloarthritis (axSpA).
Methods. Following the EULAR Standardised Operating Procedures, two systematic literature reviews were conducted on non-pharmacological and pharmacological treatment of axSpA. In a task force meeting the evidence was presented, discussed and overarching principles and recommendations were updated, followed by voting.
Results. A total of 5 overarching principles (unchanged compared to the previous version of the recommendations) and 15 recommendations were formulated (Table). All recommendations included in the previous version were kept: eight unchanged (#2,3,6,7,8,13,14,15); three with minor edits, mostly on nomenclature (#1,4,5) and two with updates (#9,12), while two newly formulated recommendations (#10,11) were added. Recommendation 9 describes the indication of biological DMARDs (bDMARDs) -TNFi and IL-17i- and this was now also expanded to targeted synthetic DMARDs (tsDMARDs)- JAKi. This is indicated for patients with elevated CRP or inflammation on MRI of the SI joints or radiographic sacroiliitis who have high disease activity (ASDAS≥2.1) and failed ≥2 NSAIDs (Figure). BASDAI is no longer recommended to assess treatment start. Current practice is to start a TNFi or IL-17i as there is more accumulated evidence, particularly on safety, and experience with these drug classes. The continuation of a b/tsDMARD should be considered if an improvement of ASDAS≥1.1 has been achieved after ≥12 weeks. The new recommendation 10 addresses extra-musculoskeletal manifestations with a recurrent uveitis and inflammatory bowel disease making TNF monoclonal antibodies preferred, while for significant psoriasis IL-17i are preferred. In light of overdiagnosis and overtreatment, treatment failure should trigger re-evaluation of the diagnosis and consideration of the presence of comorbidities (recommendation 11, new). If active axSpA is confirmed, switching to another b/tsDMARD is recommended (recommendation 12); tsDMARDs were added to this recommendation.



O1. Fig. 1. ASAS-EULAR recommendations for the treatment of patients with axSpA with b/tsDMARDs

O1. Table. ASAS-EULAR recommendations for the management of axial spondyloarthritis, 2022 update.

	OVERARCHING PRINCIPLES
A	Axial Spondyloarthritis (axSpA) is a potentially severe disease with diverse manifestations, usually requiring multidisciplinary management coordinated by the rheumatologist.
B	The primary goal of treating the patient with axSpA is to maximize health related quality of life through control of symptoms and inflammation, prevention of progressive structural damage, preservation/normalisation of function and social participation.
C	The optimal management of patients with axSpA requires a combination of non-pharmacological and pharmacological treatment modalities.
D	Treatment of axSpA should aim at the best care and must be based on a shared decision between the patient and the rheumatologist.
E	axSpA incurs high individual, medical and societal costs, all of which should be considered in its management by the treating rheumatologist.
	RECOMMENDATIONS
1	The treatment of patients with axSpA should be individualised according to the current signs and symptoms of the disease (axial, peripheral, extra-musculoskeletal manifestations) and the patient characteristics including comorbidities and psychosocial factors.
2	Disease monitoring of patients with axSpA should include patient reported outcomes, clinical findings, laboratory tests and imaging, all with the appropriate instruments and relevant to the clinical presentation. The frequency of monitoring should be decided on an individual basis depending on symptoms, severity, and treatment.
3	Treatment should be guided according to a predefined treatment target.
4	Patients should be educated about axSpA and encouraged to exercise on a regular basis and stop smoking; physiotherapy should be considered.
5	Patients suffering from pain and stiffness should use an NSAID as first line drug treatment up to the maximum dose, taking risks and benefits into account. For patients who respond well to NSAIDs continuous use is preferred if needed to control symptoms.
6	Analgesics, such as paracetamol and opioid-(like) drugs, might be considered for residual pain after previously recommended treatments have failed, are contraindicated, and/or poorly tolerated.
7	Glucocorticoid injections directed to the local site of musculoskeletal inflammation may be considered. Patients with axial disease should not receive long-term treatment with systemic glucocorticoids.
8	Patients with purely axial disease should normally not be treated with csDMARDs; Sulfasalazine may be considered in patients with peripheral arthritis.
9	TNFi, IL-17i* or JAKi should be considered in patients with persistently high disease activity despite conventional treatments (Figure 1); current practice is to start a TNFi or IL-17i*.
10	If there is a history of recurrent uveitis or active IBD, preference should be given to a monoclonal antibody against TNFα**. In patients with significant psoriasis, an IL-17i* may be preferred.
11	Absence of response to treatment should trigger re-evaluation of the diagnosis and consideration of the presence of comorbidities
12	Following a first b/tsDMARD failure, switching to another bDMARD (TNFi or IL-17i*) or a JAKi should be considered.
13	If a patient is in sustained remission, tapering of a bDMARD can be considered.
14	Total hip arthroplasty should be considered in patients with refractory pain or disability and radiographic evidence of structural damage, independent of age; spinal corrective osteotomy in specialised centres may be considered in patients with severe disabling deformity.
15	If a significant change in the course of the disease occurs, causes other than inflammation, such as a spinal fracture, should be considered and appropriate evaluation, including imaging, should be performed.

*IL-17i: refers only to IL-17A-inhibitors; **This includes a pegylated Fab' fragment

Conclusions. The 2022 ASAS-EULAR recommendations provide up-to-date guidance on the management of patients with axSpA.

O2

BIMEKIZUMAB IN PATIENTS WITH ACTIVE NON-RADIOGRAPHIC AND RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: EFFICACY AND SAFETY UP TO WEEK 24 FROM THE BE MOBILE PHASE 3 STUDIES

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Introduction. Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. We assessed efficacy and safety of BKZ versus placebo in patients with active non-radiographic axial spondyloarthritis(nr-axSpA) and radiographic axSpA(r-axSpA) to Week (Wk)24 in ongoing BE MOBILE-1 (NCT03928704;nr-axSpA) and -2 (NCT03928743;r-axSpA) phase 3 studies.

Methods. Patients were ≥18 years and had active disease (BASDAI≥4, spinal pain≥4) at baseline. In BE MOBILE-1, patients met ASAS classification criteria and had elevated CRP and/or MRI sacroiliitis; patients were randomised 1:1 to BKZ 160mg Q4W:placebo. In BE MOBILE-2 patients showed radiographic evidence of axSpA, fulfilling modified New York criteria, and were randomised 2:1 to BKZ 160mg Q4W:placebo. Studies comprised 16-wk double-blind, and 36-wk maintenance period where all patients received BKZ 160mg Q4W. Efficacy endpoints were assessed through Wk24. Treatment-emergent adverse events (TEAEs; MedDRA v19.0) are reported among patients who received ≥1 dose BKZ by preferred term.

Results. 254 nr-axSpA (BKZ:128;placebo:126) and 332 r-axSpA patients (BKZ:221;placebo:111) were randomised. Primary endpoint (Wk16 ASAS40) was met; more BKZ-treated TNFi-naive/-experienced patients were responders versus placebo in both studies. Greater percentages of BKZ-treated patients achieved ASAS partial remission and complete resolution of enthesitis versus placebo at Wk16 across studies; responses maintained at Wk24 (Table). Improvements from baseline inflammation (MRI spine Berlin and SPARCC MRI SIJ score) were observed (Table). Percentage of BKZ-treated patients achieving ASDAS≤2.1 increased rapidly versus placebo across studies (Figure).

At Wk24-data cut, 50.8%(124/244) nr-axSpA and 55.5%(183/330) r-axSpA patients had ≥1TEAE; 0.4%(1/244) and 3.6%(12/330) had serious TEAEs. TEAEs in ≥5% nr-axSpA patients: upper respiratory tract infection (7.0%;17/244) and nasopharyngitis (6.6%;16/244); r-axSpA: nasopharyngitis (6.4%;21/330). Adjudicated IBD: nr-axSpA:0%(0/244), r-axSpA:0.3%(1/330); uveitis: nr-axSpA:0.8%(2/244), r-axSpA:0.3%(1/330); oral candidiasis: nr-axSpA:2.9%(7/244), r-axSpA:3.0%(10/330). No systemic candidiasis, MACE or deaths were reported.

Conclusions. BKZ treatment provided clinically relevant improvements versus placebo across the spectrum of axSpA. Safety was consistent with prior studies.

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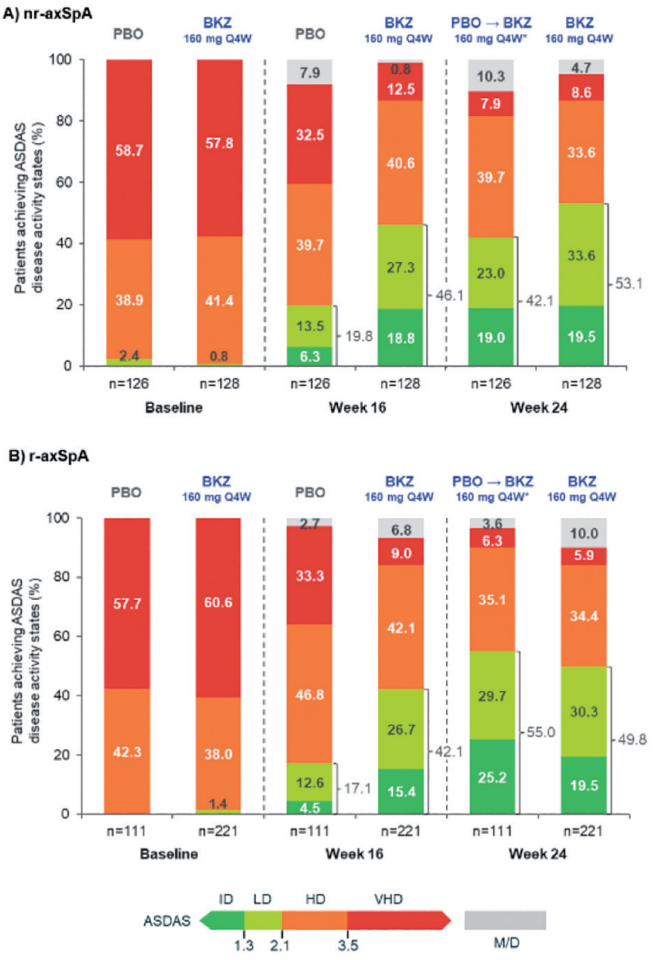
O2. Table. Efficacy outcomes for patients with nr-axSpA and r-axspA.

			Baseline		Week 16			Week 24	
			PBO	BKZ 160 mg Q4W	PBO	BKZ 160 mg Q4W	*p* value	PBO→BKZ 160 mg Q4W	BKZ 160 mg Q4W
nr-axSpA (BE MOBILE-1) r-axSpA (BE MOBILE-2)			n=126 n=111	n=128 n=221	n=126 n=111	n=128 n=221		n=126 n=111	n=128 n=221
ASAS40* n (%)	[NRI]	nr-axSpA	–	–	27 (21.4)	61 (47.7)	<0.001	59 (46.8)	67 (52.3)
		r-axSpA	–	–	25 (22.5)	99 (44.8)	<0.001	63 (56.8)	119 (53.8)
ASAS40 in TNFi-naive‡ [NRI] n (%)		nr-axSpA	–	–	25 (22.9)[a]	55 (46.6)[b]	<0.001§	–	–
		r-axSpA	–	–	22 (23.4)[c]	84 (45.7)[d]	<0.001	56 (59.6)[c]	100 (54.3)[d]
ASAS40 in TNFi-experienced [NRI] n (%)		nr-axSpA	–	–	2 (11.8)[e]	6 (60.0)[f]	N/A	–	–
		r-axSpA	–	–	3 (17.6)[e]	15 (40.5)[g]	N/A	–	–
ASAS PR† [NRI]n (%)		nr-axSpA	–	–	9 (7.1)	33 (25.8)	<0.001	35 (27.8)	37 (28.9)
		r-axSpA	–	–	8 (7.2)	53 (24.0)	<0.001	28 (25.2)	56 (25.3)
Complete resolution of enthesitis[h] [NRI] n (%)		nr-axSpA	–	–	22 (23.9)[i]	48 (51.1)[c]	<0.001§	40 (43.5)[i]	45 (47.9)[c]
		r-axSpA	–	–	22 (32.8)[j]	68 (51.5)[k]	0.006§	33 (49.3)[j]	70 (53.0)[k]
MRI spine Berlin CfB[l] [OC] mean (SD)		nr-axSpA	1.9 (3.2)[m]	1.6 (2.9)[n]	–0.1 (1.7)[o]	–0.7 (2.2)[p]	N/A	–	–
		r-axSpA	3.3 (4.9)[q]	3.8 (5.3)[r]	0.0 (1.4)[s]	–2.3 (3.9)[t]	N/A	–	–
SPARCC MRI SIJ score CfB[l] [OC] mean (SD)		nr-axSpA	10.5 (13.8)[u]	8.5 (10.3)[t]	–1.5 (9.2)[v]	–6.3 (10.0)[w]	N/A	–	–
		r-axSpA	5.8 (7.7)[q]	7.4 (10.7)[x]	1.1 (6.9)[s]	–5.6 (9.9)[t]	N/A	–	–

Randomised set. Data reported for patients with nr-axSpA (BE MOBILE-1) and patients with r-axSpA (BE MOBILE-2). *Primary endpoint; †secondary endpoint; ‡secondary endpoint of BE MOBILE-2; §p values without any multiplicity adjustment are indicated as nominal p values. Not all ranked secondary endpoints are reported. Ranked endpoints assessed at Week 16 of BE MOBILE-1 in order of statistical hierarchy: ASAS40, BASDAI CfB, ASAS20, ASAS PR, ASDAS-MI, ASAS5/6, BASFI CfB, nocturnal spinal pain CfB, ASQoL CfB, SF-36 PCS CfB. Ranked endpoints assessed at Week 16 of BE MOBILE-2 in order of statistical hierarchy: ASAS40, ASAS40 in TNFi-naive patients, ASAS20, BASDAI CfB, ASAS PR, ASDAS-MI, ASAS5/6, BASFI CfB, nocturnal spinal pain CfB, ASQoL CfB, SF-36 PCS CfB, BASMI CfB. [a]n=109; [b]n=118; [c]n=94; [d]n=184; [e]n=17; [f]n=10; [g]n=37; [h]MASES=0 in patients with MASES >0 at baseline; [i]n=92; [j]n=67; [k]n=132; [l]In patients in MRI sub-study, absolute values are shown at baseline; [m]n=65; [n]n=75; [o]n=58; [p]n=73; [q]n=45; [r]n=82; [s]n=43; [t]n=79; [u]n=68; [v]n=60; [w]n=77; [x]n=83.

O2. Fig. 1. ASDAS states over time.
Randomised set. Data reported as observed case.
*At Week 16, patients on placebo switched to BKZ.
ASAS20/40: Assessment of SpondyloAthritis International Society 20/40 response; ASAS PR: ASAS partial remission; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-MI: ASDAS major improvement; ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BKZ: bimekizumab; CfB: change from baseline; CRP: C-reactive protein; HD: high disease; IBD: inflammatory bowel disease; ID: inactive disease; IL: interleukin; LD: low disease; MACE: Major Adverse Cardiovascular Event; M/D: missing data; MRI: magnetic resonance imaging; n: number; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; OC: observed case; PBO: placebo; Q4W: every four weeks; r-axSpA: radiographic axial spondyloarthritis; SD: standard deviation; SF-36 PCS: Short Form-36 Physical Component Summary; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada; TEAE: treatment-emergent adverse event; TNFi: tumour necrosis factor inhibitor; VHD: very high disease; Wk: week.



O3

COMPARISON OF THE EFFECT OF TREATMENT WITH NSAIDS ADDED TO ANTI-TNF THERAPY VERSUS ANTI-TNF THERAPY ALONE ON PROGRESSION OF STRUCTURAL DAMAGE IN THE SPINE OVER TWO YEARS IN PATIENTS WITH ANKYLOSING SPONDYLITIS (CONSUL): AN OPEN-LABEL, RANDOMIZED CONTROLLED, MULTICENTER TRIAL

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Background. There is some evidence that NSAIDs, in particular celecoxib (CEL), might possess not only symptomatic efficacy but also disease-modifying properties in ankylosing spondylitis (AS), retarding progression of structural damage in the spine if taken continuously. For biological disease-modifying antirheumatic drugs (bDMARDs), retardation of structural damage progression has also been demonstrated, but at least 4 years of treatment seem to be necessary (at least for tumour necrosis factor inhibitors – TNFi) to see such an effect. Therefore, a combination of an NSAID with a TNFi might bring additional benefits in terms of retardation of structural damage progression especially in high-risk patients.

Objectives. The aim of this RCT was to evaluate the impact of treatment with the COX-II-selective NSAID (CEL) when added to a TNFi (golimumab - GOL) compared with TNFi (GOL) alone on progression of structural damage in the spine over 2 years in patients with r-axSpA.

Methods. Eligible patients had r-axSpA and high disease activity (BASDAI ≥4), NSAID failure and risk factors for radiographic spinal progression: C-reactive protein >5 mg/l and/or ≥1 syndesmophyte(s). The trial consisted of two phases: a 12-week run-in phase, in which all included patients received treatment with GOL 50 mg every 4 weeks sc, followed by a 96-week controlled treatment period, in which patients who achieved a BASDAI improvement of ≥2 points were randomly assigned to GOL + CEL 200 mg bid or GOL alone arms. The primary endpoint was radiographic spinal progression as assessed by the change in the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) after 108 weeks in the intent-to-treat population, read by 3 independent readers blinded for the treatment arm and the time-point.

Results. Of the 157 screened patients, 81.5% (n=128) were enrolled into the run-in phase. 109 patients fulfilled the BASDAI response criterion at w12 and were randomized 1:1 (54 vs. 55) to GOL+CEL or GOL alone; 97 (45 vs. 52) patients completed the study at w108. Clinical characteristics of the randomized patients are shown in Tab. I. The mSASSS change after w108 was 1.1 (95%CI 0.2; 2.0) vs. 1.7 (95%CI 0.8; 2.6) in the GOL+CEL vs. GOL alone groups, respectively, p=0.79. Fig. 1 shows the cumulative probability of the mSASSS change in both treatment arms. New syndesmophytes in the opinion of three readers occurred in 11% vs. 25% of the patients in the GOL+CEL vs. GOL alone groups, respectively, *p*=0.12. During the study, a total of 14 serious adverse events (SAE) were reported (7 in the GOL+CEL group, 5 in the GOL alone group and 2 during the run-in phase).

Conclusions. In this study, a combined therapy with GOL+CEL did not show significant superiority over GOL monotherapy in retarding radiographic spinal progression over two years in r-axSpA patients. However, the observed numerical reduction in radiographic spinal progression associated with the combined treatment might be, however, clinically relevant for patients at high risk for progression.

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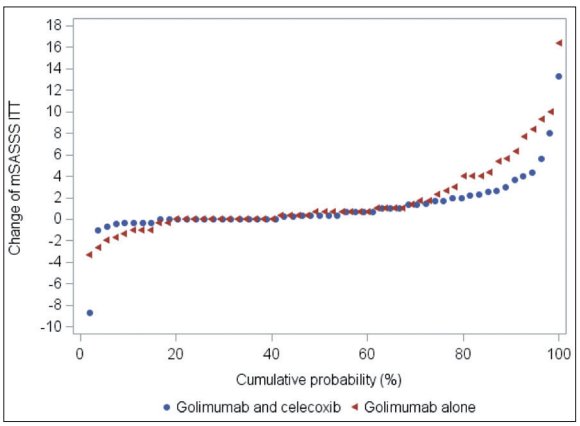
O3. Table I. Baseline characteristics of randomized patients.

Parameters		GOL+CEL n=54		GOL alone n=55		All patients n=109	
		valid n	value	valid n	value	valid n	value
Sex, male	n (%)	54	40 (74.1)	55	41 (74.5)	109	81 (74.3)
Age, years	Mean (SD)	54	39.9 (9.9)	55	37.5 (10.8)	109	38.7 (10.4)
Smoker	n (%)	53	19 (35.8)	55	22 (40)	108	41 (38)
BASDAI	Mean (SD)	54	6.2 (1)	55	6.1 (1.1)	109	6.1 (1.1)
BASMI	Mean (SD)	54	2.6 (1.9)	54	2.9 (1.4)	108	2.8 (1.6)
CRP > 5 mg/L	n (%)	54	38 (70.4)	55	38 (69.1)	109	76 (69.7)
ASDAS-CRP	Mean (SD)	54	3.6 (0.6)	55	3.7 (0.9)	109	3.7 (0.8)
HLA-B27 positivity	n (%)	54	45 (83.3)	51	47 (92.2)	105	92 (87.6)
Smoker	n (%)	53	19 (35.8)	55	22 (40)	108	41 (38)
Prior bDMARDs	n (%)	54	17 (31.5)	55	9 (16.4)	109	26 (23.9)
Presence of ≥ 1 syndesmophyte(s)	n (%)	54	27 (50)	55	28 (50.9)	109	55 (50.5)
mSASSS	Mean (SD)	54	13.5 (16.9)	55	10.3 (13.2)	109	11.9 (15.2)



O3. Fig. 1. Cumulative probability plot of mSASSS progression over 108 weeks of treatment.

O4

RECAPTURE RATES WITH IXEKIZUMAB AFTER WITHDRAWAL OF THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS AT WEEK 104 FROM A RANDOMIZED PLACEBO-CONTROLLED WITHDRAWAL STUDY

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Introduction. Here, we describe the final results of the first study of patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis re-randomized to either placebo (ixekizumab withdrawal) or ixekizumab, who experienced a flare and recaptured response either before or after open-label retreatment during COAST-Y.
Materials and methods. COAST-Y (NCT03129100) is a phase 3 extension study that included a double-blind, placebo-controlled, randomized withdrawal-retreatment period (RWP) through 104 weeks. Patients who achieved remission (Ankylosing Spondylitis Disease Activity Score (ASDAS)<1.3 (inactive disease; ID) at least once at week 16 or 20, and <2.1 (low disease activity; LDA) at both visits) were randomized 2:1 at week 24 to continue ixekizumab or withdraw to placebo. Patients who subsequently flared were switched to open-label ixekizumab Q2W or Q4W at the next visit. The proportion of patients who recaptured ASDAS LDA and ID were summarized for patients who experienced flare.

O4. Table I. Recapture of first treatment response before or after switching to open label IXE through 104 weeks among placebo (ixekizumab withdrawal)-treated patients who experienced a flare and retreated.

Total patients who flared and were switched to open-label ixekizumab retreatment	Placebo (ixekizumab withdrawal) (n=28)	
ASDAS disease activity status	LDA	ID
Recaptured response before open label ixekizumab retreatment	4	1
Recaptured response with open label ixekizumab retreatment (≤16 weeks)	23	14
Recaptured response with open label ixekizumab retreatment (>16 weeks)	0	5
Total patients who recaptured response at week 104	27/28 (96%)	20/28 (71%)

Data are presented as n, (%) for the total row and n only for all other rows. In each column, the denominator is 28. ASDAS, Ankylosing Spondylitis Disease Activity Score; ID, inactive disease; LDA, low disease activity including ID; N, number of patients in the analysis population.

Results. A total of 155 patients entered the RWP (placebo, N=53; ixekizumab Q4W, N=48; ixekizumab Q2W, N=54) and 138 completed week 104. Thirty-six percent of patients re-randomized to placebo never experienced a flare through 104 weeks. Twenty-eight placebo-treated patients experienced a flare during weeks 24-104; of those, 4/28 (14%) recaptured LDA before retreatment with open-label ixekizumab, while 23/28 (82%) recaptured LDA and 19/28 (68%) met ID after switching to open-label ixekizumab retreatment.
Conclusions. The majority of patients withdrawn from ixekizumab to placebo recaptured at least LDA and over half met ID with ixekizumab retreatment. This may provide insight for ixekizumab therapy for patients who require a short interruption in treatment.

O5

THE PREVALENCE OF INFLAMMATORY BACK PAIN AND HLA-B27 IN A LARGE POPULATION-BASED COHORT IN THE NETHERLANDS

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Introduction. Chronic low back pain before age 45 (CLBP) and inflammatory back pain (IBP) are regarded as early and key axSpA features. HLA-B27 is the most important genetic risk factor. Despite improved diagnostics, especially including sacroiliac MRI, the diagnostic delay in axSpA has not improved. Our objective was to explore the presence of CLBP and IBP in combination with HLA-B27 and the presence of other axSpA associated features in the general population.
Methods. Participants of the Lifelines cohort, a large population-based cohort of the northern region of The Netherlands, responded to a survey with questions concerning the presence of CLBP and the ESSG criteria for IBP. HLA-B haplotypes were imputed from genome-wide SNPs genotyped with the Illumina GSA beadchip-24 v1.0, using the R-package HIBAG with published parameter estimates. Analyses were performed on participants with available HLA-B haplotype and CLBP/IBP data. Logistic regression was performed to identify axSpA features that were independently associated with the presence of the key axSpA features HLA-B27, CLBP and IBP.
Results. 20,619 participants had data available on CLBP, IBP and HLA-B haplotype. In total, 226 (1.1%) participants had the combination of CLBP/IBP/HLA-B27. Only 11 (4.9%) of them reported a previous SpA diagnosis. Participant characteristics and other available SpA related features are presented in Table I. In multivariable logistic regression analysis, current NSAID use and a reported history of peripheral arthritis were independently associated with the axSpA key features CLBP, IBP, and IBP+HLA-B27.
Conclusions. In this large Dutch population-based cohort only 4,9% of participants presenting the combined axSpA key features IBP and HLA-B27 reported a previous axSpA diagnosis, indicating possible underdiagnosis. Although not all SpA features were available in Lifelines, NSAID use and a history of peripheral arthritis in combination with the axSpA key features may have additional value in identifying patients with axSpA in primary care.

O5. Table I. Characteristics and features associated with SpA in the different subgroups of Lifelines participants.

	Available data in Lifelines of CLBP/IBP & HLA-B (n=20,619)	Self-reported SpA diagnosis (n=47)	CLBP+ (n=3,698[1])	CLBP+/IBP+ (n=2,653[1])	HLA-B27+ (n=1,585[1])	CLBP+/IBP+/ HLA-B27+ (n=226[1])
General characteristics						
Male	8173 (39.6%)	24 (51.1%)	1443 (39.0%)	1058 (39.9%)	630 (39.7%)	89 (41.4%)
Age	44.2 ± 14.2	48.1 ± 12.6	42.5 ± 13.2	44.0 ± 12.8	44.1 ± 14.1	41.7 ± 12.5
BMI	25.7 ± 4.1	26.7 ± 4.3	26.2 ± 4.5	26.3 ± 4.3	25.7 ± 4.4	25.9 ± 4.6
Features associated with SpA						
Reported diagnosis of:						
- Uveitis	11 (0.1%)	1 (2.1%)	1 (0.0%)	0 (0%)	2 (0.1%)	0 (0%)
- IBD	179 (0.9%)	3 (6.4%)	31 (0.8%)	22 (0.8%)	14 0.9%)	2 (0.9%)
- Psoriasis	588 (2.9%)	8 (17%)	491 (2.8%)	79 (3.0%)	52 (3.3%)	7 (3.3%)
Current NSAID use	766 (3.7%)	20 (42.6%)	252 (6.8%)	189 (7.1%)	82 (5.2%)	22 (10.2%)
History of peripheral arthritis	609 (3.0%)	7 (14.9%)	229 (6.2%)	196 (7.4%)	43 (2.7%)	17 (7.9%)
Reported rheumatism in FDR	3572 (17.3%)	12 (25.5%)	724 (19.6%)	535 (20.2%)	315 (19.9%)	47 (21.9%)
At least 1 of above features	4803 (23.3%)	30 (63.8%)	1013 (27.4%)	744 (28.0%)	418 (26.4%)	69 (32.1%)
At least 2 of above features	302 (1.5%)	7 (14.9%)	85 (2.2%)	66 (2.5%)	34 (2.1%)	7 (3.3%)

Data presented as mean ± SD or n (%). [1]Participants already reporting a previous SpA diagnosis excluded from this group.

O6

A MACHINE LEARNING PIPELINE FOR PREDICTION OF BONE MARROW OEDEMA ALONG THE SACROILIAC JOINTS ON MAGNETIC RESONANCE IMAGING

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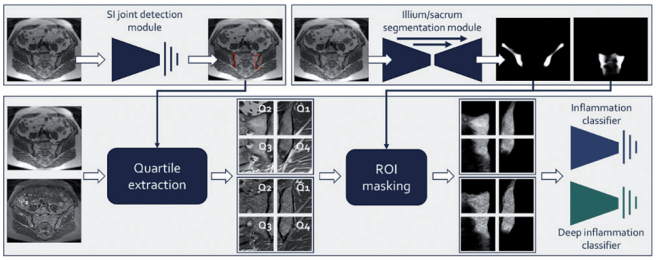
Objectives. Detection and semi-quantitative assessment of bone marrow oedema (BMO) on magnetic resonance imaging (MRI) of the sacroiliac (SI) joints is essential for the diagnosis and follow-up of spondyloarthritis (SpA) patients. A machine learning (ML) algorithm could address intra- and inter-reader variability and the time-consuming nature of these assessments.

Methods. We developed a deep learning workflow that automatically locates the SI joints, segments regions of interest (ilium and sacrum), performs quadrant extraction and predicts presence of BMO, suggestive of inflammatory lesions, on a quadrant-level in semi-coronal slices of T1/T2 weighted MRI scans (Fig. 1). Using a ResNet18 backbone, the inflammation classifier was trained and tested (5-fold cross-validation) on scans of SpA patients (n=279), postpartum women (n=71), and healthy individuals (n=114); while 243 SpA MRIs served as external validation. Patient-level predictions were derived from aggregating quadrant-level predictions, i.e. at least one positive quadrant.

Results. The proposed method automatically detects the SI joints and segments the ilium and sacrum. A ROC AUC score of 94.7%, balanced accuracy (B-ACC) of 82.2% and an F1 score of 62.1% is reported for the proposed inflammation prediction algorithm in cross validation. In the external validation dataset, ROC AUC was 88.2%, B-ACC 72.1% and F1 score 50.8%. On a patient-level, the model achieved an accuracy of 81.6% and 81.4% in the cross validation and external validation dataset, respectively.



O6. Fig. 1. Proposed pipeline for automated scoring of the MRI data. The T1-weightes sequence is used for locating the SI joints and segmentation of the ilium/sacrum. Based on this, the SI regions of interest (ROI) are extracted, and (optionally) masked with the ilium/sacrum segments. These ROIs are then fed to a convolutional neural network to predict presence of (deep) inflammatory lesions.

Conclusions. We propose a fully automated ML pipeline for detection of BMO on MRI of the SI joints that has the potential to assist clinicians in early diagnosis and reliable quantification of inflammatory lesions in patients with (suspected) SpA.

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O7

AN AI-BASED ALGORITHM FOR AUTOMATIC DETECTION OF EROSION AND ANKYLOSIS ON CT IMAGES OF THE SACROILIAC JOINTS: MULTICENTRE DEVELOPMENT AND VALIDATION

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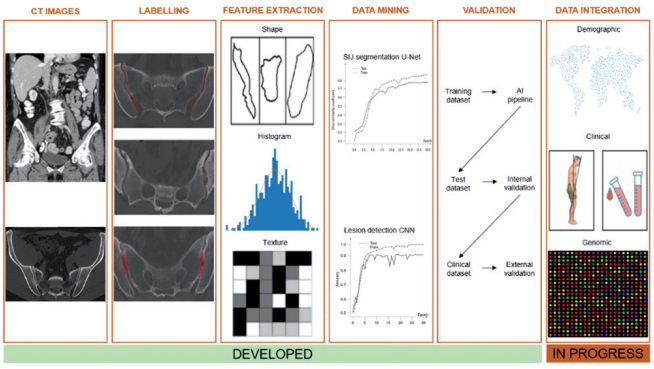
Introduction. Axial spondyloarthritis affects the sacroiliac joints (erosion and ankylosis). We developed an AI pipeline for automatic lesion detection on CT images and validated its diagnostic accuracy.

Methods. Patients with clinical symptoms of sacroiliitis who underwent a SIJ CT were included (n=145, 40±13y, 81 female, 2 hospitals, 84 axSpA, 15 mechanical back pain, 46 without final diagnosis). Ground truth segmentation of the SIJs was performed by three independent and blinded radiologists who annotated erosions >1mm and ankylosis >2mm. A deep learning pre-processing, U-Net and convolutional neural network pipeline was developed to segment the SIJs and detect structural lesions. Internal in-training validation assessed the diagnostic performance of the algorithm on a slice and patient level.

Results. A dice similarity coefficient of 0.75±0.03 was obtained for segmentation. Slice-by-slice, erosions and ankylosis were detected with a PPV, NPV, sensitivity and specificity of 89/90/90/89% and 91/93/93/91%, respectively. On a patient level, erosions were depicted with an accuracy of 74% (threshold confidence level (TCL) 98%, threshold number of windows (TNW) 15). Ankylosis was depicted with an accuracy of 88% (TCL 70%, TNW 27). Optimization to reduce false negatives rendered a NPV of 94% and a sensitivity of 95% for erosions (TCL 97%, TNW 11) and a NPV of 95% and specificity of 90% for ankylosis (TCL 97%, TNW 12). Optimization to reduce false positives rendered a PPV of 73% and a specificity of 85% for erosions (TCL 99%, TNW 40) and a NPV of 88% and specificity of 97% for ankylosis (TCL 39%, TNW 44).

Conclusions. Erosions and ankylosis in patients with sacroiliitis can be automatically detected on CT images in an objective way using an AI pipeline (Fig. 1). This opens opportunities to automatic objective and early diagnosis and treatment of patients with SpA, even if the scan was obtained for different clinical use.



O7. Fig. 1. Pipeline for the automated segmentation of the sacroiliac joints and detection of hallmark lesions of sacroiliitis in CT images. CT images are labelled for the presence of erosion and ankylosis. After manual segmentation of the sacroiliac joints and annotation of structural lesions, preprocessing steps (image centering, rescaling, resizing and slice selection/centreline detection) are performed. Shape, histogram and texture features are extracted on the original images. 32*32 pixel training images are fed to an automatic sacroiliac joint segmentation U-Net and subsequently to an automatic lesion detection convolutional neural network to build the pipeline architecture and subsequent diagnostic models. In-training internal and external validation is performed on a validation dataset to assess the algorithm's performance. In the future, demographic, clinical and genomic data integration can increase the diagnostic performance. SIJ: sacroiliac joint. CNN: convolutional neural network. AI: artificial intelligence.

O8

DOES GENDER INFLUENCE OUTCOME MEASURES SIMILARLY IN PATIENTS WITH SPONDYLOARTHRITIS? RESULTS FROM THE ASAS-PERSPA STUDY

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Introduction. There is growing evidence revealing that females report worse patient-reported outcomes compared to males in axial spondyloarthritis (axSpA). However, in which precise outcomes there is a meaningful difference across gender and whether this also occurs in patients with peripheral spondyloarthritis (pSpA) and psoriatic arthritis (PsA) is not fully understood. The main objective of this work is to investigate the influence of gender on disease outcomes in patients with SpA, including axSpA, pSpA and PsA, in a worldwide setting.
Methods. Data from 4185 patients of 23 countries with a diagnosis of axSpA, pSpA or PsA from the ASAS-PerSpA study were analysed. Associations between gender and disease activity [ASDAS, BASDAI, CRP], function [BASFI], and overall health [ASAS HI, EQ-5D] outcomes were investigated. Multilevel multivariable linear mixed models adjusted for relevant confounders (and stratified by disease phenotype in case of relevant interactions).
Results. In total, 65%, 10% and 25% of patients had axSpA, pSpA, and PsA respectively. AxSpA was more frequent in males (68%) whereas pSpA and PsA were more frequent in females (53% and 52%, respectively). A significant interaction between gender and disease phenotype was found for ASDAS, BASDAI and BASFI. While being female independently contributed to higher BASDAI across the three disease phenotypes (with varying magnitude), female gender was only associated with higher ASDAS in pSpA [β(95%CI):0.36(0.15;0.58)] and PsA [0.25(0.12;0.38)] but not in axSpA [0.016(-0.07;0.11)] (Table I). No associations were observed between gender and CRP levels. Female gender was associated with higher ASAS-HI and EQ5D, without differences across disease phenotype.

O8. Table I. Multivariable multilevel model by disease phenotype.

Outcome	Determinant of interest	Disease phenotype		
		AxSpA	**pSpA**	**PsA**
ASDAS [+]	Gender (female vs male)	0.02 (-0.07, 0.11)	**0.36 (0.15, 0.58)**	**0.25 (0.12, 0.38)**
BASDAI [*]		**0.39 (0.20, 0.58)**	**1.22 (0.77, 1.69)**	**0.88 (0.59, 1.16)**
BASFI [-]		0.01 (-0.14, 0.17)	0.30 (-0.12, 0.71)	**0.46 (0.20, 0.72)**
CRP[^]			-1.36 (-3.17, 0.44)	
ASAS-HI[#]			**0.90 (0.70, 1.10)**	
EQ-5D[°]			**-0.02(-0.03, -0.01)**	

All models are adjusted by age, gender and education.
[+]Also adjusted for marital status, BMI, smoking, axial involvement, peripheral arthritis, enthesitis, fibromyalgia, NSAIDs, steroids, csDMARDs, bDMARDs
[*] Also adjusted for marital status, BMI, smoking, axial involvement, peripheral arthritis, enthesitis, psoriasis, fibromyalgia, NSAIDs, bDMARDs
[-] Also adjusted for marital status, BMI, ASDAS, radiographic damage, fibromyalgia, NSAIDs, bDMARDs
[^]Also adjusted for marital status, BMI, radiographic damage, concomitant NSAIDs, steroids, csDMARDs
[#]Also adjusted for smoking, ASDAS, BASFI, peripheral arthritis, enthesitis, fibromyalgia
[°] Also adjusted for BMI, smoking, ASDAS, BASFI, radiographic damage, HLA-B27, enthesitis, fibromyalgia
Results are expressed in β (95% CI). Estimates with $p<0.05$ are highlighted in bold.

Conclusions. Female gender was associated with less favorable outcome measures across the SpA spectrum. However, while female gender influenced BASDAI across the three phenotypes, ASDAS was associated with gender only in pSpA and PsA but not in axSpA. Therefore, ASDAS is an appropriate instrument both for females and males with axSpA.

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O9

MIF IS AN IMPORTANT MEDIATOR IN SPA ASSOCIATED GUT INFLAMMATION IN SKG MOUSE

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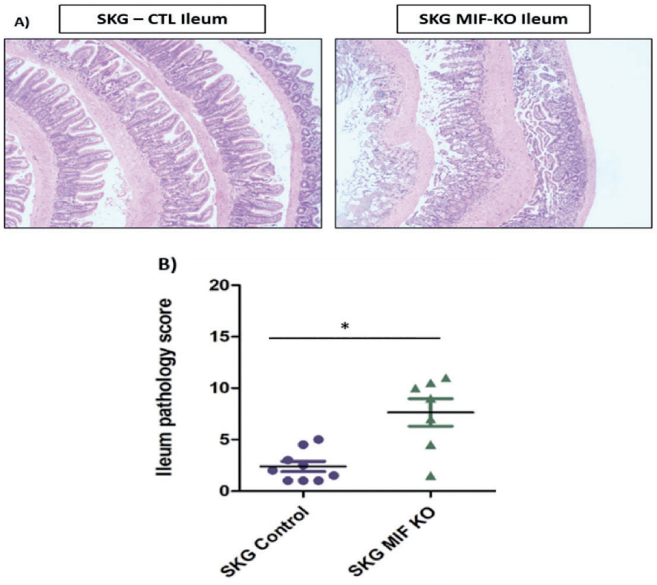
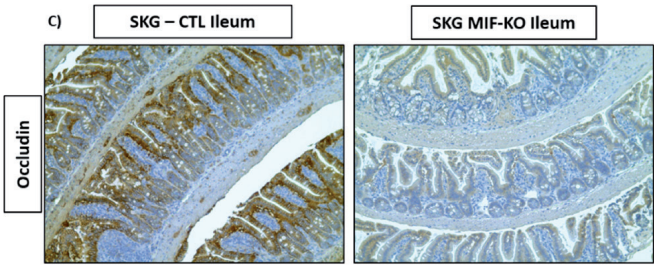
Introduction. Axial Spondyloarthritis (AxSpA) is a chronic inflammatory disease with multifactorial origins, primarily affecting the musculoskeletal system. AxSpA often is accompanied by extra-articular manifestations, such as Inflammatory Bowel Disease (IBD). Over the years many pathways and cell populations have been linked to the pathogenesis of gut inflammation in AxSpA.
Macrophage migration inhibitory factor (MIF) plays a critical role in the pathogenesis of AxSpA. Over-expression of MIF in a mouse model of SpA (SKG mice) causes major clinical features of AxSpA. On the other hand, blocking or depletion of MIF significantly suppresses these symptoms. However, it is mostly unknown what is the role of MIF in gut inflammation in AxSpA. We hypothesized that MIF is a key player driving gut inflammation in AxSPA.
Methods. 6 SKG-MIFKO and 6 SKG control 16 weeks old mice were used for this study. H&E slides were prepared for histopathology assessment on formalin-fixed paraffin-embedded (FFPE) blocks of ileum tissue (2 individual persons scored the samples blindly). Immunohistochemistry (IHC) was performed for occludin. qPCR was performed to measure the expression level of IL-17, Muc2, Mmp7, and Lyz1. Mann Whitney test was used to analyze the difference between the two groups.
Results. We observed significantly increased levels of inflammation in the ileum of MIFKO SKG compared to SKG mice (p=0.01) (Fig. 1). We also observed disruption of ileum epithelium in MIFKO SKG mice compared to the SKG control group which was confirmed with decreased expression of occludin suggesting disruption of tight junctions (Fig. 2). IL-17 and Muc2 levels were decreased in MIFKO-SKG ileum. Expression of Mmp7 and Lyz1 were increased in the ileum of MIFKO-SKG mice.



O9. Fig. 1. Histopathology of ileum. Inflammation is increased in SKG MIFKO mice compared to the control group.



O9. Fig. 2. IHC staining for occludin. Expression of occludin is decreased in SKG MIFKO mice compared to the control group.

Conclusions. Knocking out MIF in SKG mice has shown improvement in AxSpA symptoms. However, based on our findings, MIF seems to have a protective role in the gut of SKG mouse unlike what we see in joints. MIF can stimulate IL-17. Thus, decreased levels of IL-17 in the MIFKO group can contribute to gut inflammation as well. The absence of MIF leads to decreased production of mucin and increased production of Mmp7 and Lyz1 from goblet and paneth cells, respectively. These findings together suggest that MIF is essential for the integrity of the gut epithelial barrier in the SKG mouse model of SpA.

O10

HIGH DIMENSIONAL IMMUNOPHENOTYPING OF PERIPHERAL BLOOD POPULATIONS BY MASS CYTOMETRY IN AXIAL SPONDYLOARTHRITIS

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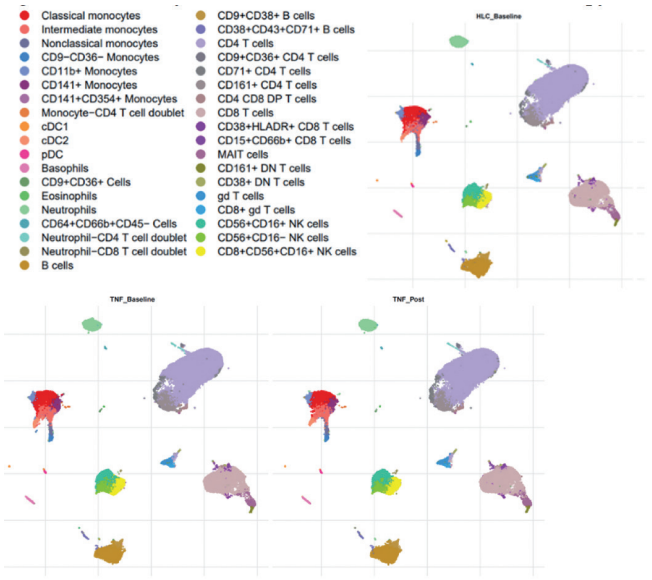
Introduction. Axial spondyloarthritis (AxSpA) is an immune-mediated inflammatory disease of unknown pathogenesis. Two cytokine pathways are currently targeted by licenced therapies: inhibitors of tumour necrosis factor (TNF)-alpha and interleukin (IL)-17A. It is not known which treatment is best for which patients. Other immune pathways being explored for therapeutic benefit include Granulocyte-macrophage colony-stimulating factor (GM-CSF) blockade. We wish to determine if there is a distinct immunologic signature in the blood of AxSpA patients and if this changes with treatment response to biological therapy. We investigated the blood immune phenotypes of AxSpA patients participating in the first in-disease, double-blind, randomised, placebo-controlled, phase II clinical trial of a GM-CSF neutralising monoclonal antibody (namilumab) in AxSpA (NAMASTE trial), together with those initiating TNF inhibitor therapy.

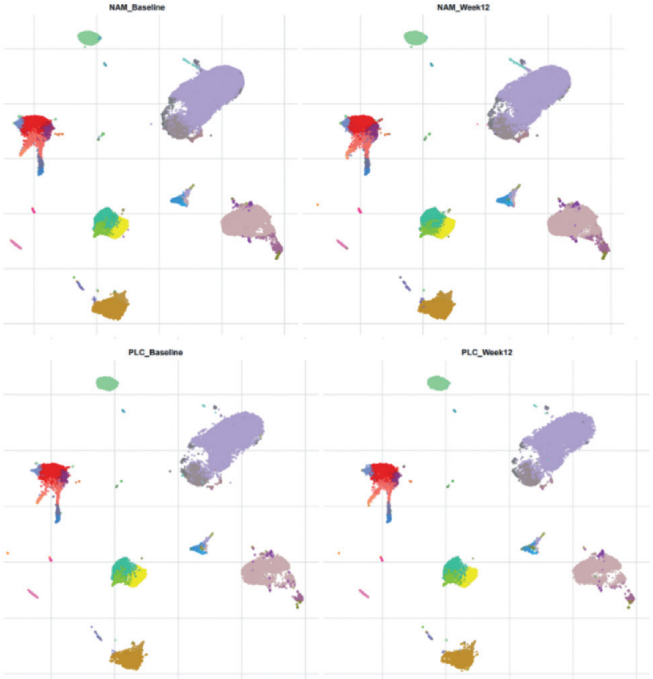
Methods. Peripheral blood mononuclear cells were obtained from 20 healthy controls, and pre- and post-treatment for 46 AxSpA patients. 20 AxSpA patients commenced TNF inhibitor therapy, and 26 namilumab/placebo as part of the NAMASTE clinical trial. Myeloid and T cell populations have been enumerated by a 41-marker high dimensional Cytometry by Time of Flight (CyTOF) panel. Results. Data was obtained from between 26697 and 489323 cells for 20 healthy control subjects and 46 SpA patients (at multiple time points). Immunophenotyping clearly delineated multiple myeloid and lymphoid cell populations and was robust to multiple seed analysis with or without downsampling (Fig.1). Differences in myeloid and neutrophil population frequencies were observed between SpA patients and controls. Changes in myeloid and B cell populations were observed after therapy. These are currently being examined in detail.

Conclusions. High dimensional enumeration of immune cell populations by CyTOF mass spectrometry is a powerful technique capable of simultaneously distinguishing multiple myeloid and lymphoid populations. It gives valuable insights into the immunobiology and treatment response of therapeutic TNF and GM-CSF blockage in AxSpA patients.

Acknowledgements. The NAMASTE clinical trial was funded by Izana Bioscience (EudraCT number: 2018-000176-15). The research in this article was supported by the Arthritis Therapy Acceleration Programme (A-TAP) (grant number KENN161704) and Versus Arthritis (grant no. 22287).



A) Healthy controls (n=20); **B**) Pre-TNF inhibitor therapy (n=20); **C**) Post-TNF inhibitor therapy (n=20)



D) Pre-GM-CSF inhibitor therapy (n=21); **E**) Post-GM-CSF inhibitor therapy (n=21); **F**) Pre-placebo treatment (n=5); **G**) Post-placebo treatment (n=5)

O10. Fig. 1. Myeloid and lymphoid cell population enumeration by CyTOF mass spectrometry in anti-TNF and anti-GM-CSF/placebo treated AxSpA patients and healthy controls. Uniform Manifold Approximation and Projection (UMAP) plots of high dimensional CyTOF immune profiles are shown for 20 healthy controls (panel A) and 20 anti-TNF treated patients pre- and post-treatment (panels B and C). CyTOF immune profiles were obtained for 26 patients of the NAMASTE trial, a first-in-disease phase II clinical trial of the anti-GM-CSF monoclonal antibody namilumab. Pre- and post-namilumab treatment UMAP visualisation plots are shown for 21 namilumab treated patients (panels D and E) and 5 placebo treated patients (panels F and G). Additional early treatment samples at week two of therapy are available for NAMASTE patients (not shown).

O11

MECHANICAL LOADING-INDUCED BHLHE40 PROMOTES INFLAMMATORY ARTHRITIS

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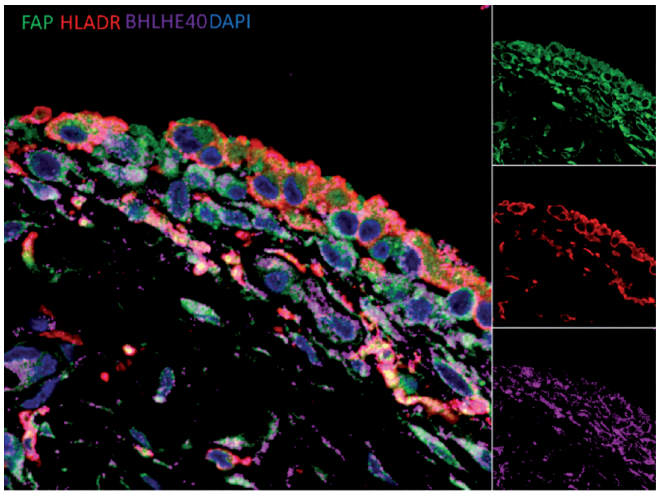
Background. Force induced microdamage to joint tissue is hypothesized to trigger inflammatory events in the joint. Patients with inflammatory arthritis, such as rheumatoid arthritis (RA) and spondyloarthritis (SpA), are found to have inflammation in "mechanical hotspots" and mechanical loading in mice is pro-arthritogenic (1, 2). To date, the molecular mechanism involved in converting force to a pro-arthritic biological signal is not known.
Objectives. This study aims to identify stretch induced genes in synovial fibroblasts, and the effect of these "mechano-sensitive" genes on arthritis.
Methods. Human synovial fibroblasts were stretched in vitro (FlexCell system) and analysed by microarray. Top stretch induced genes were measured in synovial tissue by qPCR and IHC. Bhlhe40 deficient mice were subjected to collagen induced arthritis (CIA) and KBxN serum transfer arthritis (STA). FACS was performed on ankle synovium.
Results. 600 genes were found to be differentially expressed in stretched synovial fibroblasts (fold change > ±1.5, adjusted $p<0.05$). 25% of these genes were found to be transcription factors, which included BHLHE40. BHLHE40 mRNA was elevated in the synovial tissue of RA/SpA vs healthy subjects (1.56 fold change), and BHLHE40 protein was widely detectable in synovial fibroblasts and macrophages (Fig. 1). Bhlhe40 deficient mice were completely protected against CIA (incidence: 0% vs 40%), but Bhlhe40 did not block the generation of anti-collagen antibodies. Bhlhe40 deficient mice were partially protected against STA (peak clinical score at day 7; 5.2 vs 6.8), with reduced synovial macrophage (CD11b+Ly6G-F4/80+) frequency observed in the arthritic Bhlhe40 deficient mice.



O11. Fig. 1. BHLHE40 is widely expressed in human synovium. Synovium obtained from total knee replacement. FFPE samples were stained for synovial macrophages (HLADR+) and fibroblasts (FAP+). Images acquired with the Zeiss LSM 780.

Conclusions. BHLHE40 was identified as a force-induced gene in synovial fibroblasts and was found to be upregulated in patients with inflammatory arthritis. Importantly, Bhlhe40 strongly promotes joint inflammation in murine models of arthritis and uncouples systemic autoimmunity from joint tissue inflammation. Thus, we have identified BHLHE40 as a novel regulator of mechanical loading-associated inflammation.
Acknowledgements. E. Gracey is supported by a Fonds Wetenschappelijk Onderzoek (FWO) senior postdoctoral fellowship.

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O12

SINGLE CELL ANALYSIS OF ANKYLOSING SPONDYLITIS SYNOVIAL T CELLS IDENTIFIES CD8 AND TREG CLONAL EXPANSION AND PHENOTYPIC PATTERNS OF TISSUE ADAPTATION

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Introduction/objectives. In Ankylosing Spondylitis (AS), a pathogenic role for acquired immune response to an unknown antigen or antigens has long been hypothesised. We wished to look for evidence of possible antigen-driven response in AS synovial fluid (SF) by studying both T cell phenotype and immune T cell receptor (TCR) repertoire.
Materials and methods. We first performed single cell RNA sequencing of matched blood and synovial fluid (SF) $CD4^+$ and $CD8^+$ T cells from 2 patients with HLA-$B27^+$ AS presenting with active knee arthritis. A previously published Psoriatic Arthritis (PsA) single cell dataset[1] was used as disease control. Multicolor flow cytometry and in vitro cell-based assays were used to confirm findings that emerged from the gene expression analysis.
Results. Functionally distinct specialised T cell subtypes, and specific changes in transcriptional profile occurring in SF cells, provide evidence of cellular adaptation during inflammation. Through unsupervised analysis, we identify multiple clusters of distinct transcriptomic profiles, associated to both regulatory and effector markers. In the SF, clonal expansion of CD8 with identical TCRa/b sequences, including previously published sequences, indicates likely antigen-driven clonal expansion and dynamic fate changes. TCR clonality is also seen in Tregs, which also show upregulation of interferon signature and TNF receptor superfamily genes. We demonstrate that LAG-3, expressed on SF Tregs, directly inhibits IL-12/23 and TNF secretion by patient-derived monocytes.
Discussion. Our detailed characterization of T cells at an AS inflammatory site identifies transcriptional changes consistent with tissue adaptation and antigen contact. We find evidence of both Treg and CD8 clonal expansion, both of which may be driven by antigen. Notably individual sister clones can adopt different phenotypic characteristics indicative of specialised functions within the joint. We also propose a new Treg functional mechanism through LAG-3 which in turn suggests a possible novel therapeutic approach to immune-driven diseases.

Reference
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O13

REDUCED FREQUENCY OF RORγT REGULATORY T CELLS IN AXIAL SPONDYLOARTHRITIS: EFFECT OF SECUKINUMAB TREATMENT

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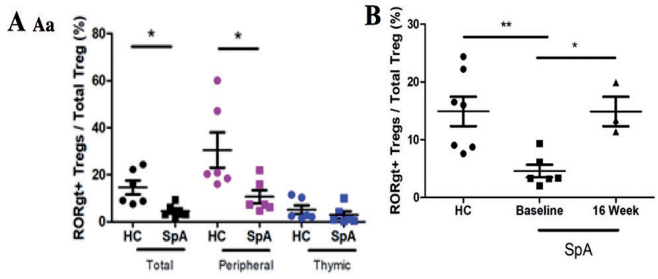
Introduction. Axial spondylarthritis (axSpA) is an inflammatory disease that predominantly affects the spine and the sacroiliac joints. Although the pathobiology of axSpA is not completely known, biologics that target the cytokine IL17a, such as secukinumab, have demonstrated improved clinical outcome in a majority of patients. Our study aims to address biomarkers that may be associated with treatment response. We hypothesized a decrease in the frequency of IL-17-producing cell subsets in secukinumab responders and an increase in frequency of anti-inflammatory cell subsets such as $CD4^+$ regulatory T cells (Tregs).
Methods. Patients with axSpA treated with secukinumab were recruited to the study. Peripheral mononuclear cells (PBMCs) were collected at baseline prior to treatment, and at 16 weeks follow-up. Multi-parametric flow cytometry analysis of several IL-17-producing cell subsets was used to assess differences between responders and nonresponders during secukinumab treatment.
Results. Compared to baseline, we found no difference in the Treg frequencies relative to total $CD4^+$ T cells in patients after secukinumab treatment. However, baseline frequencies of RORγt+ Tregs in PBMC of SpA patients

were significantly reduced (mean=4.59%) compared to healthy controls (mean=14.7%) (Fig. A). At 16 weeks after treatment with secukinumab, the frequencies of RORγt+ Tregs in SpA patients recovered to levels comparable to healthy controls (mean=14.9%) (Fig. B). An increase in RORγt+ Tregs during secukinumab treatment suggests an important role of Treg changes during anti-IL17a treatment.

Conclusions. We report that secukinumab treatment in axSpA restores suppression of type 3 immunity through an increase in frequencies of RORγt+ Tregs. Our findings underscore the importance of regulating type 3 immunity to reduce inflammation in axSpA patients. Further understanding of the immunobiology of RORγt+ Tregs may address how this immune dysregulation may contribute to the chronic inflammation characteristic of axSpA.



O13. Fig. 1.

O14

DO FATTY LESIONS EXPLAIN THE ASSOCIATION BETWEEN INFLAMMATION AND NEW SYNDESMOPHYTES IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS?

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Introduction. We assessed how much of the effect of vertebral corner inflammation (VCI) on the development of new syndesmophytes is explained by subsequent vertebral corner fat deposition (VCFD).

Methods. Two datasets (SIAS cohort, ASSERT clinical trial) were analyzed. Patients with r-axSpA were assessed at T0, T1 (SIAS:1 year; ASSERT:24 weeks) and T2 (SIAS:2 years; ASSERT:102 weeks). Syndesmophytes on whole spine low dose CT (SIAS) or spinal radiographs (ASSERT) at T0 and T2 were considered present if seen by 2/2 readers. VCI (T0) and VCFD (T0 and T1) on MRI were present if seen by ≥2/3 readers (SIAS) or 2/2 readers (ASSERT). Corners with VCFD or a syndesmophyte at baseline were excluded. We used the counterfactual approach to decompose the total effect of VCI at T0 on the formation of a new syndesmophyte in the same corner at T2 into the effect that is explained (average natural indirect effect, aNIE) and the effect that is not explained (average natural direct effect, aNDE) by new VCFD at T1. Effects were estimated taking into account the 2-level structure of the data (corners nested within patients).

Results. Forty-nine patients (2667 corners) in SIAS and 168 patients (2918 corners) in ASSERT were included. A new syndesmophyte occurred in 124/2667 (5%) corners in SIAS and 91/2918 (3%) corners in ASSERT (Table I). In SIAS, the presence of VCI increased the probability of a new syndesmophyte by 9.3% (Table II). Only 0.2% increase in this probability was mediated by the formation of new VCFD, while 9.1% of the increase in probability remained unexplained. This means that only 2% (0.2/9.3) of the total effect of VCI on the formation of new syndesmophytes was explained by new VCFD. Effects were similar in ASSERT.

Conclusions. In these two datasets we see that VCI only infrequently leads to syndesmophyte formation via visible VCFD.

O14. Table I. Marginal and conditional probabilities.

SIAS					
VCI T0	New VCFD T1	New SYND T2	n	P (SYND|VCI, VCFD)	P(VCFD|VCI)
0	0	0	2302	P (SYND|0,0) =90/2392 = 0.038	P(VCFD|0) = 74/2466= 0.030
0	0	1	90		
0	1	0	70	P (SYND|0,1) =4/74 = 0.054	
0	1	1	4		
1	0	0	152	P (SYND|1,0) = 25/177 = 0.141	P(VCFD|1) = 24/201 = 0.119
1	0	1	25		
1	1	0	19	P (SYND|1,1) = 5/24 = 0.208	
1	1	1	5		
ASSERT					
VCI T0	New VCFD T1	New SYND T2	n	P (SYND|VCI, VCFD)	P(VCFD|VCI)
0	0	0	2660	P (SYND|0,0) = 76/2736 = 0.028	P(VCFD|0) = 35/2771 = 0.013
0	0	1	76		
0	1	0	34	P (SYND|0,1) =1/35 = 0.029	
0	1	1	1		
1	0	0	112	P (SYND|1,0) = 9/121 = 0.074	P(VCFD|1) = 26/147 = 0.177
1	0	1	9		
1	1	0	21	P (SYND|1,1) = 5/26 = 0.192	
1	1	1	5		

The table provides the frequencies and probabilities of all possible scenarios: VCI: vertebral corner inflammation; VCFD: vertebral corner fat deposition; Synd: syndesmophytes, T0. baseline; T1. intewrmediate visit, T2: end of follow-up; n: number of vertebral corners; P: probability.

O14. Table II. Effects of vertebral corner fat deposition in the association between vertebral corner inflammation and syndesmophyte formation.

	SIAS	ASSERT
Total effect	9.3% (4.5 - 15.0)	7.3% (2.0 – 16.0)
Average natural direct effect	9.1% (4.3 - 15.0)	6.5% (1.3 – 14.0)
Average natural indirect effect	0.2% (-0.4 - 1.0)	0.8% (-0.2 – 3.0)
Proportion mediated	2.0% (-4.0 - 13.0)	10.2% (-3.1 – 44.0)

Values are the average increase in probability (95% CI) of a new syndesmophyte at the end of follow-up driven by the presence of VCI at baseline (total effect), the increase in this probability that is unexplained (natural direct effect) and explained (natural indirect effect) by the formation of fat deposition in the intermediate visit; and the proportion mediated (natural indirect effect/total effect).

O15

A PHASE 2 RANDOMIZED CONTROLLED TRIAL OF THE JANUS KINASE (JAK) INHIBITOR FILGOTINIB IN PATIENTS WITH NONINFECTIOUS UVEITIS

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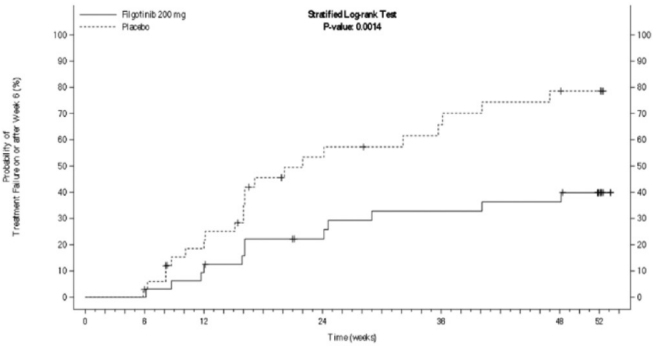
Introduction. Noninfectious uveitis (NIU) is a major cause of visual impairment, with limited treatment options. A randomized, placebo-controlled, double-masked trial of filgotinib, a JAK1 preferential inhibitor, assessed its efficacy and safety in NIU.

Methods. Adults with intermediate-, posterior- or pan-uveitis that was active despite ≥2 weeks of prednisone treatment were eligible. Subjects were randomized 1:1 to filgotinib 200 mg (FIL200) daily or placebo for up to 52 weeks. All subjects completed a prednisone taper from 60 mg (Day 1) to 0 mg (by Week 15). Primary endpoint was the proportion of subjects failing treatment by Week 24. Treatment failure was defined as: new chorioretinal

and/or retinal vascular lesion, worsening of best corrected visual acuity by ≥15 letters, or: inability to achieve an anterior chamber cell or vitreous haze grade 0.5+ at Week 6 or a 2-step increase after Week 6. Efficacy was evaluated in subjects receiving study drug and completing ≥6 weeks of treatment. The trial was terminated before full enrolment (planned n=248); therefore, hypothesis testing was done without multiplicity adjustment.

Results. Seventy-four subjects were randomized. Most (57%) had idiopathic uveitis. Missing data were imputed as treatment failures. Of n=66 evaluable subjects, 12/32 (37%) receiving filgotinib and 23/34 (68%) receiving placebo failed treatment (p=0.006). Median time to treatment failure was 22 weeks for placebo; this was not estimable for filgotinib as >50% of subjects had no treatment failure (hazard ratio 0.309; 95% CI [0.144 to 0.663]) (Figure). Adverse events (AEs) were more frequent with filgotinib than placebo (AEs: 81% vs. 69%; serious AEs: 14% vs. 6%). No arterial or venous thromboembolic events, major adverse cardiovascular events, opportunistic infections or cases of tuberculosis or herpes zoster were reported.

Conclusions. In patients with vision-threatening NIU, FIL200 reduced risk of uveitis flare compared to placebo and had an acceptable safety profile.



O15. Fig. 1. Time to treatment failure on or after Week 6.

Funding. Gilead.

O16

COMORBIDITIES IN EARLY PSORIATIC ARTHRITIS: BELGIAN PROSPECTIVE METAPSA COHORT

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Objectives. To investigate prevalence of comorbidities and cardiovascular risk factors (CV RF) in treatment naive early psoriatic arthritis (ePsA) compared to healthy volunteers and to identify factors that contribute to the metabolic burden of the patients.

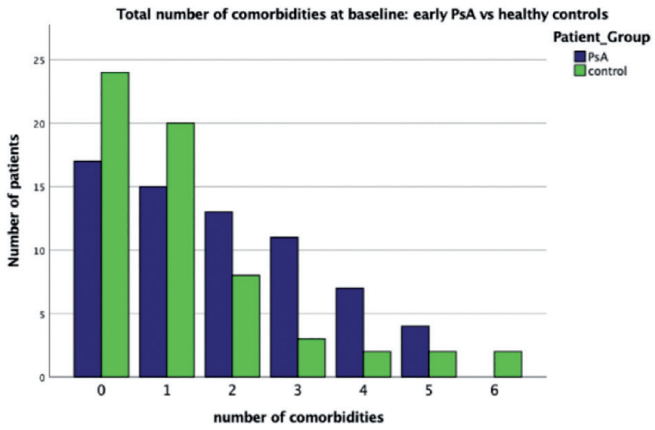
Methods. In observational multicenter study from UZ Leuven, we compared clinical, demographic characteristics, CV RFs and comorbidities of newly diagnosed naive to DMARD-treatment adult patients with PsA to sex- and age matched controls.

Results. EPsA patients (67) were matched to healthy volunteers (61). Majority of ePsA had oligoarticular disease and 95% had skin involvement, mostly mild. Median (IQR) symptom duration before diagnosis was 0.6 (0.22-2.3) years. EPsA group had above normal BMI, higher than controls (28.2 vs 25.7, Cohen's d=0.49, p=0.006), higher rate of obesity, abdominal obesity and metabolic syndrome (Table I). Number of comorbidities was higher in ePsA and 82% of ePsA and patients had ≥1 CV RFs present at baseline as compared to 38% of healthy volunteers (OR [95%CI]: 1.6 [1.14-2.26], p=0.017) (Fig. 1). Patients with ePsA had higher odds of having multiple cardiovascular risk factors (OR [95%CI] 2.1 [1.3-3.2], p<0.001) than the controls. Duration of skin psoriasis had no mediation effect on comorbidities or CV RF in ePsA. Diagnosis of PsA was the strongly associated with the number of comorbidities and CV RF after adjusting for age, sex and BMI. Dyslipidemia was the most prevalent comorbidity in the PsA (64.2% vs 39.3% in controls; OR [95%CI]: 1.6 [1.1-2.3], p=0.008). Rate of insulin resistance, arterial hypertension was similar in ePsA and in controls.

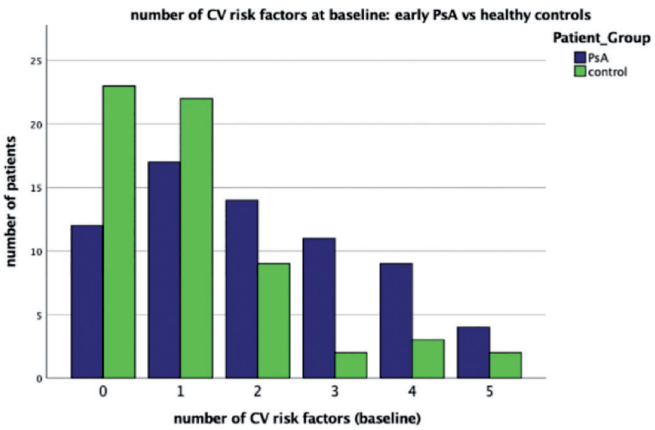
Conclusions. PsA patients have higher comorbidities and cardiovascular burden already at early stages of the disease. Rates of dyslipidemia, metabolic syndrome and obesity are significantly higher in early PsA population as compared to healthy volunteers. This suggests a bidirectional relationship between metabolic disturbances and PsA.

O16. Table 1. Comorbidities in patients with psoriatic arthritis as compared to age and sex matched controls at baseline.

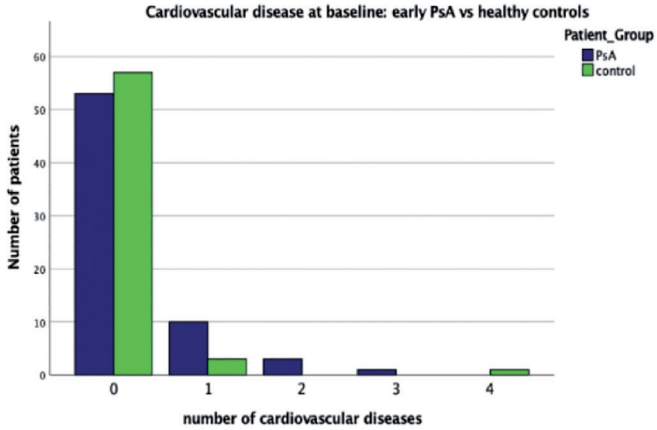
	early PsA (n= 67)	healthy controls (n=61)	p-value	ODDs ratio [95% CI]
male gender, n (%)	47 (70.1)	35 (57.4)	0.144	
age, mean (±SD)	47.9 (±14.3)	45 (±14.2)	0.25	
Patients with ≥1 comorbidities, n (%)	50 (74.6)	37 (60.7)	0.129	0.7 [0.5-1.1]
Patients with ≥2 comorbidities, n (%)	35 (52.2)	17 (27.9)	0.007*	1.9 [1.2-3.0]
Patients with ≥1 CV RF, n (%)	55 (82.1)	23 (37.7)	0.017*	1.6 [1.14-2]
Patients with ≥2 CV RF, n (%)	38 (56.7)	16 (26.2)	<0.001*	2.1 [1.3-3.2]
Patients with CV morbidity, n (%)	14 (20.7%)	4 (6.6)	0.023	2.3 [0.9-5.6]
Charlson comorbidity index ≥1, n (%)	21 (31.3)	4 (6.6)	<0.001*	4.8 [1.7-13.1]
dyslipidemia[&], n (%)	43 (64.2)	24 (39.3)	0.008*	1.6 [1.1-2.3]
dyslipidemia treated	14 (20.9)	7 (11.5)	0.162	
dyslipidemia documented	29 (43.3)	17 (27.9)	0.097	
presence of metabolic syndrome, n (%)	15 (22.4)	5 (8.2)	0.03*	2.7 [1.1-7.1]
Obesity (BMI ≥30), n (%)	27 (40.3)	11 (18.3)	0.011*	2.2 [1.2-4.0]
Abdominal obesity[#] n (%)	34 (50.7)	18 (29.5)	0.019*	1.7 [1.1-2.7]
W/H ratio, mean (±SD)	0.99 (±0.12)	0.91 (±0.14)	< 0.001*	NA
waist/hip ratio				NA
males, mean (±SD)	1.02 (±0.12)	0.94 (±0.09)	0.002*	
females, mean (±SD)	0.93 (±0.11)	0.87 (±)	0.23	
Smoking, n (%)	15 (22.4)	4 (6.6)	0.013*	0.6 [0.4-0.8]
presence of type 2 diabetes mellitus, n (%)	8 (11.9)	1 (1.6)	0.034*	7.2 [0.9-56.5]
arterial hypertension, n (%)	19 (28.4)	12 (19.7)	0.304	0.8 [0.6-1.4]
Smoking, n (%)	15 (22.4)	4 (6.6)	0.013*	0.6 [0.4-0.8]
Alcohol consumption (≥ 6 units/week), n (%)	20 (29.9)	17 (27.9)	0.85	0.6 [0.7-1.6]



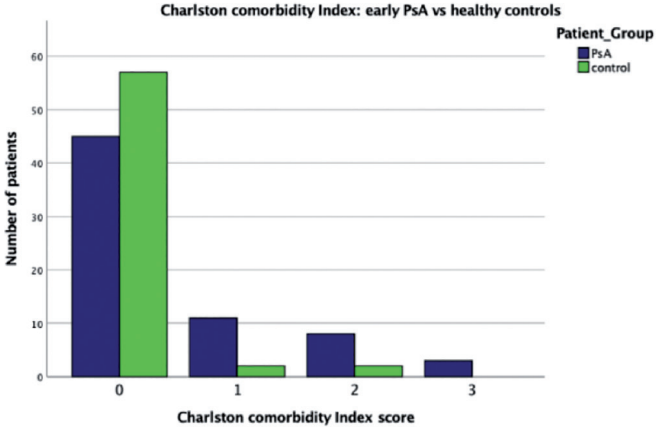
A. Number of comorbidities is significantly higher in early PsA (p=0.045, χ^2 test).



B. Number of CV RF is significantly higher in early PsA than in controls (p=0.011, χ^2 test).



C. Cardiovascular disease was not significantly different in two groups (p=0.07, χ^2 test).



D. CCI is significantly higher in early PsA (p=0.005, χ^2 test).

O16. Fig. 1. Comparison of comorbidities (**A**), cardiovascular risk factors (**B**), cardiovascular disease (**C**) and Charlson comorbidity index (**D**) in early PsA and healthy controls.

O17

BIMEKIZUMAB IN BDMARD-NAIVE PATIENTS WITH PSORIATIC ARTHRITIS: 24-WEEK EFFICACY AND SAFETY FROM BE OPTIMAL, A PHASE 3, MULTICENTRE, RANDOMISED, PLACEBO-CONTROLLED, ACTIVE REFERENCE STUDY

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Introduction. Assess the efficacy and safety of bimekizumab, a monoclonal IgG1 antibody that selectively inhibits IL-17F and IL-17A, versus placebo in bDMARD-naive patients with active PsA to Wk24 of BE OPTIMAL.

Methods. BE OPTIMAL (NCT03895203) comprises 16-wk double-blind placebo-controlled and 36-wk treatment-blind periods. Patients were bDMARD-naive, aged ≥18 years, with adult-onset, active PsA, ≥3 tender and ≥3 swollen joints. Patients were randomised 3:2:1, subcutaneous bimekizumab 160 mg Q4W:placebo:adalimumab 40 mg Q2W (reference arm). From Wk16, placebo patients received bimekizumab 160 mg Q4W. Primary endpoint: ACR50 at Wk16.

Results. 821/852 (96.4%) randomised patients completed Wk16 and 806 (94.6%) Wk24. Baseline characteristics were comparable across arms: mean age 48.7 years, BMI 29.2 kg/m^2, time since diagnosis 5.9 years, 46.8% male. The primary endpoint was met (Wk16 ACR50: 43.9% bimekizumab vs 10.0% placebo, p<0.001; adalimumab: 45.7%; Figure). All ranked secondary endpoints were met at Wk16 (Table). Additional outcomes, including ACR20/70 and TJC/SJC CfB, demonstrated improvement with bimekizumab versus placebo (Table). As early as Wk2, ACR20 response was higher in bimekizumab vs placebo (27.1% vs 7.8%, nominal p<0.001; adalimumab: 33.6%). At Wk24, outcomes continued to improve (Table). Over 16 wks, patients with ≥1 TEAE, bimekizumab: 59.9%; placebo: 49.5%; adalimumab: 59.3%. SAEs were low (1.6%; 1.1%; 1.4%). Most frequent (≥5%) AEs for all arms: nasopharyngitis (9.3%; 4.6%; 5.0%), URTI (4.9%; 6.4%; 2.1%), increased ALT (0.7%; 0.7%; 5.0%). *Candida* infections, 2.6%; 0.7%; 0.0%. No systemic candidiasis reported. Two malignancies reported (bimekizumab: basal cell carcinoma; placebo: breast cancer stage 1). No MACE, uveitis, IBD or deaths reported.

Conclusions. Dual inhibition of IL-17A and IL-17F with bimekizumab in bDMARD-naive patients with active PsA resulted in rapid, clinically relevant improvements in musculoskeletal and skin outcomes vs placebo. No new safety signals observed.

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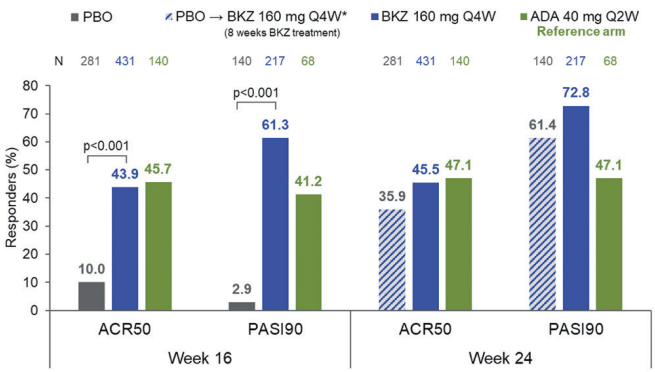
O17. Table. Week 16 and 24 efficacy

		BL			Week 16				Week 24*		
		PBO N=281	BKZ 160 mg Q4W N=431	ADA 40 mg Q2W N=140†	PBO N=281	BKZ 160 mg Q4W N=431	ADA 40 mg Q2W N=140†	*p* value (BKZ vs PBO)	PBO→BKZ 160 mg Q4W[a] N=281	BKZ 160 mg Q4W N=431	ADA 40 mg Q2W N=140†
Ranked endpoints[b]	ACR50 [NRI], n (%)	-	-	-	28 (10.0)	189 (43.9)	64 (45.7)	<0.001	101 (35.9)	196 (45.5)	66 (47.1)
	HAQ-DI CfB [MI] mean (SE)	0.89 (0.04)	0.82 (0.03)	0.86 (0.05)	–0.09 (0.03)	–0.26 (0.02)	–0.33 (0.04)	<0.001c	–0.28 (0.03)	–0.30 (0.02)	–0.34 (0.05),
	PASI90d [NRI], n (%)	-	-	-	4 (2.9)[e]	133 (61.3)[f]	28 (41.2)[g]	<0.001	86 (61.4)[e]	158 (72.8)[f]	32 (47.1)[g]
	SF-36 PCS CfB [MI], mean (SE)	36.9 (0.6)	38.1 (0.5)	37.6 (0.7)	2.3 (0.5)	6.3 (0.4)	6.8 (0.8)	<0.001c	6.2 (0.5)	7.3 (0.4)	7.3 (0.8)
	MDA [NRI], n (%)	5 (1.8)	14 (3.2)	1 (0.7)	37 (13.2)	194 (45.0)	63 (45.0)	<0.001	106 (37.7)	209 (48.5)	67 (47.9)
	vdHmTSS CfB (subgroup)h [MI], mean (SE)	15.67 (1.80)[i]	15.56 (1.69)[j]	17.39 (2.89)[k]	0.36 (0.10)[i]	–0.01 (0.04)[j]	–0.06 (0.08)[k]	<0.001[c]	-	-	-
	vdHmTSS CfB [MI], mean (SE)	13.31 (1.56)[l]	13.44 (1.47)[m]	14.55 (2.44)[n]	0.31 (0.09)[l]	0.00 (0.04)[m]	–0.03 (0.07)[n]	0.001[c]	-	-	-
Other endpoints	ACR20 [NRI], n (%)	-	-	-	67 (23.8)	268 (62.2)	96 (68.6)	<0.001[o]	175 (62.3)	282 (65.4)	99 (70.7)
	ACR70 [NRI], n (%)	-	-	-	12(4.3)	105 (24.4)	39 (27.9)	<0.001[o]	53 (18.9)	126 (29.2)	42 (30.0)
	PASI100d [NRI], n (%)	-	-	-	3 (2.1)[e]	103 (47.5)[f]	14 (20.6)[g]	<0.001[o]	60 (42.9)[e]	122 (56.2)[f]	26 (38.2)[g]
	TJC CfB [MI], mean (SE)	17.1 (0.7)	16.8 (0.6)	17.5 (1.1)	–3.2 (0.7)	–10.0 (0.5)	–10.9 (1.0)	<0.001[o]	–9.4 (0.7)	–11.5 (0.5)	–11.8(0.9)
	SJC CfB [MI], mean (SE)	9.5 (0.4)	9.0 (0.3)	9.6 (0.6)	–3.0 (0.5)	–6.6 (0.3)	–7.5 (0.6)	<0.001[o]	–6.8 (0.4)	–7.2 (0.3)	–7.9 (0.6)

Randomised set. *Interim results. †Reference arm; study not powered for statistical comparisons of ADA to BKZ or PBO. [a] PBO/BKZ pts received PBO to Week 16, switched to BKZ 160 mg Q4W through Week 24 (8 weeks BKZ); [b] Resolution of enthesitis/dactylitis in pts with LEI>0/LDI>0 at BL pooled with BE COMPLETE (Week 16 LEI=0 BKZ: 124/249 [49.8%], PBO: 37/106 [34.9%], p=0.008; LDI=0 BKZ: 68/90 [75.6%], PBO: 24/47 [51.1%], p=0.002); [c] Continuous outcome p values calculated with RBMI data; [d] Pts with PSO and ≥3% BSA at BL; [e] n=140; [f] n=217; [g] n=68; [h] Pts with hsCRP ≥6 mg/L and/or bone erosion at BL; [i] n=221; [j] n=357; [k] n=108; [l] n=261; [m] n=416; [n] n=131; [o] Nominal, not powered or adjusted for multiplicity. ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology criteria; ADA: adalimumab; BKZ: bimekizumab; BL: baseline; CfB: change from baseline; HAQ-DI: health assessment questionnaire disability index; hsCRP: high-sensitivity C-reactive protein; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; MDA: minimal disease activity; MI: multiple imputation; NRI: non responder imputation; PASI: psoriasis area and severity index; PASI75/90/100: ≥75/90/100% improvement in PASI; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks; RBMI: reference-based multiple imputation; SF-36 PCS: 36-item short form survey Physical Component Summary; SJC: swollen joint count; TJC: tender joint count; vdHmTSS: van der Heijde-modified Total Sharp Score.



O17. Fig. 1. ACR50 and PASI90 response at Weeks 16 and 24.
Randomised set. Data reported as NRI. *PBO/BKZ pts received PBO through Week 16 then switched to BKZ 160 mg Q4W through Week 24 (8 weeks BKZ treatment). ACR50: ≥50% improvement in American College of Rheumatology criteria; ADA: adalimumab; BKZ: bimekizumab; PASI: psoriasis area and severity index; PASI90: ≥90% improvement in PASI; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks.

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O18

MRI SPINAL LESIONS IN PATIENTS WITHOUT MRI OR RADIOGRAPHIC LESIONS IN THE SACROILIAC JOINTS TYPICAL OF AXIAL SPONDYLOARTHRITIS

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Introduction. We assessed the frequency of MRI lesions of the spine in the ASAS-Classification Cohort according to the presence/absence of MRI SIJ lesions typical of axSpA and/or radiographic sacroiliitis (mNY+), as well as a clinical diagnosis of axSpA.

Methods. MRI spine lesions were recorded by 9 central readers in an eCRF that captures global assessment of the spine ("Is the MRI consistent with axSpA: yes/no") (yes=MRI_{global} spine+) and detailed anatomical-based scoring of each discovertebral unit plus lateral and posterior structures. Independently, readers globally assessed SIJ scans for active and/or structural lesions typical of axSpA. We compared the frequency of MRI_{global} spine+ and frequencies of different types of spinal lesions according to the presence/absence of axSpA on global evaluation of SIJ scans by ≥5 of 9 readers (MRI_{global} SIJ+) and mNY+ sacroiliitis using Fisher's exact test. Analysis was also stratified by rheumatologist diagnosis of axSpA.

Results. Among 51 cases with SIJ as well as spine MRI scans and radiographs of the SIJ,19 (37.3%) had MRI_{global} SIJ+, and 12 (23.5%) and 7 (13.7%) had MRI_{global} spine+ by ≥2 and ≥5 reader agreement, respectively. MRI_{global} spine+ occurred significantly more frequently in the presence of mNY+ sacroiliitis and MRI_{global} SIJ+ but was also recorded in 4 of 32(12.5%) (≥2 readers) and 1 of 32(3.4%) (≥5 readers) cases that were MRI_{global} SIJ- ***and*** x-ray negative, all 4 cases being clinically diagnosed with axSpA. Moreover, vertebral corner BME lesions, but not spinal structural lesions, were significantly more frequent in MRI_{global} SIJ- cases that had been clinically diagnosed as axSpA versus non-axSpA (Table).

Conclusions. Spinal lesions on MRI indicative of axSpA per majority read occurred in about 3% of patients without positive imaging in the SIJ. Frequency of spinal BME lesions was higher in cases with negative SIJ imaging but clinically diagnosed with axSpA.

O19

PATHOGENICITY OF IL-17 PRODUCING CELLS IN HLA-B27 TRANSGENIC RAT MODEL OF SPONDYLOARTHRITIS

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Introduction. Spondylarthritis (SpA) is a group of chronic inflammatory disorders with osteoarticular and extraarticular symptoms, including colitis, highly associated with the human leukocyte antigen (HLA) class I molecule B27. A strong association of SpA with HLA-B27 has been known for nearly 50 years but its pathogenic role remains largely unexplained. Transgenic rats expressing HLA-B27 and human β2-microglobulin (B27-rat) develop clinical manifestations resembling human SpA (rat SpA). Previous studies revealed that IL-17 and TNF-α are two major cytokines implicated in both SpA and rat SpA.

Objectives. In this study, we aimed to determine which cell subset(s) produce both proinflammatory cytokines (IL-17 and TNF-α) during rat SpA and characterize their tissue distribution. Then, we tested the pathogenicity of these proinflammatory cell subsets by transfer experiments in nude B27-rats.

Methods. Lymphoid cells were isolated from both inflamed tissues and lymphoid organs draining those tissues before and during rat SpA development and were characterized. Non transgenic (NTG) littermates were used as control. Blood samples were used to translate B27-rat findings to HLA-$B27^+$ SpA patients. The pathogenicity of purified $CD4^+$ T cell subsets was assessed by transfer in SpA-resistant athymic nude B27-rats.

Results. First, we showed that conventional T cells ($CD4^+$ $Foxp3^-$) were the main producers of both IL-17 and TNF-α. Those Th17 cells were significantly expanded in blood, bone marrow (BM), lymph nodes and colon from B27-rats. Similar findings were observed in SpA patients. Importantly, this expansion was already present in BM and colon of premorbid B27-rats. Finally, transfer of HLA-$B27^+$ purified Th17 induced SpA symptoms in nude B27-rats, directly evidencing for the first time a specific proarthritogenic role of Th17 cells in SpA.

Conclusions. Our study demonstrates that Th17 cells are expanded before disease development and are involved in SpA development. Further studies are required to determine the pathogenic mechanism of such cells.

O18. Table. Frequency of spinal MRI lesions according to SIJ imaging for AxSpA.

MRI spinal lesions, N (%)	All Cases (n=51)	*MRI_{global} SIJ+ (n=19)	MRI_{global} SIJ- (n=32)	*p*-value	MRI_{global} SIJ+ and/or mNY+ (n=22)	MRI_{global} SIJ- and mNY- (n=29)	*p*-value	MRI_{global} SIJ- and axSpA Diagnosis+ (n=17)	MRI_{global} SIJ- and axSpA Diagnosis- (n=15)	*p*-value
MRI_{global} consistent with axSpA* (≥2/9 readers agree)	12 (23.5%)	8 (42.1%)	4 (12.5%)	0.04	8(36.4%)	4(13.8%)	0.10	4 (23.5%)	0 (0%)	0.10
MRI_{global} consistent with axSpA* (≥5/9 readers agree)	7 (13.7%)	6 (31.6%)	1 (3.1%)	0.01	6 (27.3%)	1 (3.4%)	0.03	1 (5.9%)	0 (0%)	1.0
VC BME ≥1	24 (47.1%)	9 (47.4%)	15(46.9%)	1.0	10(45.5%)	14(48.3%)	1.0	11 (64.7%)	4 (26.7%)	0.04
VC BME ≥2	16 (31.4%)	6 (31.6%)	10(31.3%)	1.0	6(27.3%)	10(34.5%)	0.76	9 (52.9%)	1 (6.7%)	0.007
VC BME ≥3	13 (25.5%)	6 (31.6%)	7 (21.9%)	0.52	6(27.3%)	7(24.1%)	1.0	7 (41.2%)	0 (0%)	0.008
VC BME ≥4	10 (19.6%)	5 (26.3%)	5 (15.6%)	0.47	5(22.7%)	5(17.2%)	0.73	5 (29.4%)	0 (0%)	0.046
Vertebral Endplate BME ≥1	5 (9.8%)	2 (10.5%)	3 (9.4%)	1.0	2(9.1%)	3(10.3%)	1.0	2 (11.8%)	1 (6.7%)	1.0
Lateral vertebral BME	6 (11.8%)	3 (15.8%)	3 (9.4%)	0.66	3(13.6%)	3(10.3%)	1.0	3 (17.6%)	0 (0%)	0.23
Facet BME ≥1	5 (9.8%)	4 (21.1%)	1 (3.1%)	0.06	4(18.2%)	1(3.4%)	0.15	1 (5.9%)	0 (0%)	1.0
Posterior BME ≥1	7 (13.7%)	5 (26.3%)	2 (6.3%)	0.09	5(22.7%)	2(6.9%)	0.22	1 (5.9%)	1 (6.7%)	1.0
VC Fat ≥1	18 (35.3%)	8 (42.1%)	10(31.3%)	0.55	8(36.4%)	10(34.5%)	1.0	5 (29.4%)	5 (33.3%)	1.0
VC Fat ≥2	12 (23.5%)	7 (36.8%)	5 (15.6%)	0.10	7(31.8%)	5(17.2%)	0.32	3 (17.6%)	2 (13.3%)	1.0
VC Fat ≥3	9 (17.6%)	6 (31.6%)	3 (9.4%)	0.06	6(27.3%)	3(10.3%)	0.15	1 (5.9%)	2 (13.3%)	0.59
VC Fat ≥4	7 (13.7%)	6 (31.6%)	1 (3.1%)	0.01	6(27.3%)	1(3.4%)	0.03	0 (0%)	1 (6.7%)	0.47
Lateral Fat ≥1	8 (15.7%)	6 (31.6%)	2 (6.3%)	0.04	6(27.3%)	2(6.9%)	0.06	0 (0%)	2 (13.3%)	0.21
Erosion ≥1	5 (9.8%)	3 (15.8%)	2 (6.3%)	0.35	3(13.6%)	2(6.9%)	0.64	1 (5.9%)	1 (6.7%)	1.0
Bone Spur ≥1	9 (17.6%)	4 (21.1%)	5 (15.6%)	0.71	4(18.2%)	5(17.2%)	1.0	4 (23.5%)	1 (6.7%)	0.34
Ankylosis ≥1	2 (3.9%)	2 (10.5%)	0 (0%)	0.13	2(9.1%)	0(0%)	0.18	0 (0%)	0 (0%)	-

*18 of 19 patients diagnosed with axSpA.

Poster Presentations

P1

WORK PARTICIPATION AND PRODUCTIVITY IS UNAFFECTED IN BELGIAN SPONDYLOARTHRITIS PATIENTS COMPARED TO THE GENERAL POPULATION: DATA FROM THE BELGIAN INFLAMMATORY ARTHRITIS AND SPONDYLITIS COHORT (BE-GIANT)

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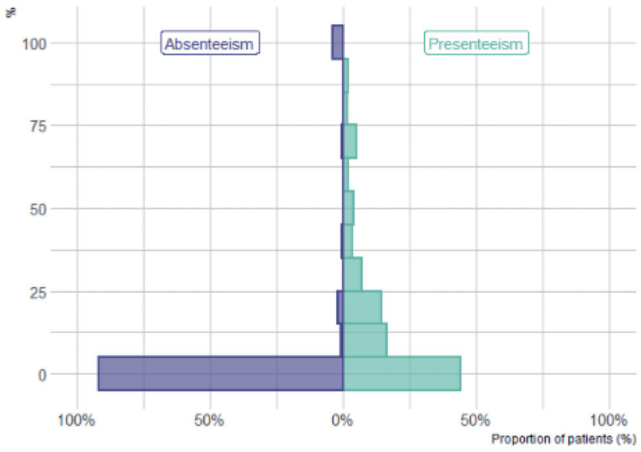
Objectives. To investigate actual work participation and productivity in Belgian spondyloarthritis (SpA) patients compared to the general population, taking into account recent advances in diagnosis and disease management strategies.
Methods. Adult SpA patients, who consulted a rheumatologist at Ghent University Hospital between May 2018 and May 2019, were cross-sectionally questioned on their socio-economic status and completed a Work Productivity and Activity Impairment questionnaire. Patients fulfilled ASAS classification criteria for axial or peripheral SpA and were involved in a clinical care path (BelGian Inflammatory Arthritis and spoNdylitis cohort, Be-Giant), providing standardized collection of clinical data and patient reported outcomes. Flemish socio-economic information was used for comparison of employment rate (applying indirect standardization of age and sex), working hours/week and long-term work disability (Belgian statistical office/Health Interview Survey, reference year 2018-2019).
Results. In the working-age population (<65 y/o), 215/262 (82%) patients had a paid job. Adjusted employment rate was 76%, corresponding to a standardized employment ratio of 1.00 (95%CI 0.88;1.14). Patients worked 39.4±10.5h/week, compared to an average of 39.7h (full-time) for Flemish employees. The median career duration was 42.1y (95%CI 40.1;43.7) compared to an average of 33.6y in Belgium. 102/208 (49%) patients with a paid job reported sick leave in the previous year (n=7 missing) with a mean±SD number of 7±22 absent days, compared to 42% of sick leave in the working Flemish population with an average of 11.1 days absence from work. Absenteeism (% of time absence from work) and presenteeism (% productivity loss while at work) in the past week was reported by 9% and 56% of the working population (Fig. 1). 25/262 (9.5%) were work disabled, compared to 6.7% in the Flemish population.



P1. Fig. 1. Proportion of working SpA patients reporting absenteeism (%) and presenteeism (%) in the previous week.

Conclusions. This study refutes the common perception that SpA patients experience excess sick leave and productivity loss compared to the general population.

Acknowledgements. This study was supported by Fund Benevermedex.

P2

DEVELOPMENT OF INTERNATIONAL CONSENSUS ON A STANDARDIZED IMAGE ACQUISITION PROTOCOL FOR DIAGNOSTIC EVALUATION OF THE SACROILIAC JOINTS BY MRI – AN ASAS-SPARTAN COLLABORATION

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Introduction. There is still no diagnostic image acquisition protocol (IAP) for MRI evaluation of the sacroiliac joints (SIJ) in axial spondyloarthritis (axSpA) that has been widely accepted as a minimum standard worldwide. We conducted an international consensus exercise to develop these minimal requirements for a standardized IAP.
Methods. All radiologist members of the ASAS and SPARTAN Classification in axSpA (CLASSIC) project, along with one European and one North American rheumatologist with extensive experience in MRI of axSpA, were invited to participate. A draft IAP was circulated along with justification for the draft proposal. Feedback on all issues was received by email, tabulated and recirculated. Remaining points of contention were resolved by teleconference. Examples of the proposed IAP performed on new and old MRI scanners were made available for review in DICOM format. The IAP was presented at the 2022 ASAS annual meeting and voted on.
Results. A 4-sequence IAP, 3-semicoronal and 1-semiaxial, is recommended for diagnostic ascertainment of sacroiliitis and its differential diagnoses (Table). It must meet the following requirements: Semicoronal sequences should be parallel to the dorsal cortex of the S2 vertebral body, and include: 1) a sequence sensitive for the detection of active inflammation being T2-weighted with suppression of fat signal; 2) a sequence sensitive for the detection of structural damage in bone and bone marrow with T1-weighting; 3) a sequence designed to optimally depict the bone-cartilage interface of the articular surface and be sensitive for detection of bone erosion; plus 4) a semiaxial sequence sensitive for inflammation detection. The IAP was approved at the ASAS annual meeting by a vote of 91%.
Conclusions. A standardized IAP for MRI of the sacroiliac joints in axSpA should be comprised of a minimum of 4 sequences, in 2-planes, that will optimally visualize inflammation, structural damage, and the bone-cartilage interface.

P2. Table. A standardized SIJ MRI Acquisition Protocol for diagnostic ascertainment of sacroiliitis

Orientation	Sequence	Target Lesion(s)
Semicoronal Parallel to the dorsal cortex of the S2 vertebral body	T1-w Spin Echo	Fat lesions, erosion, backfill & ankylosis.
	T2-w with suppressed fat signal (STIR, T2FS or =)	Bone marrow edema (BME)
	T1-w with suppressed fat signal (2D or 3D T1FS)	Erosion of the articular surface
Semiaxial	T2-w with suppressed fat signal (STIR, T2FS or =)	Bone marrow edema (BME)

P3

MAGNETIC RESONANCE IMAGING CHARACTERISTICS OF SPINE AND SACROILIAC JOINTS IN PATIENTS WITH PSORIATIC ARTHRITIS AND AXIAL MANIFESTATIONS

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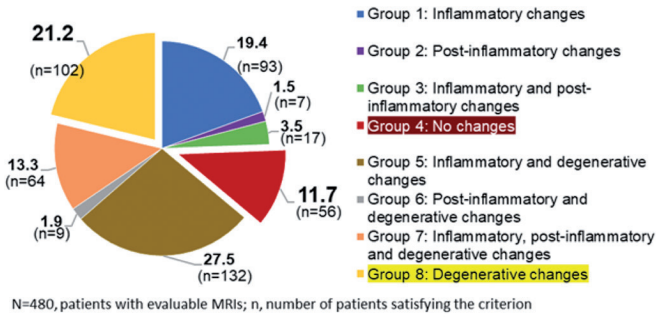
Introduction. Axial psoriatic arthritis (axPsA), one of the six PsA domains, lacks definition and universally acceptable clinical and imaging criteria. This *post hoc* analysis of MAXIMISE, the RCT to demonstrate the efficacy of secukinumab in PsA patients with axial manifestations, aimed to investigate the presence of additional inflammatory, post-inflammatory and degenerative changes (DC) in baseline spinal MRIs and their potential to predict differential treatment effect in PsA patients and axial manifestations.
Methods. The re-reading protocol of 485 baseline MRIs of the spine included assessment of: inflammatory changes of the spinal processes (SPi), post-inflammatory changes assessed by FAt Spondyloarthritis Spine Score (FASSS), and DC as Modic type-1 and type-2 lesions, Schmorl's nodes with/without vertebral endplate BME, erosion, sclerosis and Pfirrmann changes. The potential for differential treatment effect of inflammatory, post-inflammatory and DC groups was investigated using logistic regression modelling.
Results. SPi and FASSS were documented in 11.1% and 20.2% of patients, respectively. At least one type of DC was revealed in 64% of patients with Pfirrmann grade ≥3 (51.1%) being the most common one (Table). Overall, 67.1% of patients presented with inflammatory/post-inflammatory changes at the spine and/or the sacroiliac joints, potentially suggestive of axPsA, while 21.2% and 11.7% of patients had only DC and normal MRIs, respectively (Figure). Trends for better outcomes in terms of ASAS20, ASAS40 and BASDAI50 responses were observed for post-inflammatory changes, and worse outcomes for the presence of DCs (results previously presented) (1).



P3. Fig. 1. Proportion of patients at baseline in each of the 8 mutually exclusive groups with inflammatory, post-inflammatory and degenerative changes at the spine and the SIJ.

Conclusions. Re-reading the baseline MRIs from the MAXIMISE trial revealed additional inflammatory and post-inflammatory changes suggestive of axPsA, while DCs were the only MRI finding in 21.2% of patients. These results shed light on imaging characteristics and improve our understanding of axPsA thereby supporting the design of future trials.

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P4

SEX DIFFERENCES IN THE EFFECTIVENESS OF FIRST-LINE TUMOR NECROSIS FACTOR INHIBITORS IN AXIAL SPONDYLOARTHRITIS; RESULTS FROM FIFTEEN COUNTRIES IN THE EUROPEAN SPONDYLOARTHRITIS (EUROSPA) RESEARCH COLLABORATION NETWORK

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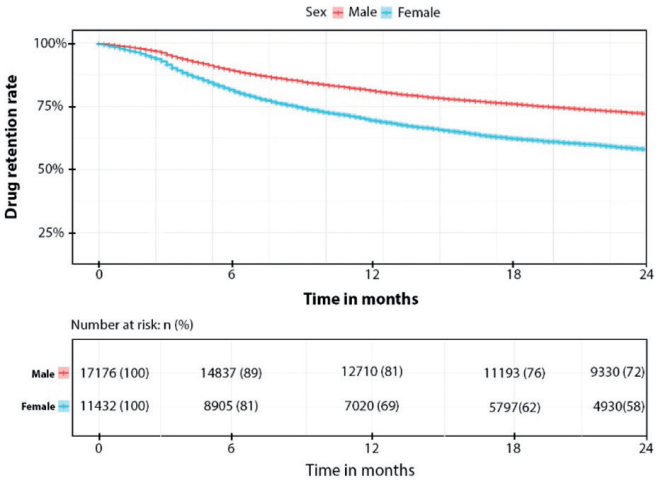
European Spondyloarthritis (EuroSpA) Research Collaboration, on behalf of SRQ (Sweden), DANBIO (Denmark), ATTRA (Czech Republic), TURKBIO (Turkey), NOR-DMARD (Norway), SCQM (Switzerland), Reuma.pt (Portugal), ROB-FIN (Finland), RRBR (Romania), biorx.si (Slovenia), ICEBIO (Iceland), AmSpA (Netherlands), BIOBADASER (Spain), GISEA (Italy), BSRBR-AS (UK)

Background. Previous evidence reveals reduced treatment effectiveness of tumor necrosis factor inhibitors (TNFis) in females with axial spondyloarthritis (axSpA). We sought to validate prior studies using data from a large multinational cohort based on real-life clinical practice.
Objectives. To investigate sex differences in treatment response and drug retention rates in clinical practice among patients with axSpA treated with their first TNFi.
Methods. Data from biologic-naive axSpA patients initiating a TNFi in the EuroSpA registries were pooled. In the primary analysis, propensity-score weighting was applied to assess the effect of sex on clinically important improvement (CII) according to ASDAS-CRP at six months. Logistic regression was used to estimate relative risk (RR) and risk difference (RD). The analysis was adjusted for covariates determined a priori, namely, country, age, and TNFi start year. In the secondary analysis, drug retention was assessed over 24 months of follow-up by Kaplan-Meier curves.
Results. In total, 6,451 axSpA patients with available data on CII were assessed for treatment response. Baseline characteristics are shown in the Table. In the adjusted analysis, the probability for females to have CII was 15% (RR, 0.85; 95% confidence interval [CI], 0.82 to 0.89) lower compared to males, and the difference in probability for having CII was 9.4 percentage points (RD, 0.094; 95% CI, 0.069 to 0.12). The survival analysis included 28,608 axSpA patients. The TNFi 6/12/24-month retention rates were significantly lower in females (81%/69%/58%) compared to males (89%/81%/72%), see Figure.
Conclusions. Treatment efficacy and retention rates are lower among female patients with axSpA initiating their first TNFi. Females presented with lower CRP levels and higher scores on patient-reported outcomes at baseline, reflecting differences in disease expression. Recognizing these sex differences is relevant for customized patient care and may improve patient education.



P4. Fig. 1. Sex differences in 24-month retention rates in first-line tumor necrosis factor inhibitors in patients with axial spondyloarthritis in EuroSpA (Kaplan-Meier, log-rank test; $p<0.001$).

P4. Table Baseline characteristics of all biologic-naive axSpA patients treated with their first TNFi and available ASDAS-scores, data pooled across all countries.

	Female Mean (SD), median [IQR], or percentages	Male Mean (SD), median [IQR], or percentages
Age (years)	42.0 (12.1)	41.4 (12.3)
Fulfillment of mNYC	66%	80%
Disease duration (years)	2.0 [1.0 to 7.0]	3.0 [1.0 to 9.0]
TNFi start year		
Start 1999-2009	7.2%	9.8%
Start 2010-2013	26%	27%
Start 2014-2016	37%	36%
Start 2017-2020	30%	27%
BASDAI, mm	59 (20)	54 (21)
BASFI, mm	48 (25)	46 (24)
ASDAS, units	3.5 (0.9)	3.5 (1.0)
CRP (mg/L)	6.7 [2.5 to 16.0]	11.9 [4.0 to 25.0]
SJC (0-28)	0 [0 to 0]	0 [0 to 0]
TJC (0-28)	0 [0 to 2]	0 [0 to 1]
VAS pain, mm	63 (22)	59 (24)
VAS fatigue, mm	65 (25)	59 (26)

mNYC: modified New York criteria; TNFi: tumor necrosis factor inhibitor; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; CRP: C-reactive protein; SJC: swollen joint count; TJC: tender joint count; VAS: visual analogue scale.

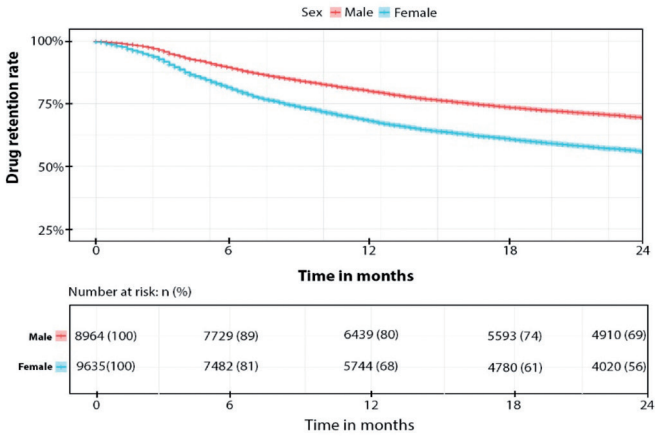
Acknowledgments. Novartis Pharma AG and IQVIA for supporting the EuroSpA collaboration.

P5

SEX DIFFERENCES IN THE EFFECTIVENESS OF FIRST-LINE TUMOR NECROSIS FACTOR INHIBITORS IN PSORIATIC ARTHRITIS; RESULTS FROM THIRTEEN COUNTRIES IN THE EUROPEAN SPONDYLOARTHRITIS (EUROSPA) RESEARCH COLLABORATION NETWORK

Hellamand P., Van de Sande M.G., Midtbøll Ørnbjerg L.M., Klausch T., Trokovic N., Sokka-Isler T., Santos M.J., Vieira-Sousa E., Loft A.G., Glintborg B., Østergaard M., Lindström U., Wallman J.K., Michelsen B., Möller B., Micheroli R., Codreanu C., Mogosan C., Laas K., Rotar Z., Tomsic M., Castrejon I., Pombo-Suarez M., Gudbjornsson B., Love T.J., Fagerli K.M., Pavelka K., Závada J., Kenar G., Yarkan H., Hetland M.L., Van der Horst- Bruinsma I.E.
European Spondyloarthritis (EuroSpA) Research Collaboration, on behalf of SRQ (Sweden), DANBIO (Denmark), ATTRA (Czech Republic), TURKBIO (Turkey), NOR-DMARD (Norway), SCQM (Switzerland), Reuma.pt (Portugal), ROB-FIN (Finland), RRBR (Romania), biorx.si (Slovenia), ICEBIO (Iceland), AmSpA (Netherlands), BIOBADASER (Spain), GISEA (Italy)

Background. Previous evidence demonstrates reduced treatment efficacy in females with psoriatic arthritis (PsA). We sought to validate prior studies using data from a large multinational cohort based on real-life clinical practice.
Objectives. To investigate sex differences in treatment response and drug retention rates in clinical practice among patients with PsA treated with their first TNFi.
Methods. Data from biologic-naive PsA patients initiating a TNFi in the EuroSpA registries were pooled. In the primary analysis, propensity-score weighting was applied to assess the effect of sex on low disease activity (LDA) according to DAS28-CRP at 6 months. Logistic regression was used to estimate relative risk (RR) and risk difference (RD). The analysis was adjusted for covariates determined a priori, namely, country, age, and TNFi start year. In the secondary analysis, drug retention was assessed over 24 months of follow-up by Kaplan-Meier curves.
Results. In total, 7,679 PsA patients with available data on DAS28-CRP at six months were assessed for treatment response. Baseline characteristics are shown in the Table. In the adjusted analysis, the probability for females to have LDA was 17% (RR, 0.83; 95% confidence interval [CI], 0.81 to 0.85) lower compared to males, and the difference in probability of having LDA was 13 percentage points (RD, 0.13; 95% CI, 0.11 to 0.15). The survival analysis included 18,599 PsA patients. The TNFi 6/12/24-month retention rates were significantly lower in females (81%/68%/56%) compared to males (89%/80%/69%), see Figure.



P5. Fig. 1. Sex differences in 24-month retention rates in first-line tumor necrosis factor inhibitors in patients with psoriatic arthritis in EuroSpA (Kaplan-Meier, log-rank test; $p<0.001$).

P5. Table Baseline characteristics of all biologic-naive PsA patients treated with their first TNFi and available DAS28-CRP at six months, data pooled across all countries.

	Female Mean (SD), median [IQR], or percentages	Male Mean (SD), median [IQR], or percentages
Age (years)	49.7 (12.5)	47.8 (11.9)
Disease duration (years)	4.0 [1.0 to 10.0]	4.0 [1.0 to 10.0]
TNFi start year		
1999-2009	29%	29%
2010-2013	26%	27%
2014-2016	25%	24%
2017-2020	20%	20%
Concomitant csDMARD	75%	77%
DAS28-CRP	4.4 (1.2)	4.2 (1.2)
DAPSA28	32 (16)	29 (16)
CRP (mg/L)	7.0 [3.0 to 17.0]	8.0 [3.3 to 19.0]
SJC (0-28)	3.0 [1.0 to 6.0]	3.0 [1.0 to 6.0]
TJC (0-28)	6.0 [2.0 to 10.0]	4.0 [2.0 to 9.0]
VAS pain, mm	61 (23)	55 (23)
VAS fatigue, mm	62 (26)	53 (27)

Data are as observed, mean (SD), median [IQR], or percentage.
TNFi, tumour necrosis factor inhibitor; csDMARD, Conventional synthetic disease-modifying antirheumatic drugs; DAS28-CRP, Disease Activity Score 28-joint count C reactive protein; DAPSA28, Disease Activity in PsA 28; CRP, C-reactive protein; SJC, swollen joint count; TJC, tender joint count.

Conclusions. Treatment efficacy and retention rates are lower among female patients with PsA initiating their first TNFi. Females presented with higher 28-tender joint count and higher scores on patient-reported outcomes at baseline, reflecting differences in disease expression. Recognizing these sex differences is relevant for customized patient care and may improve patient education.

Acknowledgments. Novartis Pharma AG and IQVIA for supporting the EuroSpA collaboration.

P6

COMPARISON OF ESTABLISHED AND NEW, PRELIMINARILY PROPOSED ASAS CUT-OFFS FOR INFLAMMATORY MRI LESIONS IN THE SACROILIAC JOINTS IN AXIAL SPONDYLOARTHRITIS AND IMPLICATIONS FOR RECRUITMENT IN CLINICAL STUDIES

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Introduction. The ASAS recently proposed preliminary, more stringent, data-driven definitions for active and structural MRI lesions of the SIJ typical of axSpA (1). In this post hoc analysis, we applied both the existing and newly proposed definitions to the C-OPTIMISE trial dataset. We assessed the efficacy of certolizumab pegol (CZP) in patients who were MRI-positive (MRI+) and negative (MRI-) according to each definition, as well as those who were MRI+ using the existing definition but MRI- by the newly proposed definition (discordant group).

Materials and methods. C-OPTIMISE (NCT02505542) enrolled 736 patients with active axSpA who received 400mg CZP at Weeks (Wks) 0, 2, and 4, then 200mg CZP every two wks to Wk48. We report percentage of patients achieving ASAS40 response alongside mean BASDAI and ASDAS change from baseline (CfB) to Wk48. Outcomes are stratified by axSpA subgroup (r-/nr-axSpA) and MRI definition. Missing values were imputed using non-responder imputation for ASAS40 and last observation carried forward for continuous variables.

Results. Baseline MRI data were available for 657/736 (89.3%) patients: 333/657 (50.7%) were classified as MRI+ according to the newly proposed definition versus 386/657 (58.8%) using the existing definition. A numerically higher proportion of newly proposed definition MRI+ patients achieved ASAS40 at Wk48 versus those fulfilling the existing MRI+ definition; patients in the discordant group (18/358 [5.0%] among r-axSpA, 35/299 [11.7%] among nr-axSpA) responded similarly to those originally classified as MRI- (Fig. 1). Similar results were observed for mean BASDAI and ASDAS CfB (Fig. 2).

Conclusions. Application of the preliminary MRI definition needs to be evaluated in future clinical trials to confirm its translation into fewer false-positive recruited patients.

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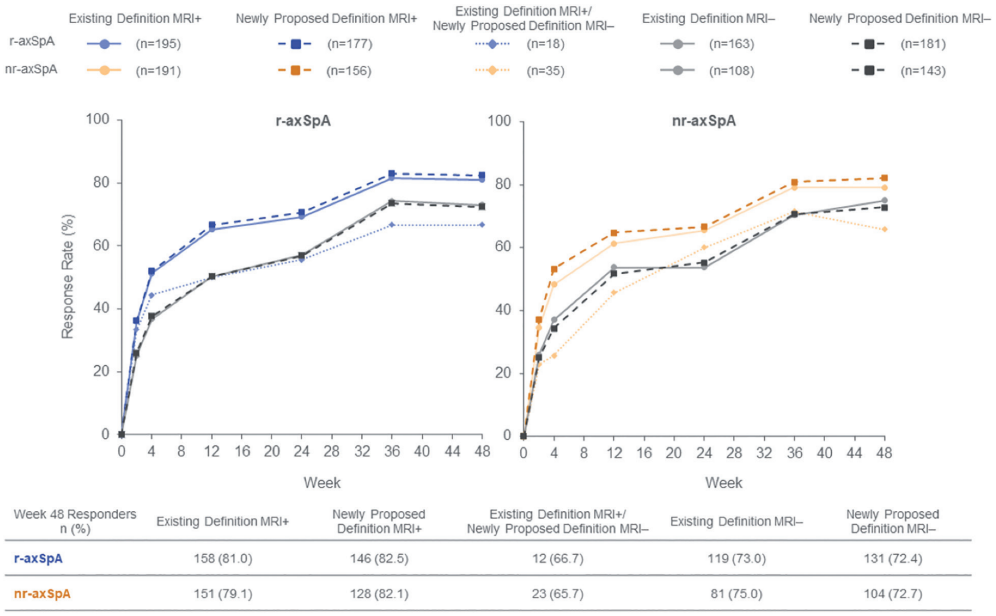
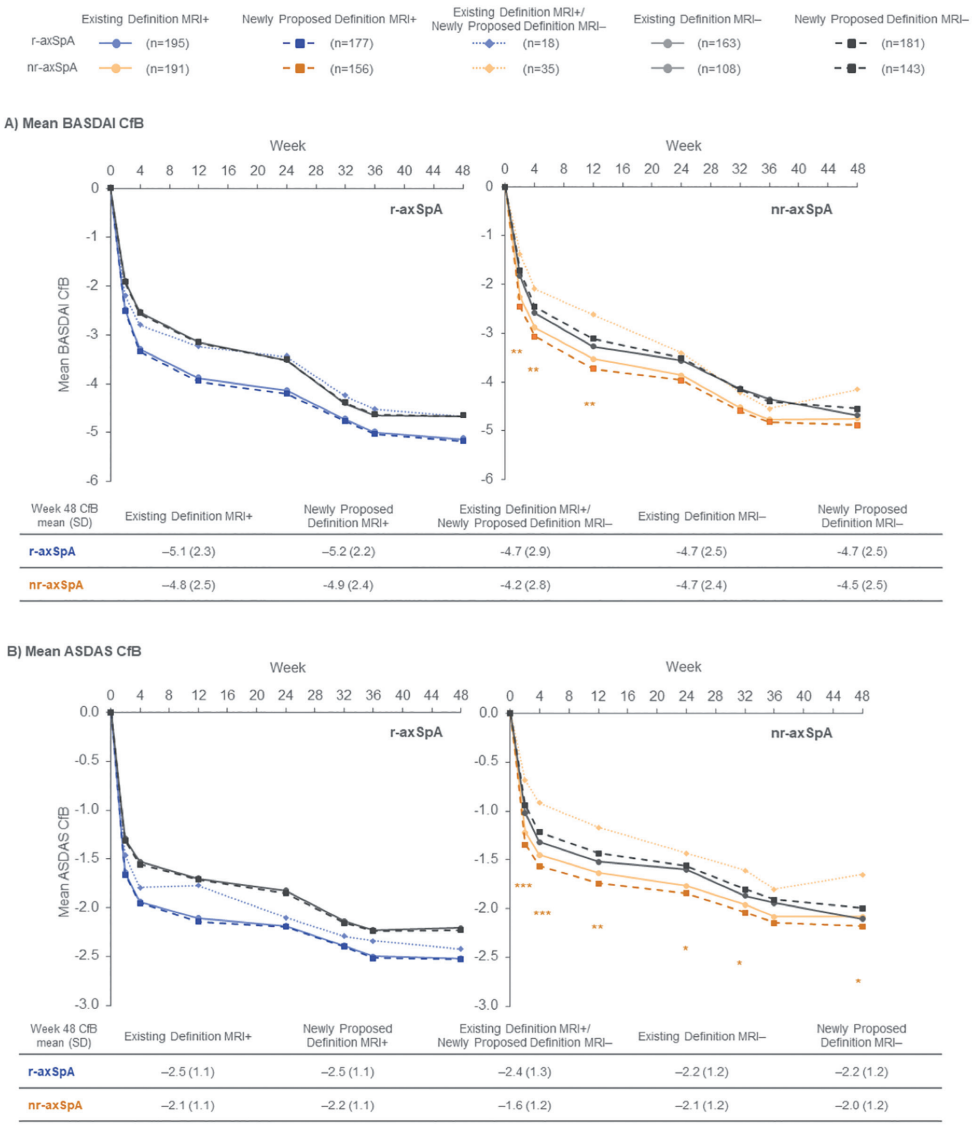


Week 48 Responders n (%)	Existing Definition MRI+	Newly Proposed Definition MRI+	Existing Definition MRI+/ Newly Proposed Definition MRI–	Existing Definition MRI–	Newly Proposed Definition MRI–
r-axSpA	158 (81.0)	146 (82.5)	12 (66.7)	119 (73.0)	131 (72.4)
nr-axSpA	151 (79.1)	128 (82.1)	23 (65.7)	81 (75.0)	104 (72.7)

P6. Fig. 1. Proportion of patients achieving ASAS40 stratified by both existing, and newly proposed, ASAS SIJ MRI definitions.
Missing data imputed using non-responder imputation.
ASAS40: Assessment of Spondyloarthritis international Society ≥40% improvement; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; r-axSpA: radiographic axial spondylo-arthritis.



Week 48 CfB mean (SD)	Existing Definition MRI+	Newly Proposed Definition MRI+	Existing Definition MRI+/ Newly Proposed Definition MRI–	Existing Definition MRI–	Newly Proposed Definition MRI–
r-axSpA	–5.1 (2.3)	–5.2 (2.2)	-4.7 (2.9)	-4.7 (2.5)	-4.7 (2.5)
nr-axSpA	–4.8 (2.5)	-4.9 (2.4)	-4.2 (2.8)	-4.7 (2.4)	-4.5 (2.5)

Week 48 CfB mean (SD)	Existing Definition MRI+	Newly Proposed Definition MRI+	Existing Definition MRI+/ Newly Proposed Definition MRI–	Existing Definition MRI–	Newly Proposed Definition MRI–
r-axSpA	–2.5 (1.1)	–2.5 (1.1)	–2.4 (1.3)	–2.2 (1.2)	–2.2 (1.2)
nr-axSpA	–2.1 (1.1)	–2.2 (1.1)	–1.6 (1.2)	–2.1 (1.2)	–2.0 (1.2)

P6. Fig. 2. Change from baseline in mean (**A**) BASDAI and (**B**) ASDAS scores stratified by both existing, and newly proposed, ASAS SIJ MRI definitions
Missing data imputed using last observation carried forward. †One sample t-tests were performed to identify significant differences between Existing Definition MRI+/New Definition MRI– and Existing New Definition MRI+ patients.
*$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$.
ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CfB: change from baseline; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; r-axSpA: radiographic axial spondyloarthritis; SD: standard deviation.

P7

BIMEKIZUMAB IN BDMARD-NAIVE PATIENTS WITH PSORIATIC ARTHRITIS: INTERIM ANALYSIS OF INHIBITION OF RADIOGRAPHIC STRUCTURAL PROGRESSION AT 16 WEEKS OF TREATMENT IN BE OPTIMAL, A PHASE 3, MULTICENTRE, RANDOMISED, PLACEBO-CONTROLLED, ACTIVE REFERENCE STUDY

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Introduction. Bimekizumab (BKZ) is a monoclonal antibody that selectively inhibits IL-17F in addition to IL-17A. This interim analysis assessed radiographic progression after 16 weeks (wks) BKZ treatment compared with placebo (PBO) in the phase 3 BE OPTIMAL study.

Methods. BE OPTIMAL (NCT03895203) comprises a 16-wk double-blind, PBO-controlled period, followed by 36 weeks treatment-blind. Randomisation was 3:2:1 to receive subcutaneous BKZ 160 mg every four weeks (Q4W), PBO, or subcutaneous adalimumab (ADA) 40 mg Q2W (reference arm for standard of care over the whole study). Patients were ≥18 years, biologic DMARD-naive, with adult-onset, active PsA involving ≥3 tender and ≥3 swollen joints. Radiographic outcomes at Wk16 included the van der Heijde-modified Total Sharp Score (vdHmTSS, 0–528), vdH Joint Narrowing sub-score and vdH Erosion sub-score. Radiographs were read centrally and independently by two readers blind to treatment and image time course; outcomes reported for overall radiographic set (RAD) and a subpopulation potentially at higher risk of progression (At Risk [AR]; hs-CRP levels ≥6 mg/L and/or ≥1 bone erosion at baseline).
Results. Of 852 randomised patients (Table), 808 (BKZ:416, PBO:261, ADA:131) were included in the RAD. The mean change from baseline (CfB) in vdHmTSS was significantly lower in BKZ-treated patients in the RAD (both overall and AR) compared with PBO (overall: p=0.001; AR: p<0.001; Fig. 1A). Overall 85.3% of BKZ-treated patients (AR: 84.3%) experienced no radiographic joint damage progression (vdHmTSS ≤0.5, non-responder imputation), compared with 80.1% (AR: 78.3%) for PBO. Of ADA-treated patients, 80.2% (AR: 81.5%) experienced no progression. CfB in VdH Joint Narrowing and Erosion sub-scores in BKZ-treated patients were numerically smaller than PBO (Fig. 1B-C).
Conclusions. Treatment with BKZ 160 mg Q4W demonstrated inhibition of radiographic progression at Wk16, compared with PBO. BKZ showed numerically lower progression of joint narrowing and erosion compared with PBO.

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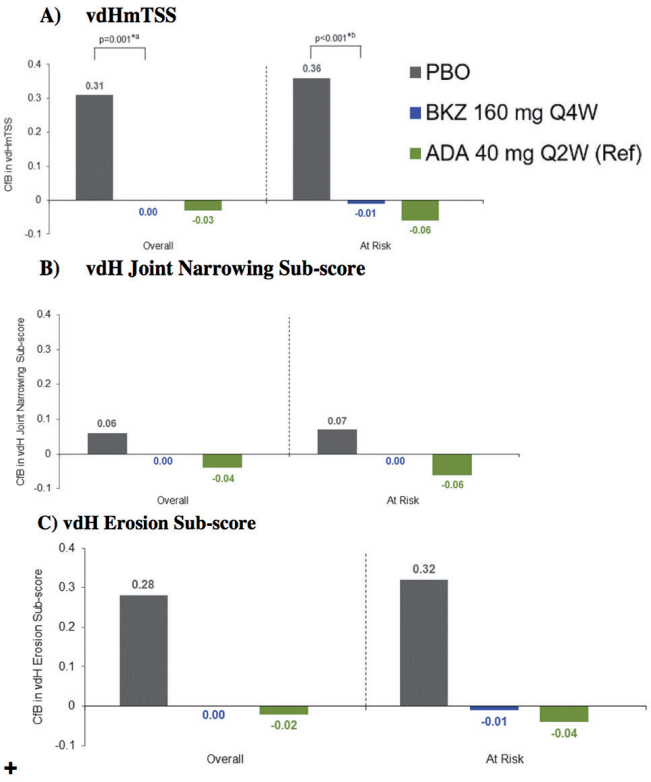

P7. Fig. 1. Mean change from baseline in efficacy endpoints to Week 16, radiographic set (MI).
*Nominal p value, not powered or adjusted for multiplicity. ANCOVA with reference-based MI to compare differences in least squares means. [a]Difference versus placebo = –0.282 (95% CI: –0.453, –0.111). [b]Difference versus placebo = –0.335 (95% CI: –0.533, –0.137). Figures depict both the radiographic (overall) set and at risk subpopulation. Radiographic set consists of patients in the randomised set with valid radiographic imaging of hands and feet at screening. At risk subpopulation includes patients in the radiographic set with hs-CRP ≥6 mg/L and/or ≥1 bone erosion at baseline. The ADA 40 mg Q2W treatment arm served as an active reference. The study was not powered for statistical comparisons of ADA to BKZ or PBO. ADA: adalimumab; ANCOVA: Analysis of Covariance; BKZ: bimekizumab; CfB: change from baseline; MI: multiple imputation; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks; Ref: reference arm; vdHmTSS: van der Heijde modified Total Sharp Score.

P7. Table. Baseline demographics and patient characteristics in BE OPTIMAL.

	Radiographic Set (RAD)			At Risk Subpopulation (AR)		
	Placebo N=261	BKZ 160 mg Q4W N=416	ADA 40 mg Q2W (Ref) N=131	Placebo N=221	BKZ 160 mg Q4W N=357	ADA 40 mg Q2W (Ref) N=108
Age, years, mean (SD)	48.9 (11.9)	48.7 (12.4)	48.9 (13.1)	50.5 (11.8)	49.5 (12.3)	50.4 (13.2)
Sex, male, n (%)	121 (46.4)	194 (46.6)	66 (50.4)	107 (48.4)	177 (49.6)	56 (51.9)
BMI, kg/m^2, mean (SD)	29.7 (6.1)	29.3 (6.8)	28.5 (6.0)	30.0 (6.2)	29.6 (6.8)	28.5 (6.1)
Time since first diagnosis of PsA, years,[a] mean (SD)	5.6 (6.5)	6.0 (7.3)	6.1 (6.8)	–	–	–
TJC, mean (SD)	16.8 (12.5)	16.7 (11.8)	17.2 (12.8)	16.9 (12.5)	16.9 (11.6)	17.2 (13.1)
SJC, mean (SD)	9.3 (7.2)	8.9 (6.2)	9.4 (6.8)	9.6 (7.5)	9.1 (6.4)	9.3 (7.0)
hs-CRP ≥6 mg/L, n (%)	115 (44.1)	154 (37.0)	41 (31.3)	115 (52.0)	154 (43.1)	41 (38.0)
At risk subpopulation: Bone erosion ≥1 and/or hs-CRP ≥6 mg/L, n (%)	221 (84.7)	357 (85.8)	108 (82.4)	221 (100)	357 (100)	108 (100)
vdHmTSS						
Mean (SD)	13.3 (25.2)	13.4 (30.1)	14.5 (27.9)	15.7 (26.8)	15.6 (32.0)	17.4 (30.0)
BL score >0, n (%)	216 (82.8)	361 (86.8)	111 (84.7)	209 (94.6)	345 (96.6)	104 (96.3)
Mean score (SD) in patients with score >0	16.1 (26.9)	15.5 (31.8)	17.2 (29.6)	16.6 (27.3)	16.1 (32.4)	18.1 (30.4)
vdH Joint Narrowing sub-score						
Mean (SD)	7.6 (14.4)	7.8 (15.9)	8.7 (16.8)	8.9 (15.3)	9.0 (16.9)	10.3 (18.1)
BL score >0, n (%)	168 (64.4)	276 (66.3)	95 (72.5)	161 (72.9)	260 (72.8)	88 (81.5)
Mean (SD) in patients with score >0	11.8 (16.5)	11.7 (18.3)	12.1 (18.8)	12.2 (16.7)	12.3 (18.7)	12.7 (19.3)
vdH Erosion sub-score, mean (SD)	5.7 (12.0)	5.7 (15.1)	5.7 (11.5)	6.7 (12.7)	6.6 (16.1)	7.0 (12.3)
Number of bone erosions						
Bone erosions ≥1, n (%)	204 (78.2)	337 (81.0)	101 (77.1)	204 (92.3)	337 (94.4)	101 (93.5)
Mean number of erosions (SD) in patients with ≥1 erosion	7.3 (13.1)	7.0 (16.5)	7.4 (12.6)	7.3 (13.1)	7.0 (16.5)	7.4 (12.6)

[a]Safety set (all patients who received at least one dose of the IMP whether PBO, BKZ or ADA), PBO n=279, BKZ 160 mg Q4W n=423, ADA 40 mg Q2W n=139). Randomisation was stratified by geographic region and presence of bone erosions. Actual stratum is used for analysis. RAD set consists of patients in the randomised set with valid radiographic imaging of hands and feet at screening. Patients in RAD except where otherwise specified. ADA: adalimumab; AR: At Risk subpopulation; BL: baseline; BMI: body mass index; BKZ: bimekizumab; hs-CRP: high-sensitivity C-reactive protein; IMP: investigational medicinal product; PsA: psoriatic arthritis; Q2W: every 2 weeks; Q4W: every 4 weeks; RAD: radiographic set; SD: standard deviation; SJC: swollen joint count; TJC: tender joint count; vdHmTSS: van der Heijde modified Total Sharp Score.

P8

BIMEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AN INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS: 16-WEEK EFFICACY & SAFETY FROM BE COMPLETE, A PHASE 3, MULTICENTRE, RANDOMISED PLACEBO-CONTROLLED STUDY

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Introduction. Assess the efficacy and safety of bimekizumab, a monoclonal IgG1 antibody that selectively inhibits IL-17F and IL-17A, versus placebo in patients with active PsA and prior inadequate tumour necrosis factor inhibitor (TNFi) response in the phase 3 study, BE COMPLETE.

Methods. BE COMPLETE (NCT03896581) comprises a 16-wk double-blind, placebo-controlled period. Patients were ≥18 years, had adult-onset, active PsA, ≥3 tender and ≥3 swollen joints, and inadequate response/intolerance to 1–2 TNFi. Patients were randomised 2:1, subcutaneous bimekizumab 160mg Q4W: placebo. From Wk16, patients were eligible to enter an OLE, receiving subcutaneous bimekizumab 160mg Q4W. Primary endpoint: ACR50 at Wk16. Efficacy endpoints were assessed at Wk16.

Results. 388/400 (97.0%) randomised patients completed Wk16 (bimekizumab: 263/267 [98.5%]; placebo: 125/133 [94.0%]). Baseline characteristics were comparable between groups: mean age 50.5 years, BMI 29.8 kg/m^2, time since diagnosis 9.5 years; 47.5% male. The primary endpoint (ACR50: 43.4% bimekizumab versus 6.8% placebo; $p<0.001$; Figure) and all ranked secondary endpoints were met (Table). Additional outcomes, including ACR20/70, TJC/SJC CfB, and PASI75/100, demonstrated improvement with bimekizumab compared with placebo (Table). 107/267 (40.1%) patients on bimekizumab had ≥1 TEAE versus 44/132 (33.3%) patients on placebo; the three most frequent TEAEs on bimekizumab were nasopharyngitis (bimekizumab: 3.7%; placebo: 0.8%), oral candidiasis (bimekizumab: 2.6%; placebo: 0%) and upper respiratory tract infection (bimekizumab: 2.2%; placebo: 1.5%). Incidence of SAEs was low (bimekizumab: 1.9%; placebo: 0%); none led to discontinuation. Two patients discontinued due to a TEAE (bimekizumab: 0.7%; placebo: 0%). No systemic candidiasis, IBD, MACE, uveitis, VTE or deaths were reported.

Conclusions. Dual inhibition of IL-17A and IL-17F with bimekizumab in patients with active PsA and prior inadequate TNFi response resulted in clinically relevant and statistically significant improvements in efficacy outcomes versus placebo. No new safety signals were observed.

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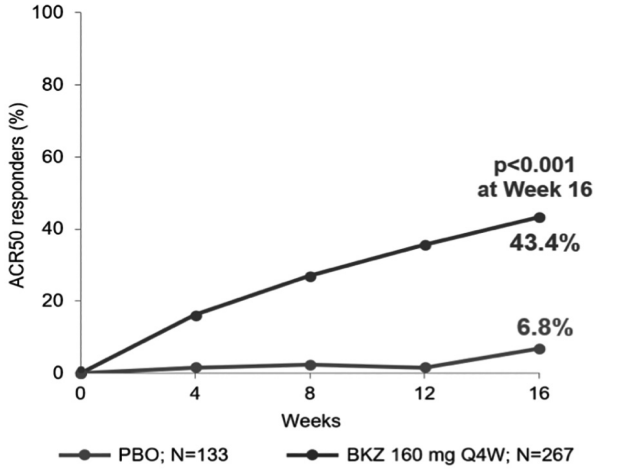

P8. Fig. 1. ACR50 responder rate over time to Week 16.
Randomised set (N=400). Data reported as NRI. p value nominal, not powered or adjusted for multiplicity. ACR50: ≥50 improvement in American College of Rheumatology criteria; BKZ: bimekizumab; PBO: placebo.

P8. Table. Disease characteristics at baseline and efficacy at Week 16.

		PBO N=133	BKZ 160 mg Q4W N=267	*p* value
Baseline characteristics	**TJC**, mean (SD)	19.3 (14.2)	18.4 (13.5)	-
	SJC, mean (SD)	10.3 (8.2)	9.7 (7.5)	-
	PtGA-PsA, mean (SD)	63.0 (22.0)	60.5 (22.5)	-
	PtAAP, mean (SD)	61.7 (24.6)	58.3 (24.2)	-
	Psoriasis BSA, n (%)			
	<3%	45 (33.8)	91 (34.1)	-
	≥3 to ≤10%	63 (47.4)	109 (40.8)	-
	>10%	25 (18.8)	67 (25.1)	-
	PASI[a], mean (SD)	8.5 (6.6)[b]	10.1 (9.1)[c]	-
	Prior TNFi, n (%)			
	Inadequate response to 1 TNFi	103 (77.4)	204 (76.4)	-
	Inadequate response to 2 TNFi	15 (11.3)	29 (10.9)	-
	Intolerance to TNFi	15 (11.3)	34 (12.7)	-
	Current cDMARDs, n (%)	63 (47.4)	139 (52.1)	-
Ranked endpoints in hierarchical order	**ACR50*** [NRI], n (%)	9 (6.8)	116 (43.4)	<0.001
	HAQ-DI CfB† [RBMI] mean (SE)	–0.1 (0.0)	–0.4 (0.0)	<0.001
	PASI90†[a] [NRI], n (%)	6 (6.8)[b]	121 (68.8)[c]	<0.001
	SF-36 PCS CfB† [RBMI], mean (SE)	1.4 (0.7)	7.3 (0.5)	<0.001
	MDA Response† [NRI], n (%)	8 (6.0)	118 (44.2)	<0.001
Other endpoints	**ACR20**† [NRI], n (%)	21 (15.8)	179 (67.0)	<0.001‡
	ACR70† [NRI] n (%)	1 (0.8)	71 (26.6)	<0.001‡
	TJC CfB [MI] mean (SE)	–2.4 (0.9)	–10.9 (0.8)	<0.001‡
	SJC CfB [MI] mean (SE)	–2.0 (0.5)	–7.0 (0.4)	<0.001‡
	PASI75[a] [NRI] n (%)	9 (10.2)[b]	145 (82.4)[c]	<0.001‡
	PASI100[a] [NRI] n (%)	4 (4.5)[b]	103 (58.5)[c]	<0.001‡

Randomised set (N=400). *Primary endpoint; †Secondary endpoint; ‡Nominal p-value, not powered or adjusted for multiplicity. [a]In patients with ≥3% BSA with PSO at BL; [b]n=88; [c]n=176. ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology criteria; BKZ: bimekizumab; BL: baseline; BSA: body surface area; cDMARD: conventional disease-modifying antirheumatic drug; CfB: change from baseline; HAQ-DI: health assessment questionnaire disability index; MI: multiple imputation; NRI: non responder imputation; PASI: psoriasis area and severity index; PASI75/90/100: ≥75/90/100% improvement in PASI; PBO: placebo; PtAAP: patient's assessment of arthritis pain; PtGA-PsA: patient's global assessment of psoriatic arthritis; Q4W: every 4 weeks; RBMI: reference-based multiple imputation; SD: standard deviation; SE: standard error; SF-36 PCS: 36-item short form survey Physical Component Summary; SJC: swollen joint count; TJC: tender joint count; TNFi: tumour necrosis factor inhibitor.

and UCB Pharma; **RL** has received consultancy fees from Abbott, Ablynx, Amgen, AstraZeneca, Bristol-Myers Squibb, Centocor, GSK, Novartis, Merck, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth; Research grants from Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth; Speaker's bureau from Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth; **AA** has received honoraria and/or research grants from AbbVie, Amgen, Eisai, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Maruho, Mitsubishi Tanabe Pharma, Pfizer, Sun Pharma, Taiho Pharma, Torii Pharmaceutical, and UCB Pharma; **YT** is a member of the speakers' bureaus for AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer-Ingelheim, Chugai, Eisai, Eli Lilly, Gilead, Mitsubishi-Tanabe, YL Biologics; Research Grants for Asahi-Kasei, AbbVie, Chugai, Mitsubishi-Tanabe, Eisai, Takeda, Corrona, Daiichi-Sankyo, Kowa, Boehringer-Ingelheim, and Consultant fee for Eli Lilly, Daiichi-Sankyo, Taisho, Ayumi, Sanofi, GSK, AbbVie; **RBW** has received consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; research grants to his institution from AbbVie, Almirall, Janssen, LEO Pharma, Novartis, and UCB Pharma; honoraria from Astellas, DiCE, GSK, and Union; **LG** has received research grants from Amgen, Galapagos, Lilly, Pfizer, Sandoz; consulting fees: AbbVie, Amgen, Bristol-Myers Squibb, Galapagos, Gilead, GSK, Janssen, Lilly, Novartis, Pfizer, Samsung Bioepis, Sanofi-Aventis, UCB Pharma; **DDG** has received grants from AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer and UCB Pharma; Consulting fees from AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer and UCB Pharma; **FB** has been a consultant for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Chugai, Eli Lilly, Galapagos, Genzyme, GSK, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi and UCB Pharma; **BI** is an employee of UCB Pharma and a shareholder of GSK and UCB Pharma; **DA, RB, JC** are all employees and stockholders of UCB Pharma; **LCC** has received grants/research support from AbbVie, Amgen, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer and UCB Pharma; worked as a paid consultant for AbbVie, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Domain, Eli Lilly, Gilead, Galapagos, Janssen, Moonlake, Novartis, Pfizer and UCB Pharma; and has been paid as a speaker for AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Medac, Novartis, Pfizer and UCB Pharma.

P9

THE IMPACT OF MRI SLICE THICKNESS ON THE DETECTION OF SPINAL SYNDESMOPHYTES IN AXIAL SPONDYLOARTHRITIS

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Introduction. Conventional radiographs (CR) are the gold standard for detecting syndesmophytes in axSpA, mainly because magnetic resonance imaging (MRI) is not able to detect thin bony structures due to its slicing technique. We assessed the ability and performance of detection of syndesmophytes using different MRI slice thicknesses and compare them with CR.
Methods. MRI (T1W and STIR) with slice thicknesses of 1-6mm and CR of the lower thoracic and lumbar spine were prospectively performed in 43 axSpA patients. Each vertebral corner (VC) from the thoracic (Th11) to the lumbar (L5) vertebral body were assessed for the presence/absence of syndesmophytes but also fat lesion (FL) on MRI by two readers.
Results. A total of 1.204 VCs was assessed from all patients. Syndesmophytes were detected in 19.3% VCs on CR and in 38.3%, 37.5%, 34.8%, 33.7%, 31.4%, 28.7% VCs on MRI slice thicknesses of 1-6mm, respectively ($p \leq 0.001$ for all MRI vs. CR and within MRI slice thicknesses). The anterior superior VC of L1 was the most affected site among all VCs in all MRI slice thicknesses and CRs. In thoracic spine, the anterior superior corner of T12 was the most frequently affected site in both MRI and CR. Although MRI could detect more syndesmophytes than CR, MRI at any slice thickness could not detect 15.4%-23.2% of syndesmophytes detected in CR (Table). FLs were detected in 38.3%, 37.5%, 34.8%, 33.7%, 31.4%, 28.7% of VC with MRI slice thicknesses of 1-6mm, respectively. MRI slice thickness had no role in detecting FLs ($p > 0.05$ within MRI slice thicknesses).

P9. Table Agreement and disagreement of CR and MRI for syndesmophyte detection per MRI slice thickness.

		CR		Agreement CR/MRI	False positive MR based on CR as gold standard
MRI		yes	no		
1mm	yes	182	279	72,6%	23,2%
	no	51	692		
2mm	yes	184	267	73,8%	22,2%
	no	49	704		
3mm	yes	181	238	75,9%	19,8%
	no	52	733		
4mm	yes	175	231	76,0%	19,2%
	no	58	740		
5mm	yes	169	209	77,3%	17,4%
	no	64	762		
6mm	yes	160	186	78,5%	15,4%
	no	73	785		

Conclusions. MRI at any slice thickness detected more syndesmophytes than CR, but the best agreement and least false-positive findings on MRI based on CR as gold standard was found in the thicker slice thicknesses. These results may influence the performance of MRI in identification of SpA specific spinal lesions in daily practice.

P10

PAIN RESPONSE IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH GUSELKUMAB IS DRIVEN PREDOMINANTLY BY INFLAMMATION-INDEPENDENT EFFECTS

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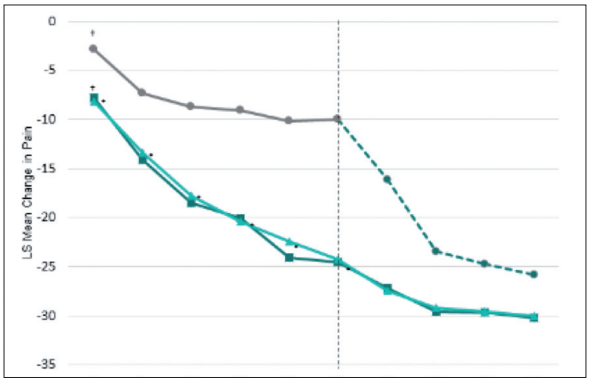
Introduction. Although reducing inflammation has been associated with pain improvement, the two do not always correlate. Using mediation modelling, we quantified the role of reducing inflammation on the observed relationship between guselkumab (GUS, a selective IL-23 inhibitor) and pain response in PsA patients from DISCOVER-1&2 trials.
Methods. Pooled data from DISCOVER-1 (≥3 swollen and ≥3 tender joints [SJC/TJC]; CRP≥0.3mg/dL; 31% patients received 1-2 prior TNFi) and DISCOVER-2 (≥5 SJC and ≥5 TJC; CRP≥0.6mg/dL; bio-naive) were analyzed. Patients were randomized 1:1:1 to GUS-100mg every-4-weeks (Q4W); GUS-100mg at W0/W4, then Q8W; or placebo with crossover to GUS-100mg Q4W at W24. Least-squares mean changes in patient-reported pain through W52 was estimated with a repeated measures linear mixed model adjusting for known pain determinants. Mediation modelling was performed separately for Q4W/Q8W, W4/W24, and TNFi-naive/TNFi-experienced patients (Table).
Results. Baseline pain levels are shown in Figure (footnotes). GUS treatment induced significantly greater pain improvement versus placebo as early as W4 ($\Delta_{Q4W\text{-}PBO}$ [95%CI]: -4.9 [-7.6, -2.2]; $\Delta_{Q8W\text{-}PBO}$ [95%CI]: -5.2 [-7.9, -2.5]) (Figure), which were further enhanced by W24 ($\Delta_{Q4W\text{-}PBO}$ [95%CI]: -14.6 [-17.6, -11.5]; $\Delta_{Q8W\text{-}PBO}$ [95%CI]: -14.3 [-17.3, -11.2]) and W52 (approximate 30-point [~50%] decrease in pain). The majority of GUS effect on pain at W4 was not attributable to SJC (direct effect); specifically, ≤6% (W4)/≤10% (W24) was mediated by inflammation assessed by changes in SJC (indirect effect; Table). Results were consistent when using CRP as the mediator variable (Table). All findings were similar for TNFi-naive/TNFi-experienced patients.



P10. Fig. 1. LS mean changes in patient-reported pain over time by treatment group - Pooled DISCOVER-1 and DISCOVER-2 patients.
*p<0.0001. †Mean (SD) BL pain scores were; Q4W=80.4 (19.8), Q8W=62.0 (20.2), PBO=81.1 (19.8).
▲p-values comparing GUS with PBO from linear mixed effects model for repeated measures adjusting for treatment (Q4W, Q8W, PBO), age, sex, BL pain, BMI, BL SF-36 MCS, BL NSAID use, and treatment by time interaction. No multiplicity adjustment has been applied.
■ Vertical dotted line represents time of patient crossover from PBO to GUS.
BL: baseline; BMI: body mass index, GUS: guselkumab; LS: least-squares; NSAID: nonsteroidal anti-inflammatory drug; PBO: placebo; Q4W: every 4 weeks; Q8W: every 8 weeks; SD: standard deviation; SF-36 WCS: Short form 36 mental component summary.

P10. Table. Direct (D) treatment effect vs. indirect (IND) effect via inflammation markers on pain improvement.

Mediator	Week	Patient group	Effect	GUS Q4W	GUS Q8W
SJC	4	All	D	96.7%*	97.0%*
			IND†	3.3%	3%
		TNFi-naive	D	93.7%*	98.5%*
			IND†	6.3%	1.5%
		TNFi-Exp	D	100%*	100%*
			IND†	0%	0%
	24	All	D	94.8%*	92.0%*
			IND†	5.2%*	8.0%*
		TNFi-naive	D	89.6%*	90.1%*
			IND†	10.4%*	9.9%*
		TNFi-Exp	D	99.8%*	95.7%*
			IND†	0.2%	4.3%
CRP	4	All	D	97.6%*	95.0%*
			IND‡	2.4%	5.0%
		TNFi-naive	D	98.2%*	95.4%*
			IND‡	1.8%	4.6%
		TNFi-Exp	D	97.6%*	95.3%*
			IND‡	2.4%	4.7%
	24	All	D	97.2%*	94.2%*
			IND‡	2.8%	5.8%*
		TNFi-naive	D	98.1%*	95.9%*
			IND‡	1.9%	4.1%
		TNFi-Exp	D	96.5%*	91.4%*
			IND‡	3.5%	8.6%

*p<0.05; †via SJC; ‡via CRP
Mediation modelling: In each model, change in patient-reported pain: dependent variable; treatment regimen: independent variable; inflammation (measured by change in SJC or CRP): designated mediator; covariates: age, sex, baseline pain score, BMI, SF-36 MCS score, and NSAID use.
BMI: body mass index; CRP: C-reactive protein; Exp: experienced; GUS: guselkumab; NSAID: nonsteroidal anti-inflammatory drug; Q4W: every 4 weeks; Q8W: every 8 weeks; SF-36 MCS: Short Form 36 Mental Component Summary; SJC: swollen joint count; TNFi: tumor necrosis factor inhibitor.

Conclusions. GUS induced significant improvement in patient-reported pain as early as W4 of treatment, which was continuously enhanced through W52. While the known mediation effect of SJC and CRP, as markers of inflammation, on pain was confirmed, the majority of GUS's effect on pain reduction was independent of its effect on these markers, regardless of dosing regimen or prior TNFi experience.

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P11

GENETIC AND MOLECULAR DISTINCTIONS BETWEEN AXIAL PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS

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Introduction. Despite overlapping symptoms, axial psoriatic arthritis (axPsA) and ankylosing spondylitis (AS) may be distinct disorders with differing clinical manifestations, genetic associations, and radiographic findings. A better understanding of molecular distinctions between axPsA and AS is needed to differentiate these diseases and guide treatment choice.
Methods. Patient whole blood/serum samples were collected in studies of guselkumab in PsA (NCT03162796/NCT0315828) and ustekinumab in AS (NCT02437162/NCT02438787). Human leukocyte antigen (HLA) genotypes were determined by RNA sequencing, limited to Caucasians to reduce genetic variability, and serum cytokine levels were analyzed. Differential prevalence of HLA alleles in axPsA versus AS was determined. Statistical significance of differential baseline serum cytokine expression among axPsA/non-axPsA/AS patients, and of guselkumab effect on serum cytokine reduction versus placebo among axPsA/non-axPsA patients were determined.
Results. Among 186/234 Caucasian axPsA/AS patients, 34%/15% were female, 70%/14% used methotrexate at baseline, mean serum CRP levels were 2.8/2.4mg/dL and mean BASDAI scores were 6.4/7.5, respectively. The prevalence of class-I HLA alleles -B27, -C01, and -C02 carriers was significantly lower in axPsA than AS patients (30.7% versus 92.3%, 5.9% versus 31.6%, and 28.0% versus 62.0%, respectively [all p<0.001]), while HLA-C06 prevalence was significantly higher in axPsA (36.0%) than AS populations (8.6%, p<0.001). Baseline serum levels of IL-17A/IL-17F were significantly higher in axPsA (N=71) versus AS (N=58) patients (p<0.01/p<0.001, respectively). Comparable IL-17A/F expression was seen for axPsA and non-axPsA (N=229) patients (both p=non-significant). Significant and comparable reductions from baseline in serum IL-17A/F in axPsA and non-axPsA patients were seen with guselkumab (axPsA N=41, non-axPsA N=160) versus placebo (axPsA N=30, non-axPsA N=69) at Week4/24 (all p<0.05).
Conclusions. AxPsA and AS patients exhibit different genetic risk factors and serum IL-17 levels, supporting the concept of distinct disorders. Guselkumab demonstrated significant pharmacodynamic effects in axPsA patients that aligned with such effects in non-axPsA patients, consistent with observed clinical improvement.

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P12

RADIOGRAPHIC PROGRESSION FROM NON-RADIOGRAPHIC TO RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: RESULTS FROM A 5-YEAR MULTICOUNTRY PROSPECTIVE OBSERVATIONAL STUDY

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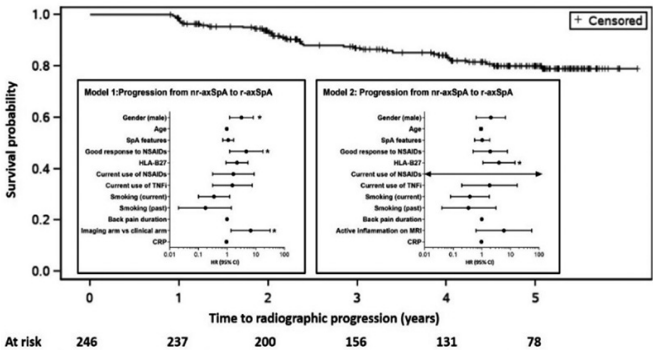
Objectives. Evaluate axial spondyloarthritis(axSpA) patient progression from non-radiographic axSpA(nr-axSpA) to radiographic axSpA(r-axSpA) over 5yrs.
Methods. Prospective, observational study, PROOF, enrolled adults with chronic back pain for ≥3mos and onset before age 45. Analysis included axSpA patients fulfilling Assessment of SpondyloArthritis international Society(ASAS) classification criteria. Baseline and follow-up radiographs of sacroiliac joints(SIJ) in nr-axSpA patients were evaluated independently by 2 central readers according to modified New York criteria. Radiographic progression from nr-axSpA to r-axSpA over 5yrs was evaluated by Kaplan-Meier analysis. Cox proportional hazards regression analyses(model 1=imaging arm vs clinical arm; model 2= active inflammation on magnetic resonance imaging highly suggestive of sacroiliitis associated with SpA) evaluated radiographic progression from nr-axSpA to r-axSpA. Potential predictive factors were age, gender, back pain duration, numbe r of SpA parameters, smoking, CRP, good response to NSAIDs, HLA-B27, and current use of NSAIDs and TNF inhibitors.
Results. 2165(82%)/2633 patients, with axSpA fulfilled ASAS criteria with 1612(74%) having r-axSpA(1050[65%]) or nr-axSpA(562[35%]) by central reading. Majority of nr-axSpA patients (77%) fulfilled ASAS criteria due to positive imaging findings(plus ≥1 SpA feature) and 23% were classified according to the clinical arm. Among 246 patients with ≥1 follow-up SIJ radiograph, progression from initial nr-axSpA to r-axSpA was observed in 40(16%) patients over 5yrs. Mean time to radiographic progression was 2.4yrs in descriptive analysis (Kaplan-Meier, Figure). In model 1 of Cox regression analysis, male gender(hazard ratio[HR]: 3.16[95% CI: 1.22–8.17]; p=0.0174), fulfilment of the imaging arm(HR: 6.64[1.37–32.25]; p=0.0188), and good NSAIDs response, (HR: 4.66[1.23–17.71]; p=0.0237), were significantly associated with progression to r-axSpA. In model 2, HLA-B27 positivity showed significant association with progression(HR: 3.99[1.10–14.49]; p=0.0353; Figure).



P12. Fig. 1. Time to Radiographic Progression and Cox Regression Analysis for Progression from to r-axSpA (inset).
Cox proportional hazards regression analyses were conducted for patients with initial nr-axSpA classification. The target variable was Time to radiographic progression from nr-axSpA to AS. In model 1, ''imaging arm vs clinical arm'' was included as an independent variable. In model 2, ''active inflammation on MRI highly suggestive of sacroiliitis associated with SpA'' was included as an independente variable. *Statistically significant p>0.05. HLA-B27, human leukocyte antigen B27; nr-axSpA. non-radiographic axial SpA; NSAIDs: nonsteroidal anti-inflammatory drugs; r-axSpA: radiographic axial SpA; SpA: spondyloarthritis; TNFI: tumor necrosis factor inhibitor.

Conclusions. Study showed 16% of nr-axSpA patients progressed to r-axSpA within 5yrs. Mean time to disease progression was 2.4yrs. Predictors of radiographic progression were male gender, good response to NSAIDs, fulfilment of the imaging arm, andHLA-B27 positivity.

Reference

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P13

IS RADIOGRAPHIC AXIAL INVOLVEMENT ASSOCIATED WITH SYNDESMOPHYTE DEVELOPMENT AFTER 2 YEARS IN PSA PATIENTS?

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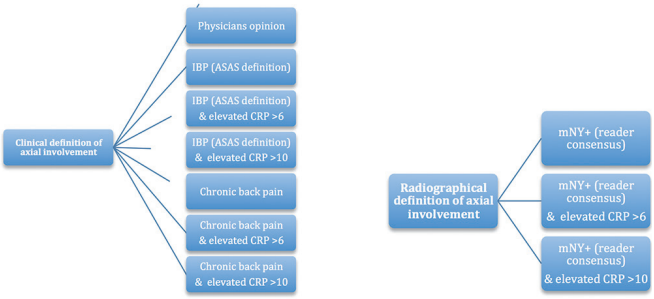
Background/objective. There is an ongoing debate on axial involvement in psoriatic arthritis (PsA). This study, using clinical and radiographical definitions of axial involvement, investigated the association between axial involvement and new syndesmophytes development over 2 years in patients with PsA.
Methods. Patients originated from the Belgian Epidemiological Psoriatic Arthritis Study (BEPAS), a prospective multicentre cohort involving 17 Belgian rheumatology practices. Recruitment was from December 2012 until July 2014. Patients were included when fulfilling the Classification criteria for Psoriatic Arthritis (CASPAR). Axial involvement included several definitions (see Figure 1).
The treating did the clinical work up. Two calibrated central readers evaluated radiographic damage by assessing the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) for the presence of syndesmophytes and assessed the modified New York criteria (mNY) for the presence of sacroiliitis. Readers assessed spinal and pelvic radiographs separately and were blinded for time sequence, clinical data, and information from other obtained images (radiographs of the hands and feet).
Generalized estimating equation models on vertebral unit level were used,taking into account that multiple corners belong to a single patient. All definitions of axial involvement were evaluated, only odds ratios (OR) with a p<0.05 were reported.
Results. In total 461 patients were included in BEPAS. Mean age was 52.79±12.29 years and 43.0% (n=198) were female; average disease duration was 8.5±9.3 years and approximately 34% of the patients reported inflammatory axial pain. From 150 patients 2 years follow-up of spinal radiographs were obtained. From the clinical definitions of axial involvement none were associated with the development of syndesmophytes in 2 years. Axial involvement was associated with syndesmophyte formation when defined as 'mNY+ reader consensus' (OR 3.72 (CI 1.06-13.06). Although few patients with PsA developed syndesmophytes after 2 years, conditional probability analysis suggests that those patients meeting the mNY criteria for axial involvement have a higher chance of developing syndesmophytes (Table I).



P13. Fig. 1. Different definitions of axial involvement in PsA patients from the Belgian Epidemiological Psoriatic Arthritis Study cohort.

P13. Table I. Conditional probability table for axial involvement defined as radiographic sacroiliitis (mNY+ reader consensus) and the development of syndesmophytes over 2 years follow-up.

mNY+ reader consensus	New syndesmophytes at 2 years	n	P (newSYND/axial involvement)
0	0	3446	P (newSYND/0) = 34/3480 = 0.0098
0	1	34	
1	0	116	P (newSYND/1) = 4/120 = 0.0333
1	1	4	

0=absent,1=present.

Conclusions. The likelihood of syndesmophyte formation in PsA is low and is more likely to be associated with axial involvement determined radiographically, particularly in the context of high CRP.

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P14

TISSUE TROPISM IN T CELL DEPENDENT REGULATORY PATHWAYS CONTROLLING TNF DRIVEN SPA-LIKE JOINT AND GUT PATHOLOGY

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Introduction. Combined gut and joint inflammation is a hallmark of SpA, which can represent a therapeutic challenge. It is therefore essential to better understand the immunobiology of common or private effector and regulatory pathways in intestine versus joints. We therefore sought to examine the role of two prototypic naturally occurring immunomodulatory T cell subsets, invariant Natural Killer T (iNKT) and $CD4^+CD25^+FOXP3^+$ regulatory T (Treg) cells, in steering gut and joint pathology in a preclinical TNF driven SpA model.
Methods. iNKT and Treg features in $TNF^{\Delta ARE}$ mice were investigated by flow cytometry and their functional role in $TNF^{\Delta ARE}$ pathology was evaluated using iNKT and/or Treg deficient strains. RNA-sequencing was performed on ileum and synovium tissues and FACSorted Tregs. Soluble TNFR2 (sTNFR2) levels were measured in serum of mice and SpA patients, along in situ hybridization of SpA gut samples.
Results. Whole-transcriptome analyses showed comparable upregulation of TNF in both inflamed synovium and ileum of $TNF^{\Delta ARE}$ mice. In contrast, other proinflammatory and TNF superfamily (TNFSF) mediators displayed a site-specific expression profile, with *Il6*, *Tnfsf9* (encoding 4-1BBL) and *Tnfsf12* (TWEAK) being upregulated in synovium while Il17a and Tnfsf10 (TRAIL) in ileum. Although both iNKT and Tregs accumulated in inflamed tissues of $TNF^{\Delta ARE}$ mice, we noted tissue restricted regulatory functions. Ileitis was suppressed by both iNKT and Tregs whereas joint inflammation was only affected by iNKTs. In line with these remarkable differences, synovial and intestinal Tregs displayed differential TNFSF receptor expression and signalling pathways. TNFR2 gene turnover was amplified in $TNF^{\Delta ARE}$ mice, along with an increase in serum sTNFR2 and TNFR2 shedding on ileal Tregs. Interestingly, this was mirrored in SpA patients presenting gut inflammation.
Conclusions. Our data highlight important differences in immune-regulatory networks in gut versus joint inflammation in SpA. Particularly, synovial Tregs seem functionally maladapted to a TNF altered immune microenvironment.

P15

IL-23 INDUCED GDF15 CONTRIBUTES TO TRABECULAR BONE LOSS, BUT DOES NOT AFFECT SKIN, GUT OR JOINT INFLAMMATION

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IL-23 mediated inflammatory diseases such as psoriasis and spondyloarthritis are associated with bone loss in addition to more classical features such as skin and joint inflammation. Inflammation-induced bone loss has long been assumed to be directly due to inflammatory cytokines, such as TNF or IL-17. Here, we provide evidence that inflammation-induced bone loss is mediated via the stress-induced cytokine, Growth Differentiation Factor 15 (GDF15). GDF15 is a well-known mediator of weight loss through aversion to food. It acts exclusively through a single receptor found in the hindbrain, GFRAL, which triggers systemic effects through activation of the sympathetic nervous system (Suriben *et al*. 2020. Nat Med).
We found serum GDF15 to be elevated in spondyloarthritis patients, especially those with co-morbid psoriasis. We used GDF15-EEV (Enhanced Episomal Vectors) to induce sustained, systemic overexpression of GDF15. GDF15 overexpression did not result in skin, gut or joint inflammation. As expected, GDF15 overexpression caused weight loss, however µCT revealed dose-dependent GDF15-induced trabecular bone loss (0.1293±0.0165 versus 0.0866±0.002404; $p<0.01$). Caloric restriction alone was not able to replicate GDF15-induced trabecular bone loss, suggesting the existence of a GDF15 mediated brain-bone axis.
IL-23 overexpression by EEV causes psoriatic-like inflammation in mice, coupled with bone and weight loss. We found serum GDF15 to be increased in mice with elevated IL-23 (control: 45.51±2.774; IL-23: 91±11.71 pg/ml, $p<0.01$). Both GDF15-KO and GFRAL-KO mice show a partial protection against IL-23 induced weight and bone loss, but had no protection against skin inflammation.
To conclude, systemic inflammation induces GDF15, which in turn mediates trabecular bone loss, but does not participate in inflammation severity.

P16

DEEP IMMUNE PROFILING OF CYTOTOXIC T CELLS (CTL) FROM PATIENTS WITH ANKYLOSING SPONDYLITIS REVEALED A SUBSET OF CTL CO-EXPRESSING PD-1 AND TIGIT THAT RESISTS IMMUNE EXHAUSTION

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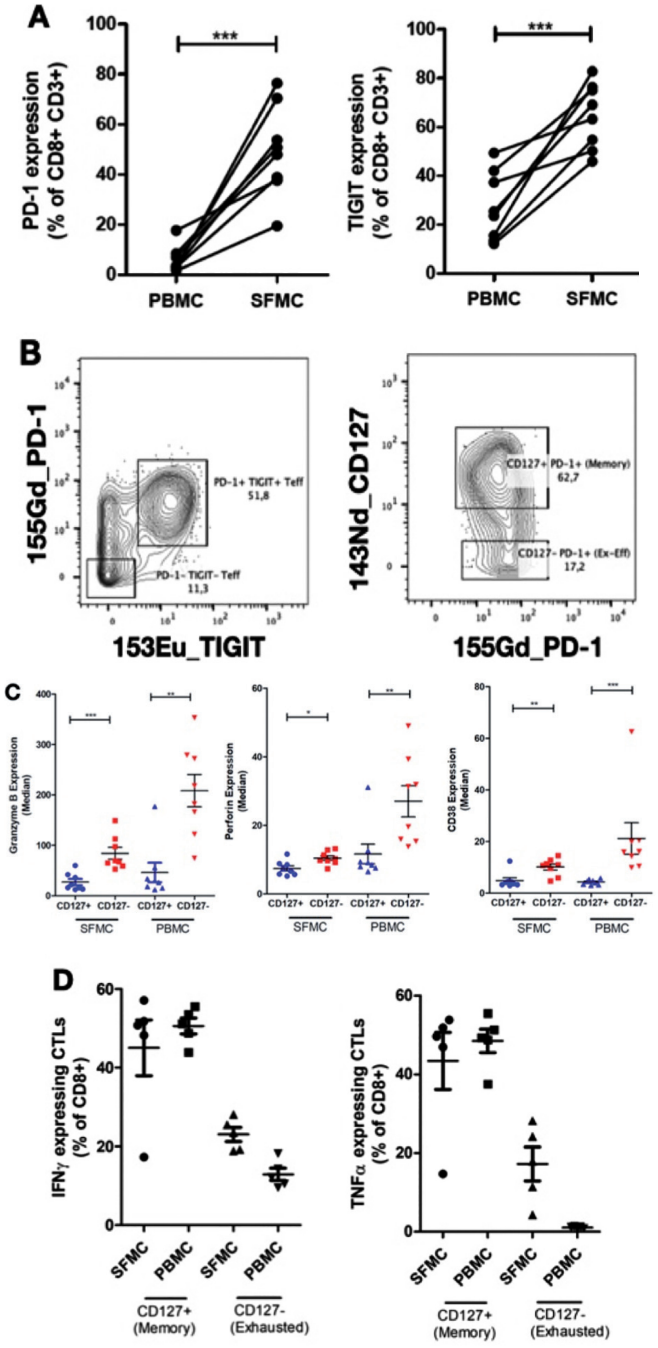
Introduction. Unresolved, chronic inflammation is a key feature of Ankylosing Spondylitis (AS) yet the immunological events perpetuating remain unclear. The strongest genetic association with AS is *HLA-B27*, a class I MHC allele, suggesting involvement of CTLs in AS pathogenesis. To date, the CTL compartment contributing to AS inflammation has not been fully defined. In the context of chronic inflammation, CTL exhaustion (often characterized by PD-1/TIGIT upregulation) represents a hyporesponsive state that limits excess effector function, which would otherwise cause inflammatory immunopathologies. Here, we sought to define how CTL dysregulation drives chronic inflammatory response in AS patients.
Methods. We performed extensive immunophenotyping of PBMCs and synovial fluid (SF) MCs, focusing on CTLs, using a 30+ parameter mass cytometry time-of-flight (CyTOF) panel. CTL in vitro functional assays were performed to assess cytotoxic functions.
Results. PD-1 and TIGIT expressions on CTLs are significantly lower (Mean = 17.2/25.5% of CD8 expressing PD-1/TIGIT respectively) in AS patients with active disease (BASDAI >5.0) compared to healthy controls (Mean = 27.1/43.4%). Contrarily, PD-1 and TIGIT were highly upregulated on CTLs from SF of AS patients, suggesting evidence of strong immune activation and possible immune exhaustion. Unsupervised clustering analysis of CyTOF data identified two subsets of CTLs that co-express PD-1 and TIGIT based on CD127 expression. The CD127- subset (terminally exhausted) from SF expressed higher levels of GZMB, perforin, and CD38

compared to CD127+ PD-1+ CTLs (memory-like). Contrary to the CD127- CTL subset from PBMC, which produced substantially less IFNγ and TNFα upon stimulation, the CD127- CTL subset from SF retained the capacity to produce both cytokines.

Conclusions. We report a subset of CTLs in SF of AS patients co-expressing classical exhaustion markers (PD-1 & TIGIT) with downregulated CD127 expression. These dysregulated CTLs are highly cytotoxic and potentially exacerbate chronic inflammation in AS.

Acknowledgements. Supported by The Arthritis Society of Canada (Strategic Operating Grant & Training Postdoctoral Fellowship).



P16. Fig. 1.

P17

VALIDATION OF THE SPARCC MRI-RETIC E-TOOL FOR INCREASING SCORING PROFICIENCY OF MRI LESIONS IN AXIAL SPONDYLOARTHRITIS

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Background. The web-based Spondyloarthritis Research Consortium of Canada (SPARCC) Real-Time Iterative Calibration (RETIC) inflammation and structural damage modules for scoring MRI lesions in axial spondyloarthritis (axSpA) have been created by SPARCC developers to enable remote training of readers to appropriately use the SPARCC MRI instruments and to attain adequate scoring proficiency.

Objectives. To test the performance of these modules in enhancing scoring proficiency in comparison to SPARCC developers.

Methods. The SPARCCRETIC sacroiliac joint (SIJ) modules are each comprised of 50 DICOM axSpA cases with baseline and follow up scans and an online interactive scoring interface based on SIJ quadrants. Participants (n=17) from the EuroSpA Imaging project were randomized, stratified by reader expertise in scoring with SPARCC, to one of two reader training strategies (groups A and B) that each comprised 3 stages (25 patients per stage, 2 timepoints, blinded to chronology; independent assessment of Inflammatory and structural lesions): Group A. 1. Review of original SPARCC manuscript describing scoring method. 2. Review of PowerPoint summary of SPARCC method plus completion of SPARCCRETIC module. 3. Re-review of PowerPoint summary. Group B. Same 3-step strategy as A except SPARCCRETIC module completed at stage 3. The reliability of scoring was compared to an expert radiologist (SPARCC developer).

Results. Very good scoring proficiency for status and change scores was evident for SPARCC BME even by non-experienced readers. The beneficial impact of the SPARCCRETIC modules on scoring proficiency was most consistently evident for the scoring of structural lesions and for Strategy B, where the impact was evident for all structural lesions, level of reader expertise, and status as well as change scores (Table). Scoring proficiency improved the most for the least experienced readers (Figure).

Conclusions. Attaining scoring proficiency for MRI structural lesions in axSpA can be consistently improved by using the SPARCCRETIC module, even for experienced readers.

P18

ELEVATED COMPLEMENT PROTEINS IN PATIENTS WITH AXSPA COMPARED WITH APPROPRIATE CONTROLS WITH LOW BACK PAIN WITH AND WITHOUT SPA-FEATURES

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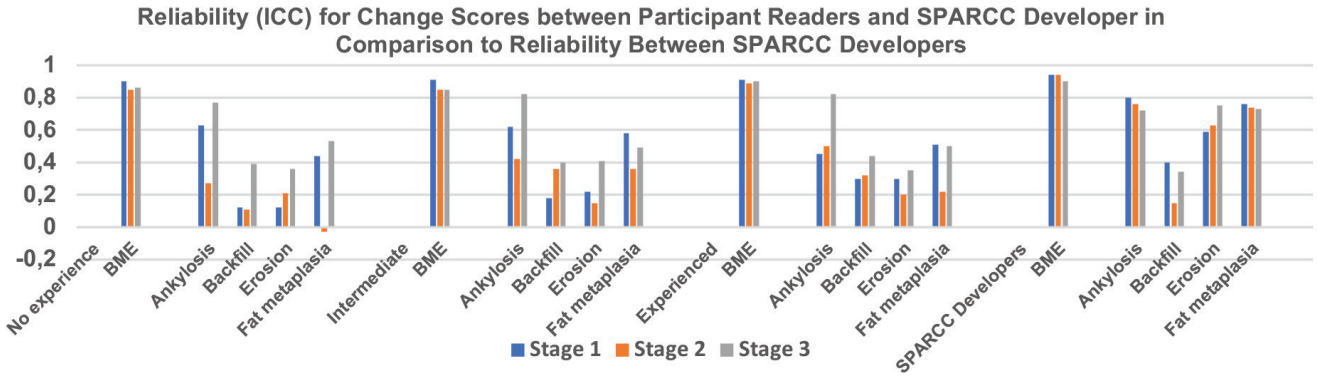
Introduction. The lectin pathway of complement activation is a vital component of the innate immune system and plays pivotal roles in homeostasis and development. Animal models of axial spondyloarthritis (axSpA) have shown that complement inhibition limits structural damage. We have previously reported elevated levels of the lectin pathway proteins L-ficolin and H-ficolin in axSpA-patients compared with blood donors.



P17. Fig. 1.

P17. Table.

MRI Lesion	Reader expertise	Strategy A			Strategy B		
		Stage 1 cases (n=25)	Stage 2 cases (n=25)	Stage 3 cases (n=25)	Stage 1 cases (n=25)	Stage 2 cases (n=25)	Stage 3 cases (n=25)
BME	None (n=6)	0.88 / 0.91	0.85/0.85	0.81/0.82	0.83/0.89	0.72/0.85	0.89/0.91
	Intermediate (n=6)	0.88/0.88	0.90/0.90	0.85/0.90	0.93/0.94	0.78/0.80	0.83/0.80
	Experienced (n=5)	0.92/0.94	0.90/0.88	0.92/0.93	0.83/0.88	0.84/0.90	0.89/0.89
ANKYLOSIS	None (n=6)	0.85/0.70	0.83/0.37	0.84/0.75	0.73/0.57	0.63/0.30	0.90/0.79
	Intermediate (n=6)	0.89/0.57	0.63/0.29	0.92/0.81	0.82/0.68	0.74/0.47	0.93/0.84
	Experienced (n=5)	0.96/0.76	0.93/0.64	0.94/0.86	0.97/0.24	0.83/0.41	0.91/0.79
BACKFILL	None (n=6)	-0.01/0.08	0.43/0.25	0.62/0.42	0.58/0.16	0.18/-0.03	0.56/0.36
	Intermediate (n=6)	0.41/0.13	0.44/42	0.69/0.39	0.50/0.22	0.30/0.30	0.70/0.42
	Experienced (n=5)	0.82/0.38	0.55/0.40	0.91/0.64	0.65/0.24	0.21/0.26	0.71/0.30
EROSION	None (n=6)	0.25/-0.09	0.64/0.30	0.51/0.33	0.42/0.30	0.33/0.13	0.45/0.38
	Intermediate (n=6)	0.42/0.17	0.56/0.12	0.51/0.44	0.33/0.27	0.45/0.18	0.53/0.39
	Experienced (n=5)	0.61/0.33	0.64/0.34	0.64/0.42	0.51/0.27	0.58/0.11	0.62/0.31
FAT METAPLASIA	None (n=6)	0.50/0.42	0.39/0.02	0.67/0.42	0.58/0.48	0.47/-0.08	0.86/0.64
	Intermediate (n=6)	0.49/0.38	0.59/0.30	0.80/0.51	0.57/0.78	0.50/0.42	0.81/0.47
	Experienced (n=5)	0.75/0.62	0.81/0.34	0.91/0.70	0.84/0.90	0.56/0.13	0.78/0.37

We aimed to investigate lectin pathway proteins in a clinical cohort of axSpA-patients and appropriate controls.

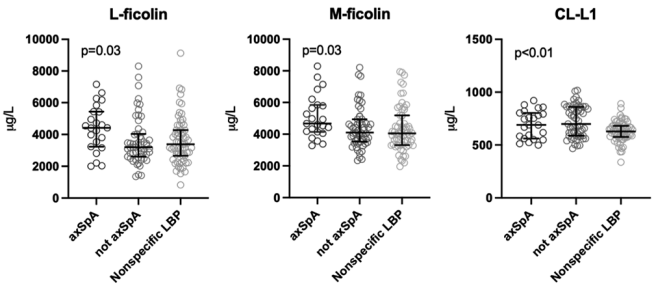
Materials and methods. Plasma samples were obtained from a cohort of patients with low back pain (LBP), including 1) 23 axSpA-patients, 2) 55 patients without axSpA but with some SpA-features (Not axSpA), and 3) 64 patients with nonspecific LBP without SpA-features or MRI findings suggestive of axSpA. Diagnosis of axSpA was based on multidisciplinary team conference consensus after 3.5 years of follow-up. Plasma levels of 10 lectin pathway proteins (MBL, CL-L1, H-ficolin, L-ficolin, M-ficolin, MASP-1, MASP-2, MASP-3, MAp44, and MAp19) were measured by immunoassays.

Results. Patient characteristics are shown in Table 1. Plasma levels of L-ficolin, M-ficolin, and CL-L1 differed significantly between the patient groups ($p \leq 0.03$). L-ficolin and M-ficolin were elevated in axSpA-patients compared with not axSpA and nonspecific LBP patients (Fig. 1). CL-L1 was elevated in axSpA-patients and not axSpA-patients compared to nonspecific LBP patients (Fig. 1). No significant differences were observed for MBL, H-ficolin, MASP-1, MASP-2, MASP-3, MAp44, and MAp19.

P18. Table I. Demographics of participants.

	axSpA (n=23)	Not axSpA (n=55)	Non-specific low back pain (n=64)	*p*-value
Median age, years (range)	32 (19-40)	33 (19-41)	32 (18-39)	0.75[a]
Males, n (%)	10 (43)	37 (67)	26 (41)	0.01[b]
HLA-B27 positive, n (%)	17 (74)	11 (20)	5 (8)	0.00[b]
Inflammatory back pain, n (%)	18 (78)	28 (51)		0.03[c]
Good response to NSAID	14 (61)	17 (31)		0.01[c]
ASAS positive SIJ MRI, n (%)	22 (96)	45 (82)		0.11[c]
Elevated CRP, n (%)	3 (13)	7 (13)		0.97
ASDAS (range)	2.5 (1.2-3.7)	2.3 (0.8-3.8)		0.52[d]
BASDAI (range)	49 (5.3-67.5)	38.3 (0-89.7)		0.92[d]

NSAID: non-steroid anti-inflammatory drug, SIJ: sacroiliac joint, MRI: magnetic resonance imaging, ASAS: Assessment of SpondyloArthritis international Society, CRP: C-reactive protein, ASDAS: The Ankylosing Spondylitis Disease Activity Score, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index
a: compared by Kruskal-Wallis test; b: all three groups compared by χ^2 test; c compared by χ^2 test; d: compared by Mann Whitney U-test.



P18. Fig. 1. Plasma levels of L-ficolin, M-ficolin and CL-L1 in the three patient groups.
axSpA: patients with axSpA.
not axSpA: patients with some SpA-features but not axSpA.
Nonspecific LBP: patients with LBP without SpA-features or MRI findings suggestive of axSpA.

Conclusions. L-ficolin and M-ficolin were increased in axSpA-patients compared to relevant controls with LBP or SpA-features but not axSpA. Our findings support a potential pathogenic role for complement in axSpA. Further studies are needed to elucidate the diagnostic potential of the specific complement proteins.

Acknowledgement. The project was supported by the Danish Rheumatism Association and Aarhus University.

P19

SEMIQUANTITATIVE ASSESSMENT OF SYNOVITIS ON US-GUIDED SYNOVIAL MEMBRANE BIOPSIES IS CONTINGENT ON DISEASE PHASE AND PREDICTIVE OF TREATMENT RESPONSE IN NAIVE TO TREATMENT PSORIATIC ARTHRITIS

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Introduction/objectives. Ultrasound (US)-guided Synovial Tissue (ST) biopsy serves as a safe procedure for basic and translational research in inflammatory arthritis. The study aims were (i) to assess the diagnostic value of the Krenn score (KSS) on ST samples obtained from US-guided biopsies in patients with Psoriatic Arthritis (PsA) across disease trajectories;(ii) to develop a multiparametric nomogram enabling treatment response prediction in naive to treatment PsA.

Materials and methods. 410 PsA who underwent US-guided ST biopsy and were categorized based on their disease phase (Table I). All ST specimens were processed for H&E-based semiquantitative synovitis quantification (KSS), implemented with the determination of lymphocytes and plasma cells presence. Each naive to treatment PsA was treated according to the EULAR recommendations and DAPSA remission rate at 6 months was recorded.

Results. The distribution of KSS was significantly different across the different PsA phases (ANOVA $p<0.001$).Specifically, KSS was significantly higher in b-DMARDs ($p<0.0001$) and c-DMARDs resistant PsA ($p<0.0001$) than remission/LDA PsA patients as well as naive to treatment PsA ($p<0.0001$).Considering the whole PsA cohort, KSS directly correlated to DAPSA disease activity (r=0.476, $p<0.001$).Particularly, naive PsA achieving LDA/remission within 6 months follow-up, had, before treatment, significantly lower KSS ($p<0.001$), lower rate of ST plasma cells presence ($p<0.001$) and shorter symptoms duration ($p=0.01$) compared to naive PsA not achieving this outcome. Considering clinical PsA domains, ST of naive PsA with concomitant dactylitis and skin disease showed significantly higher KSS ($p=0.01$ for both) compared to naive PsA without these involvements and were less likely to achieve LDA/remission ($p<0.001$).At logistic regression, having a baseline KSS <5 [OR:5.30(95%CI:2.21-12.74) $p<0.001$], absence of ST plasma cells [OR:3.87(2.11-7.10 95%CI) $p<0.001$] and not concomitant dactylitis [OR:2.55(95%CI:1.24-5.25) $p=0.01$] nor skin involvement [OR:2.06(95%CI:1.17-3.62) $p=0.01$] were independent factors associated with LDA/remission achievement at 6 months in naive PsA. Finally, a multiparametric nomogram integrating baseline clinical and histological ST characteristics of naive PsA was developed, enabling to predict up to 75% of probability to achieve DAPSA remission at 6 months.

Conclusions. KSS is contingent to inflammatory burden and included within a treatment response predictive multiparametric nomogram in naive PsA.

P19. Table I.

Variable	Naïve to treatment (n=207)	cs-DMARDs IR (n=101)	b-DMARDs IR (n=48)	Remission/LDA (n=54)
Age (years)	56.9 ± 13.3	56.1 ± 9.9	56.7 ± 11.5	59.9 ± 10.9
Gender, female (%)	134 (65.8)	64 (64.2)	27 (55.8)	33 (61.9)
Disease duration PsA (months)	5.2 ± 9.8	10.6 ± 12.5	12.5 ± 14.1	15.4 ± 9.7
Disease duration PsO (years)	16.2 ± 17.6	19.9 ± 14.2	19.1 ± 10.8	26.5 ± 17.3
Smokers, n (%)	31 (13.9)	17 (16.7)	13 (26.5)	13 (23.8)
BMI (kg/m^2)	26.9 ± 4.6	27.5 ± 4.3	29.1 ± 7.4	27.3 ± 4.4
DAPSA score	**19.5 ± 1.9**	**21.4 ± 2.6**	**23.3 ± 3.6**	**9.7 ± 4.1**
DAS28	**2.9 ± 0.4**	**3.1 ± 0.7**	**3.8 ± 1.2**	**1.6 ± 1.2**

P20

DIRECT AND INDIRECT EFFECT OF TNF INHIBITORS ON SPINAL MOBILITY IN PEOPLE WITH AXIAL SPONDYLOARTHRITIS (AXSPA) AND THE MEDIATOR ROLE OF DISEASE ACTIVITY

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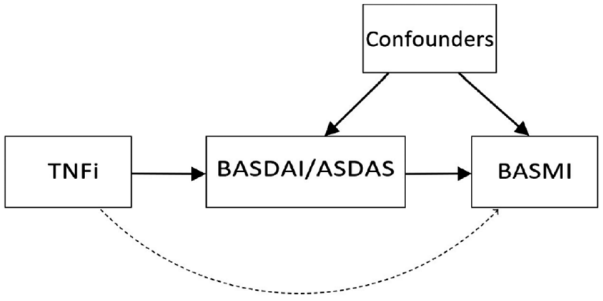
Introduction. Spinal mobility is an important measure to assess the efficacy of drugs used to treat axSpA. Our aim was to describe the long-term effect of TNFi on spinal mobility in patients with axSpA and to determine whether TNFi treatment influences spinal mobility in a direct and/or indirect way.

Methods. Retrospective observational study of patients with a clinical diagnosis of axSpA treated with TNFi. The longitudinal association between TNFi and improvement in BASDAI/ASDAS was tested using a linear mixed-effects model. To investigate whether TNFi had a direct effect on BASMI, we tested that TNFi treatment was not conditionally independent of BASMI given BASDAI/ASDAS (Figure 1). To test for the indirect effect of TNFi on BASMI reduction, we regressed BASMI on BASDAI/ASDAS, TNFi, demographics, presence of radiographic axSpA and HLA-B27 positivity.

Results. Data from 188 patients and 1326 visits were analysed. Mean age was 45.6 (SD 11.6) years, mean disease duration was 15.8 (SD 9.64) years, 152 (80.9%) were male, 120 (73.6%) had r-axSpA, and 83 (74.8%) were HLA-B27 positive. Mean follow-up time was 8.0 (SD 4.4) years. TNFi was significantly associated with long-term improvement in BASMI (B=-0.423, 95% CI=[-0.553,-0.292], $p<0.001$). An indirect effect of TNFi on BASMI improvement was observed, mediated by reduction in disease activity, measured by BASDAI (B=0.146, 95% CI=[0.092, 0.200], $p<0.001$) or ASDAS (B=0.405, 95% CI=[0.260, 0.549], $p<0.001$). A direct effect of TNFi on BASMI improvement was also observed, when BASDAI was used (B=-0.300, 95% CI=[-0.576,-0.025], $p<0.001$) as a covariate, but not when ASDAS was used ($p=0.3104$).

Conclusions. TNFi are effective at improving BASMI, which is mainly explained by the reduction in disease activity. However, a direct effect of TNFi on BASMI could also be demonstrated, when disease activity was measured by BASDAI, suggesting that ASDAS captures additional factors that can influence spinal mobility.



P20. Fig. 1. Indirect effect of TNFi on BASMI (represented by the full line), through the influence of TNFi on disease activity, adjusted by other confounders and direct effect of TNFi on BASMI (dashed line), independently of disease activity.

P21

IL-4 AND IL-13 MODULATE ENTHESEAL IL-23 PRODUCTION AND BLOCKADE WITH DUPILUMAB IS ASSOCIATED WITH EMERGENT TH17 TYPE DISEASES

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Background. IL-4 and IL-13 are Th2 cytokines that share a common receptor chain (IL-4Rα) and are known to drive allergic inflammation such as atopic dermatitis (AD) and asthma. Dupilumab is a monoclonal antibody developed to treat allergic inflammation by blocking IL-4Rα. Psoriatic arthritis (PsA), well established as a Th1/Th17 driven disease, is known to have a strong genetic risk association for IL-13, despite its pathogenic mechanism being unknown. Recent studies report that AD patients receiving dupilumab have developed clinical enthesitis and psoriasis. This study demonstrates a modulatory role for IL-4 and IL-13 by examining their effect on entheseal immune cells and assessing the association of dupilumab use with psoriatic disease.
Methods. Healthy enthesis samples were pretreated with IL-4 and IL-13 then stimulated with LPS and anti-CD3 to assess IL-23 and IL-17 production respectively. Enthesis tissue sections were also stained for IL-4Rα. 37,848 patients receiving Dupilumab were analysed for incidence of psoriasis-associated disease in VigiBase, the World Health Organization global pharmacovigilance database of ADRs.
Results. IL-4Rα+ cells were identified in the human enthesis. Pre-treatment of entheseal digested material with either IL-4 or IL-13 attenuated LPS-induced IL-23. The rate of psoriasis-associated disease including seronegative arthritis (OR 9.61) and enthesopathy (OR 12.6) was elevated amongst the 37,848 dupilumab-treated patients. No association with 10 humorally mediated autoimmune diseases including RA, systemic lupus erythematosus and Sjögren's syndrome was evident following dupilumab therapy.
Conclusions. Our combined data demonstrate a previously unknown protective role for IL-4 and IL-13 in entheseal induction of IL-23/17 axis cytokines. The translational relevance of our finding was supported by the emergence of Th17 related diseases in a large database where Th2 antagonism was used for atopic diseases. These findings point towards a novel explanation for IL-13 pathway SNPs in PsA and a molecular explanation for why anti-IL-4/13 therapy may induce entheseal pathology.

P22

SINGLE CELL ANALYSIS OF THE RESPONSE OF AXIAL SPONDYLOARTHRITIS TO TNFI THERAPY

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**Equal contribution*

Introduction. The spondyloarthropathies (SpA) including Axial Spondyloarthritis (AxSpA) are common inflammatory rheumatic diseases that characteristically affect the spine and sacroiliac joints and share a common genetic basis. While a majority (~70%) of patients respond well to biologic therapies targeting TNF, the exact mechanisms and predictors of response are poorly understood. A detailed understanding of the cell types and mechanisms responsible for both causing and resolving inflammation in SpA remains elusive.
Methods. We applied single-cell RNA-sequencing to perform an unbiased comparison of the peripheral immune system from six therapy-naive and six anti-TNF treated AxSpA patients.
Results. After performing SNP-based genetic demultiplexing, we integrated the cells from the different patients to construct an atlas of immune cells from peripheral blood. We performed a detailed comparison of the composition and transcriptional phenotype of the peripheral immune system between pre and post anti-TNF treatment. Our results demonstrate the cell-type specific effects of anti-TNF therapy on genes and pathways related to the development of AxSpA.
Conclusions. This work suggests the involvement of particular immune cell subsets in the pathogenesis of AxSpA and identifies potential targets for therapeutic intervention. It provides new insights into the effect of biologic therapy in SpA and may also have implications for the treatment of other immune-mediated inflammatory diseases.

P23

PREVALENCE OF AXSPA IN PATIENTS TREATED FOR CHRONIC BACK PAIN IN CHIROPRACTIC CLINICS: THE OREGON CHIROPRACTIC AXIAL SPONDYLOARTHRITIS STUDY (ORCAS) – AN INTERIM ANALYSIS

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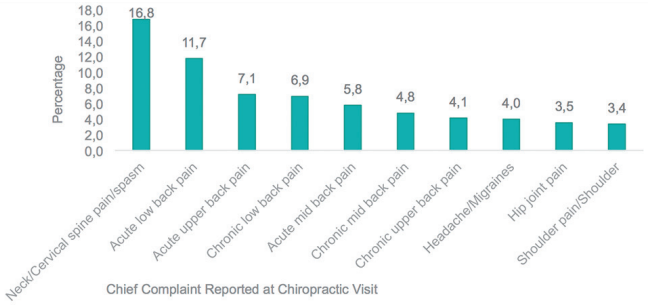
Introduction. Chiropractic clinics, where chronic back pain (CBP) patients are first seen, lack consistency in referral of patients to rheumatologists where the underlying cause may be axial spondyloarthritis (axSpA). This study aimed to estimate the prevalence of axSpA in CBP patients attending chiropractic clinics in Portland, Oregon, referred to a rheumatology clinic using a referral strategy identifying features of spondyloarthritis (SpA).
Methods. Adults attending one of four chiropractic clinics between 11/2020-11/2021 for CBP starting before age 45, without prior diagnosis of SpA were eligible for inclusion. Patients were referred to rheumatologist for diagnostic assessment, if they had inflammatory back pain (IBP) and/or ≥1 of the following features: a family history of SpA, inflammatory bowel disease, psoriasis, good response to NSAIDs, history of heel pain, uveitis, or joint swelling. The rheumatology assessment included history, CRP, HLA-B27, x-ray and MRI of the sacroiliac joints. Based on the assessment, patients were categorized as radiographic axSpA, non-radiographic axSpA, peripheral SpA, or no SpA. Endpoints were summarized using descriptive statistics.
Results. 115 patients were referred by the chiropractors and 84 patients were eligible. Of the 74 patients who provided consent, 79.7% had IBP, and 89.2% had at least one SpA feature. At interim data lock, 63 patients were fully assessed by a rheumatologist, of which 11.1% were HLA-B27 positive and 38.1% had rheumatologist-evaluated IBP. 12.7% of patients had SpA, 9.5% were diagnosed as axSpA and fulfilled Assessment of Spon-

dyloarthritis International Society (ASAS) classification criteria, 1 patient was diagnosed as psoriatic arthritis and fulfilled Classification Criteria for Psoriatic Arthritis, and 1 had undifferentiated peripheral SpA and fulfilled ASAS Classification Criteria.
Conclusions. More than 10% of patients attending chiropractic clinics for musculoskeletal complaints had undiagnosed SpA conditions, with axSpA being the most common. Educational efforts targeted at chiropractors to refer appropriate cases to rheumatologists are needed.

P23. Table 1. Demographic and clinical characteristics stratified by diagnosis as confirmed by Rheumatologist.

	Radiographic axSpA (n=1)	Non-radiographic axSpA (n=5)	Peripheral SpA Including PsA (n=2)	No SpA (n=55)
Age, years (Mean; SD)	73 (-)	36.8 (6.4)	46 (1.4)	45.1 (12.1)
Sex, Female – n (%)	0	4 (80)	2 (100)	32 (58.2)
Family history of rheumatic disease, Yes – n (%)	0	2 (40.0)	2 (100)	13 (23.6)
Chronic back pain duration, years (Mean; SD)	49 (-)	12.4 (6.0)	11 (7.0)	15 (10.8)
Confirmed during rheumatology visit – n (%)				
IBP* (4 out of 5 criteria as checked by patient)	1 (100)	3 (60.0)	1 (50.0)	27 (49.1)
IBP* (4 out of 5 criteria per rheumatologist's opinion)	0	2 (40.0)	0	22 (40.0)
History of plantar fasciitis or Achilles tendinitis	0	4 (80.0)	2 (100)	14 (25.5)
History of peripheral joint swelling	0	0	1 (50.0)	8 (14.6)
Positive response to NSAIDs	1 (100)	1 (20.0)	2 (100)	21 (38.2)
Psoriasis	1 (100)	0	1 (50.0)	2 (3.6)
Inflammatory bowel disease	0	0	0	1 (1.9)
Uveitis	0	0	0	1 (1.8)
HLA-B27 positive	0	2 (40.0)	1 (50.0)	4 (7.3)
CRP, Above 10.0 mg/L	0	2 (40.0)	1 (50.0)	1 (1.8)
SI Joints X-ray positive for sacroiliitis (modified New York criteria)	1 (100)	0	0	1 (1.8)
SI Joints MRI positive for active inflammation	1 (100)	3 (60.0)	0	0

*According to the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA.



P23. Fig. 1. Chief complaints reported by patients at chiropractor visits (n=3103).

P24

COMPARISON OF SACROILIAC CT FINDINGS IN PATIENTS WITH AND WITHOUT PSORIATIC ARTHRITIS: RESULTS OF THE CASIPSA STUDY

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Introduction. To our knowledge, no study has specifically evaluated the extent of structural lesions of the sacroiliac joints (SIJs) on computed tomography (CT) in patients with PsA compared with healthy controls.
Methods. Observational, retrospective study, patients with PsA, (CASPAR) and patients in archiving system who had undergone a CT which included the SIJs. Non-inclusion criteria were the existence of pelvic bone lesions and a history of pelvic radiotherapy. Each patient was then matched with a control of the same age and sex. CT was interpreted by two independent readers using a score previously used by Diekhoff, dividing each SIJ into 12 regions, joint space narrowing (JSN), erosions, and sclerosis are assessed. For this study, we also observed the existence of intra-articular gas and diffuse idiopathic skeletal hyperostosis (DISH) lesions for each region. Quantitative variables were compared using Student's t-test. Qualitative variables were compared using the Chi-2 test.
Results. 48 patients and 48 controls were included. Mean (SD) age was 54.76±12.91 in PsA and 54.74+12.87 in control. In PsA patients, mean (SD) disease duration was 22.87±14.95 years, 10 (43.48 %) were HLA-B27 positive, and 1 (2.86%) had a bamboo spine. CT findings are described in Table I. The only lesion found significantly more frequently in PsA patients was erosion, which appeared to be preferentially located on the anterior and middle regions of the SIJs. A positive CT scan (significant joint space narrowing, erosion and/or sclerosis) was found in 15 (32.61%) of the patients with peripheral involvement and 6 (30.00%) of the patients with axial involvement.
Conclusions. The CT characteristics of SIJs from patients with PsA were similar to those of age- and sex-matched controls, but with a higher prevalence of erosions. Structural lesions of the SIJs were found in nearly one PsA patient out of three.

P24. Table I.

Finding	PsA Patients	Controls	*p*-value
Mean (SD) total score (range 0-264)	26.37 ± 29.12	14.47 ± 10.85	0.01
Global positivity, n (%)	16 (33.33 %)	10 (20.83 %)	0.17
Bilateral ankylosis, n (%)	5 (10.42 %)	0 (0.00 %)	0.02
Positive joint space score, n (%)	15 (31.25 %)	10 (20.83 %)	0.25
Positive erosion score, n (%)	9 (18.75 %)	1 (2.08 %)	0.008
Significant sclerosis, n (%)	11 (22.92 %)	12 (25.00 %)	0.81
Intra-articular gas, n (%)	29 (60.42 %)	35 (72.92 %)	0.19
DISH, n (%)	9 (18.75%)	11 (22.92 %)	0.62

P25

PSORIASIS, WITHOUT RHEUMATOLOGICAL MANIFESTATIONS, IS ASSOCIATED WITH SRUCTURAL CHANGES OF THE SACROILIAC JOINT, A CONTROLLED STUDY USING CT SCAN

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Introduction. To our knowledge, no study has specifically evaluated the extent of structural lesions of the sacroiliac joints (SIJs) on computed tomography (CT) in patients with psoriasis (PsO), without rheumatological manifestations, compared with healthy controls.
Aim. To describe SIJ CT characteristics in patients with PsO and compare them with age- and sex-matched controls.
Methods. Observational, retrospective study patients with PsO, diagnosed by a dermatologist, and patients who had undergone a CT which included the SIJs in their entirety, matched for age and sex. Non-inclusion criteria were the existence of pelvic bone lesions and a history of pelvic radiotherapy. CT was interpreted by two independent readers using a score previously

used by Diekhoff, dividing each SIJ into 12 regions, joint space narrowing (JSN), erosions, and sclerosis are assessed. Quantitative variables were compared using Student's t-test. Qualitative variables were compared using the Chi-2 test.
Results. 60 patients and 457controls were included. Mean (SD) age was 52.2±17.7 in PsO and 53.6±16.7 in control. In PsO, BMI was 27.7±6 versus 26.9±6.44 in control (p=0.55). In PsO, mean disease duration was 20.2±17.6 years.The global SIJ score was higher in PsO (6.63±10.7) in comparison with control (2.84±4.87). Erosion and sclerosis scores were similar in both groups but joint space narrowing score was significantly higher in PsO (0.873 (±4.62) versus 4.15 (±10.8); p=0.035). There were no correlations between the global score and the disease duration (Pearson score 0.166 (-0.131; 0.435) and the severity of the psoriasis (Pearson 0.00937 (-0.259; 0.276). The number of gestation, active smoking, alcohol intake and physical work have no impact on the global score.
Conclusions. The CT characteristics of SIJs from patients with Pso were different to those of age- and sex-matched controls essentially joint space narrowing.

P26

EFFECT OF TOFACITINIB AND GLUCOCORTICOIDS ON INTESTINAL PERMEABILITY, EPITHELIAL DAMAGE AND BACTERIAL TRANSLOCATION IN RAT ADJUVANT-INDUCED ARTHRITIS

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Introduction. Growing evidence indicated a role of intestine in pathogenesis in chronic inflammatory rheumatic diseases (CIRD). Consistently, increased intestinal permeability (IP) and damage (ID) as well as bacterial translocation (BT) have been described in patients with CIRD. However, the effects of treatments used in patients with CIRD on gut health are unknown. To determine the effect of glucocorticoids (GCs) and tofacitinib on IP, ID and BT in rats with adjuvant-induced arthritis (AIA).
Methods. AIA was induced in 6-week-old male Lewis rats by a tail injection of Mycobacterium butyricum in incomplete Freund's adjuvant. At onset of arthritis, rats were treated daily with prednisolone at low (0.1 mg/kg/day, i.p.) or high dose (10 mg/kg/day, i.p.), or with Tofacitinib (10 mg/kg twice a day, s.c.) or with vehicle. After 21 days, IP, ID and BT were assessed by measurement of plasma levels of zonulin, intestinal Fatty Acid Binding Protein (iFABP) and serum levels of soluble CD14 (sCD14) by ELISA), respectively. Arthritis severity was daily evaluated through the determination of an arthritis score.
Results. Compared to vehicle, Tofacitinib and high-dose of GC both reduced arthritis score (p<0.001) and levels of sCD14 (-44%, p<0.001 and -41% p<0.001 respectively) in AIA. High dose of GC decreased iFABP (-17%, p<0.05) levels but had no effect on zonulin levels. Tofacitinib did change nor iFABP neither zonulin levels. As compared to vehicle, the low-dose of GC had no effect on arthritis severity, sCD14, iFABP and zonulin plasma levels.
Conclusions. Prednisolone at a dose efficient on arthritis reduced intestinal bacterial translocation and epithelial damage. Consistent with the positive effect of jakinibs in patients with inflammatory bowel disease, Tofacitinib blunted intestinal bacterial translocation in AIA. Our results identified a new mechanism involved in the positive effects of GC and tofacitinib in arthritis diseases.

P27

IMMUNOLOGICAL DIFFERENCES BETWEEN PSORIATIC ARTHRITIS PATIENTS WHO ARE TUMOR NECROSIS FACTOR INHIBITOR-NAIVE AND WHO HAVE INADEQUATE RESPONSE TO TUMOR NECROSIS FACTOR INHIBITORS

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Introduction. Guselkumab (GUS, an IL-23p19 subunit inhibitor) improved psoriatic arthritis (PsA) signs/symptoms in DISCOVER-1 patients with active PsA and COSMOS PsA patients with inadequate response to tumor necrosis factor inhibitor (TNFi-IR). This study assessed baseline molecular differences between TNFi-naive and TNFi-IR PsA patients and investigated GUS pharmacodynamic effect on cytokine expression over time.
Methods. Patient serum samples from DISCOVER-1 (TNFi-naive [n=101] and TNFi-IR [n=17])/DISCOVER-2 (TNFi-naive [n=150])/COSMOS (TNFi-IR [n=76]) were analyzed for selected cytokine levels. Pharmacodynamic effect of GUS every-8-weeks on cytokine levels was assessed. Differential baseline cytokine expression/associations between baseline cytokine levels and clinical response (PASI 75% improvement [PASI75]/ACR 20% improvement [ACR20])/GUS effect on cytokine levels were analyzed with a General linear model/Spearman linear regression.
Results. Baseline patient demographics/disease characteristics/conventional synthetic disease-modifying antirheumatic drug use were comparable between TNFi-naive (DISCOVER-1&2, N=251) and TNFi-IR (DISCOVER-1/COSMOS, N=93) patients, with differences in mean PASI score (8.9 vs 12.5)/swollen joint count (11.7 vs 10.3)/PsA duration (5.8 vs 9.8 years)/psoriasis duration (16.7 vs 20.4 years; Table). Baseline serum IL-22/TNF-α levels for

P27. Table. Baseline demographics, disease characteristics, and drug use in TNFi-naive and TNFi-IR* cohorts with available cytokine data in DISCOVER-1&2 and COSMOS†.

	TNFi-naïve (N=251)	TNFi-IR (N=93)
Age [years]	47.2 (11.3)	48.5 (11.1)
Female, n (%)	132 (52.6)	46 (49.5)
Body mass index [kg/m2]	29.6 (6.1)	30.3 (6.4)
Median (range) **CRP** [mg/dL]	0.9 (0.0-12.9)	1.0 (0.0-13.2)
Log2 IL-22 / TNFα [pg/mL]	2.0 (1.4) / 1.1 (0.6)	2.5 (1.5) / 1.9 (1.2)
Log2 IL-17A / F [pg/mL]	-0.4 (1.5) / 1.7 (1.5)	-0.1 (1.7) / 2.0 (1.8)
SJC [0-66]	11.7 (7.1)	10.3 (8.3)
TJC [0-68]	20.3 (13.1)	20.6 (14.2)
PsA duration [years]	5.8 (5.9)	9.8 (8.2)
PsO duration [years]	16.7 (12.8)	20.4 (12.0)
PsO body surface area (%)	14.8 (18.6)	19.1 (21.3)
IGA score [0-4]	2.3 (0.9)	2.3 (1.0)
PASI score [0-72]	8.9 (10.6)	12.5 (12.0)
Enthesitis [Yes], n (%)	160 (63.7)	58 (62.4)
csDMARD use [Yes], n (%)	164 (65.3)	62 (66.7)
Corticosteroid use (Yes), n (%)	45 (17.9)	19 (20.4)
Methotrexate use [Yes], n (%)	136 (54.2)	54 (58.1)

Data are mean (SD) unless otherwise noted
*TNFi-IR patients in this post-hoc analysis had active PsA and discontinued 1-2 TNFi due to inadequate efficacy; these patients required a TNFi-specific washout period prior to starting GUS.†Patients with serum CRP level ≥0.3 mg/dL, SJC ≥3, and TJC ≥3 (to mimic DISCOVER-1 inclusion criteria.
CRP: C-reactive protein; csDMARD: conventional synthetic disease-modifying antirheumatic drug; IGA: Investigator's Global Assessment; IL: interleukin; IR: inadequate response; PASI: Psoriasis Area Severity Index; PsA:psoriatic arthritis; PsO: psoriasis; SD: standard deviation; SJC: swollen joint count; TJC: tender joint count; TNFi: tumor necrosis factor inhibitor.

pooled treatment groups were higher in TNFi-IR than TNFi-naive patients (p<0.05). At W24, GUS reduced IL-22/IL-17A/IL-17F/IL-6/C-reactive protein/serum amyloid A protein to similar levels in both cohorts (p<0.05; Fig). W24 PASI75 responders had higher baseline IL-17F levels with GUS in both cohorts (p<0.05) and higher IL-22 levels in TNFi-IR patients only (p<0.05). A trend of upregulated baseline IL-22 expression in W24 ACR20 responders was seen for TNFi-IR GUS-treated patients (p=0.07).

Conclusions. Elevated baseline IL-22 expression and association between baseline IL-22 levels and W24 PASI75 response, and a W24 trend for an association between upregulated baseline IL-22 and ACR20 response, in TNFi-IR patients seen in this exploratory analysis may suggest increased involvement of the IL-23 pathway in TNFi-IR patients. GUS showed comparable and significant pharmacodynamic effects for TNFi-naive and TNFi-IR patients, consistent with observed clinical responses.

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P28

EFFECT OF GUSELKUMAB ON SERUM BIOMARKERS IN PSORIATIC ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE OR INTOLERANCE TO TUMOR NECROSIS FACTOR INHIBITORS: RESULTS FROM THE COSMOS STUDY

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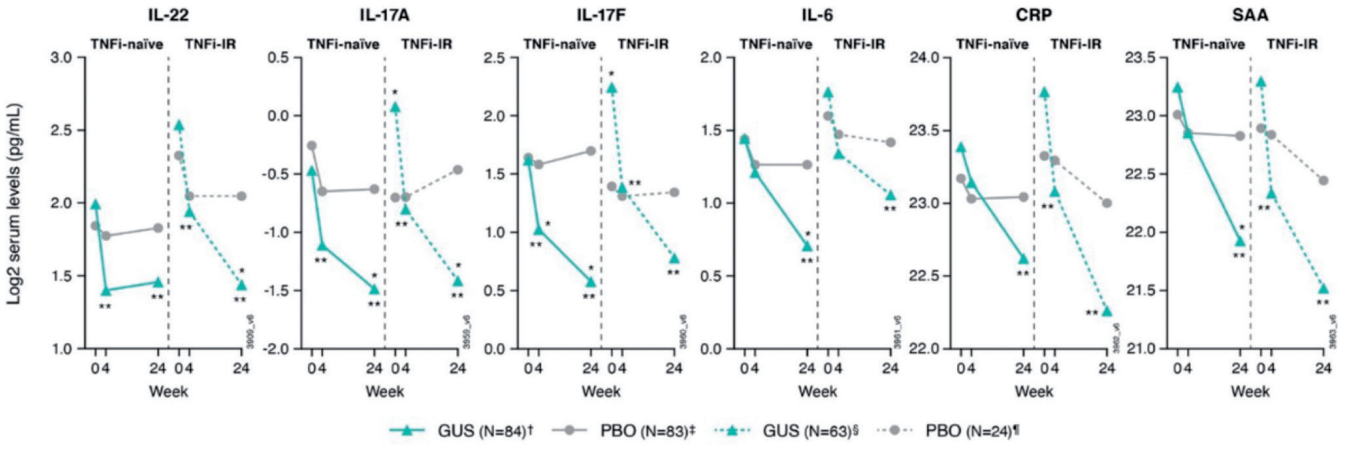
Introduction. In the COSMOS study of active PsA patients with inadequate response (IR) to 1-2 TNF inhibitors (TNFi), guselkumab (GUS) demonstrated significant improvements in PsA signs/symptoms vs. placebo (PBO) at Week (W)24. This study evaluated baseline serum levels of pro-inflammatory biomarkers (CRP/serum amyloid A [SAA]/TNF-α/IFNγ/IL-6/IL-10/IL-17F/IL-17A/IL-22), their association with baseline disease activity, change with GUS-treatment, and relationship with clinical response in COSMOS TNFi-IR patients.

Methods. Adult TNFi-IR PsA patients were randomized 2:1 to GUS-100mg every-8-weeks (Q8W) through W44 or PBO with crossover to GUS Q8W at W24 (PBOàGUS). Serum biomarker samples, collected at W0/4/16/24/48, were compared with healthy controls (HC).

Results. Biomarker data were available in 150/285 COSMOS participants (PBO: 50/95; GUS: 100/190). Baseline characteristics of the biomarker cohort were well-balanced across treatment arms. At baseline, TNF-α/ IFNγ/ IL-6/IL-10/IL-17A/IL-17F/IL-22 levels were significantly upregulated in TNFi-IR PsA patients vs. HC (Table). IL-6/CRP/SAA levels were associated with baseline joint disease severity (Disease Activity Score 28-CRP). IL-17A/ IL-17F levels were associated with baseline PASI score. Through W24, CRP/ SAA/IL-6/IL-17A/IL-17F/IL-22 levels significantly decreased from baseline in GUS-treated (but not PBO-treated) patients. Reductions in IL-17A/IL-17F/ IL-22 with GUS were significant as early as W4, decreased further through W16, and were sustained through W24/48. In GUS-treated patients, serum levels of IL-17F from W16 and IL-22 from W4 were not significantly different vs. HC. At W48, reductions in these markers were seen in PBOàGUS patients (Figure). GUS-treated patients achieving ACR20 at W24 exhibited higher baseline IL-22/IFNγ levels than nonresponders. All other biomarkers evaluated were not significantly associated with ACR20 response to GUS.

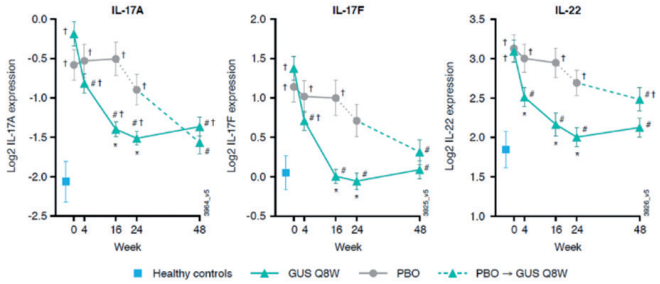


P27. Fig. 1. Longitudinal serum IL-22, IL-17A, IL-17F, IL-6, CRP, and SAA levels among TNFi-naive and-IR pts with GUS treatment.
*p<0.05 vs PBO. **p<0.05 vs baseline. †For IL-17A levels in GUS TNFi-naive pts, N=82 (W0), N=63 (W4/24). ‡For IL-17A levels in PBO TNFi-naive pts, N=81 (W0), N=60 (W4), N=61 (W24). §For IL-17A levels in GUS TNFi-IR pts, N=61 (W4), N=62 (W24). ¶For IL-17A levels in PBO TNFi-IR pts, N=23 (W0/4), N=22 (W24); for IL-22, IL-17F, IL-6, CRP, and SAA levels in PBO TNFi-IR pts, N=23 (W24).
Data should be interpreted with caution due to small sample size.
CRP: C-reactive protein; GUS: guselkumab; IL: interleukin; IR: inadequate response; PBO: placebo; SAA: serum amyloid A; TNFi: tumor necrosis factor inhibitor; W: week.

P28. Table. Select Serum Biomarkers at Baseline in TNFi-IR Patients vs. Healthy Controls†.

Biomarker, pg/mL	HC N=24	TNFi-IR N=150	Fold difference	p-value
CRP	22.1 (1.5)	22.8 (2.2)	1.6	0.2895
SAA	21.7 (1.2)	22.8 (2.4)	2.1	0.0794
IL-6	0.07 (1.1)	0.98 (1.7)	**1.9**	**0.0314***
IL-10	-2.3 (1.1)	-1.7 (1.0)	**1.5**	**0.0272***
IL-17A	-2.1 (1.3)	-0.3 (1.5)	**3.3**	**<0.0001***
IL-17F	0.05 (1.1)	1.3 (1.5)	**2.4**	**0.0007***
IL-22	1.9 (1.1)	3.1 (1.3)	**2.4**	**0.0002***
TNFα	0.5 (0.75)	1.4 (1.1)	**1.8**	**0.0002***
IFNγ	2.4 (0.84)	2.9 (1.3)	**1.5**	**0.0259***

Data are mean (SD); *p<0.05 and (fold difference) >1.4; †adjusted for confounding factors age & sex. CRP: C-reactive protein; HC: healthy controls; IFN: interferon; IL: interleukin; IR: inadequate responder; SAA: serum amyloid A; SD: standard deviation; TNFi: tumor necrosis factor inhibitor.



P28. Fig. 1. Reductions in serum levels of IL-17A, IL-17F, & IL-22 with GUS. PBO includes pts who had an early escape to GUS at W16 (dotted line; n=24), and a planned cross-over to GUS at W24 (dashed line; n=26). Statistics based on general linear model. Error bars represent 1 standard error.
*Indicates statistical significance vs. PBO by p<0.05 & | fold difference | >1.4.
#Indicates statistical significance vs. baseline by p<0.05 & | fold difference | >1.4.
†Indicates statistical significance vs. healthy controls by p<0.05 & | fold difference | >1.4.
GUS: guselkumab; IL: interleukin; PBO: placebo; pts: patients; Q8W: every 8 weeks; W: week

Conclusions. GUS-treated TNFi-IR patients showed response-specific associations with baseline biomarkers (IL-22/IFNγ/IL-6/SAA). GUS induced decreased levels of elevated CRP/SAA/IL-6/IL-17A/IL-17F/IL-22 vs. PBO. Reductions in these biomarkers were evident as early as W4 and approximated levels seen in HC, suggesting apparent normalization of effector cytokines associated with the IL-23/Th17 axis following GUS treatment.

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P29

PATIENT CHARACTERISTICS AND CLINICAL ASSESSMENTS ASSOCIATED WITH PROGRESSION FROM NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS TO ANKYLOSING SPONDYLITIS

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Introduction. Part of the patients with nr-axSpA will progress to AS. Varying factors are reported to be predictive of this progression of which the presence of elevated CRP and active sacroiliitis on MRI are most often found. Our objective was to explore patient characteristics and clinical assessments associated with progression from nr-axSpA to AS up to 6 years follow-up.
Methods. Patients from the Groningen Leeuwarden Axial SpA (GLAS) cohort classified as nr-axSpA at baseline were included. Baseline and available radiographs at 2 (n=85), 4 (n=53) and 6 years (n=30) were randomized with radiographs of patients with AS and scored by two readers according to the mNY criteria with known time sequence. In case of disagreement in classification, the score of a third independent reader was used. Progression to AS was defined as progression in mNY score to ≥2 bilaterally or ≥3 unilaterally. Patient characteristics and clinical assessments at baseline were compared between progressors and non-progressors.
Results. 85 patients were classified as nr-axSpA at baseline. Mean age was 39±11 years, 52% was male, median symptom duration was 6 (IQR 3-17) years, 75% was HLA-B27+, and mean ASDAS was 2.7±1.1.
After 2, 4 and 6 years, 9/85 (10.6%), 4/47 (8.5%) and 2/24 (8.3%) of nr-axSpA patients progressed to AS. Patients with nr-axSpA progressing to AS were significantly more often smokers and had more often a history of uveitis. Furthermore, progressors tended to have higher CRP/ASDAS, more entheseal involvement, and worse lumbar spinal mobility then non-progressors; however, in our small sample significance was not reached (Table I).
Conclusions. In our cohort, active smoking and a history of uveitis were independently associated with the progression of nr-axSpA to AS. Combining data of different cohorts will help to build a more robust picture of axSpA features and patient characteristics associated with progression to AS.

P29. Table I. Comparison of baseline characteristics between patients with nr-axSpA who did and did not progress to AS. Values presented as mean + SD, median (IQR) and n (%) for normally distributed and categorical variables, respectively.

Baseline characteristics	All patients (n=85)	No progression (n=70)	Progression (n=15)	p
Male sex	44 (52%)	39 (56%)	5 (33%)	0.115
Age	38.6 ± 10.8	38.4 ± 10.2	39.5 ± 13.8	0.774
Symptom duration	6 (3 – 17)	7 (3 – 16)	4 (2 – 20)	0.663
HLA-B27+	62 (75%)	52 (74%)	10 (67%)	0.758
Currently smoking	22 (28%)	14 (21%)	8 (53%)	0.003*
BMI	26.1 ± 4.4	26.2 ± 4.5	25.8 ± 4.2	0.750
History of uveitis	15 (18%)	8 (11%)	7 (47%)	0.001*
History of IBD	7 (8%)	6 (9%)	1 (8%)	0.808
History of psoriasis	12 (14%)	10 (15%)	2 (13%)	0.923
ASDAS	2.7 ± 1.1	2.6 ± 1.1	3.2 ± 1.0	0.107
- ASDAS >2.1	51 (72%)	41 (68%)	10 (91%)	0.126
BASDAI	5.3 (3.4 – 6.7)	5.4 (3.2 – 6.8)	4.7 (3.6 – 6.7)	0.538
CRP ≥5.0	21 (27%)	16 (25%)	5 (39%)	0.320
Start TNFi (during first 2 years of follow-up)	27 (32%)	23 (33%)	4 (27%)	0.640
Chest expansion (cm)	5.2 ± 2.1	5.3 ± 2.1	4.7 ± 2.1	0.367
Lateral spinal flexion (cm)	14.4 (10.5 – 17.5)	14.5 (10.7 – 17.7)	11.3 (9.0 – 17.5)	0.163
mSchober (cm)	14.1 ± 1.3	14.1 ± 1.3	13.7 ± 1.3	0.308

P30

TREATMENT DECISIONS IN AXIAL SPONDYLOARTHRITIS ARE MORE THAN TREAT TO TARGET

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Introduction. Currently is it unknown if treat-to-target (T2T) is applied in axSpA clinical practice and which factors influence treatment decisions. This study assessed residual disease activity according the physician's opinion, patient's opinion and disease activity measures and the subsequent treatment decisions made.

Methods. This cross-sectional multicentre study evaluated remission and low disease activity according to BASDAI (<1.9 and <3.5 respectively), physician's, and clinically diagnosed axSpA patient's opinion was assessed. Questionnaires including patient reported outcomes and satisfaction with treatment; or questions regarding motivations for treatment decisions were filled in by patients and physicians respectively.

Results. In total 115 out of 249(46%) patients were in remission according to the physician, of whom 80 out of 115(67%) perceived their disease as being inactive and only 43(37%) reached remission according to the BASDAI. In 107(93%) treatment intensity remained unchanged and in 5(6%) treatment was tapered. Physicians motivated that treatment was left unchanged because of remission in 55(48%), low disease activity in 28(24%), or complaints not related to axSpA in 13(12%) patients. Residual disease activity was present in 134/249 patients according the physician, of which 90(67%) perceived their disease as active. In 119(89%) BASDAI was >1.9 and in 83(62%) >3.5. In 51(61%) patients with residual disease and a BASDAI>3.5, treatment remained unchanged, as well as in 43(84%) of the patients with a BASDAI between 1.9 and 3.5. Physician's most frequent motives for unaltered treatment in the residual disease activity group were: low disease activity achieved in 29(25%), need to await the effect of the current treatment in 23(20%), or complaints not related to axSpA in 9(8%). The second (n=20,39%) motive was most frequent for unchanged treatment in the BASAI>3.5 group and some patients preferred to continue their current treatment despite high disease activity (n=5,10%).

Conclusions. This study shows that physicians do not always adjust treatment according to T2T-principles in patients with residual disease activity following BASDAI scores, either because low disease activity was achieved, because they classify the patient as being in remission, as having low disease activity, or because there was a need to await the efficacy of the current treatment.

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P31

EFFECT OF CIGARETTE SMOKING ON INFLAMMATORY ARTHRITIS IN CURDLAN ADMINISTERED SKG MICE

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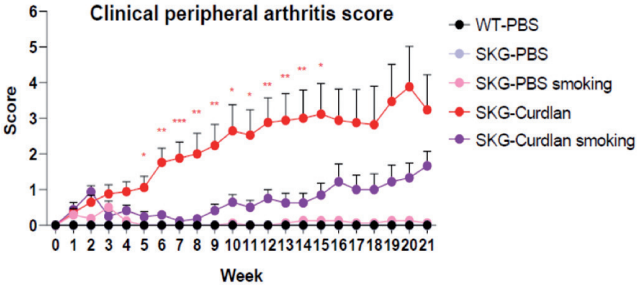
Objectives. We evaluated the effect of cigarette smoke on peripheral arthritis and axial progression in curdlan-administered SKG mice.

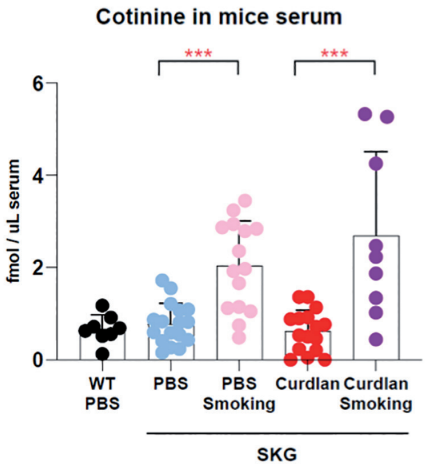
Materials and methods. Male SKG mice at 8-weeks old were injected with curdlan (n = 24) or PBS two times with 2-week intervals. The curdlan-administered SKG mice were then grouped with (n=12) or without (n=12) inhaled the cigarette smoke (3R4F cigarette) five days a week for 20-weeks since first curdlan injection. The clinical scores for peripheral arthritis were evaluated every week after curdlan injection and histological evaluation was performed at 23-weeks post-curdlan injection. To identify the presence of osteoblastic activity of spine, imaging was performed using the fluorescent *in vivo* bisphosphonate agent OsteoSense® 680 EX at 21-weeks post-curdlan injection. Splenocytes were examined for auto-reactive T cells population by flow cytometry and T cell subsets were evaluated in hind paw using immunohistochemical staining. Metabolomic analysis of serum was performed to elucidate cotinine (nicotine metabolite) at 16-weeks post-curdlan injection.

Results. Peripheral arthritis was scored lower in curdlan-administered SKG mice with smoke compared with those without smoke (Fig. 1) and, similarly to clinical score, synovial inflammation was scored lower in curdlan-administered SKG mice with smoke on the histology. However, osteoblastic activities on spine were not different between groups measured by fluorescence. In flow cytometry analysis, T_H17 and Treg population were not different between groups in splenocytes, but IL-17A$^+$Treg population was decreased in curdlan-administered group with smoke. Furthermore, proportion of IL-17A$^+$, FOXP3$^+$ and IL-17A$^+$FOXP3$^+$ cells was decreased in synovia of curdlan-administered SKG mice with smoke compared with those without. In metabolomic analysis, serum cotinine was increased in curdlan-administered SKG mice with smoke, suggesting anti-arthritogenic role of cotinine metabolized from nicotine. (Fig. 2)

Conclusions. Our results suggest cigarette smoke might ameliorate peripheral arthritis but not spinal mineralization with increase of serum cotinine in curdlan-administered SKG mice model.



P31. Fig. 1.



P31. Fig. 2.

P32

ORAL AND GUT MICROBIAL PROFILE IN ANKYLOSING SPONDYLITIS TREATED WITH SECUKINUMAB: CRONIC DISEASE RELATED DYSBIOSIS

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Objectives. To analyze the effect of secukinumab treatment in gut and oral microbiome in ankylosing spondylitis patients with recent diagnosis (AS-RD) and long disease evolution (AS-LDE).
Methods. 16S rRNA gene V3-V4 region sequencing was performed on fecal and salivary DNA isolated from 7 AS patients without previous biological therapies [4 AS-RD (<2 years) and 3 AS-LDE (>10 years)] pre-(Month-0) and post-treatment (Month-1 and Month-6) with secukinumab 150mg in monotherapy. Disease activity was assessed using ASDAS-CRP and BASDAI, and disability using HAQ.
Results. No significant shifts in richness and diversity in gut and oral microbiome were observed after 6 months secukinumab treatment. But reduced richness and diversity in fecal microbial communities in patients with AS-LDE compared to AS-RD patients was observed (Padj<0.001).
Desulfobacterota philum abundance in fecal samples was increased after 6 months of secukinumab treatment in AS-RD patients (Padj<0.001), and Synergistaceae family abundance was decreased after treatment in salivary samples (Padj<0.001), correlated with low clinical activity and disability.
The gut microbiome abundance of AS-LDE patients differ significantly from AS-RD, driven by higher abundance of Prevotella, Dialister, Desulfovibrio and Alloprevotella genera, and lower abundance of Lachnospira, Paraprevotella, Klebsiella, Ruminococcaceae_CAG_352 and Alistipes genera. In addition, higher abundance of Prevotella and Dialister and lower abundance of Lachnospira, Paraprevotella and Klebsiella correlated to high clinical activity and disability.
Oral microbiome of AS-RD patients was more enriched in Sacharimonadales and Gracillibacteria family and Phorphyromonas and Fusobacterium genera, while AS-LDE patients were more enriched in Synergistaceae, Micrococcaceae and Streptococcaceae family, all correlated to high clinical activity and disability.
Conclusions. In AS-LDE patients, oral and intestinal dysbiosis of bacterial taxa was observed, most notably in Prevotella and Dialister for fecal samples and Phorphyromonas and Fusobacterium for salivary samples. Secukinumab treatment was associated with increased Desulfobacterota abundance in fecal samples and lower Synergistaceae abundance in salivary samples.

P33

ASSOCIATION OF DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER AND AXIAL SPONDYLOARTHRITIS WITH THE M694V MUTATION

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Introduction. To evaluate the differences of demographic, clinical characteristics of patients with FMF+axSpA according to the M694V mutation results.
Methods. A total of 9630 FMF patients were identified according to the ICD-10 code (E85.0) in the electronic database of Hacettepe University Hospital. 7525 patients aged <18 years old and no follow-up after 2014 were excluded. 2105 adult FMF patients screened for accompanying axSpA according to ICD-10 code (M45) and 241 patients detected as FMF+axSpA. FMF diagnosis was confirmed with Tel-Hashomer criteria. The diagnosis of axSpA was confirmed either according to the Modified New York (mNY) criteria or the ASAS criteria. The diagnosis of FMF+AxSpA was confirmed in 136 patients. MEFV gene result was present in 113 (83%) of 136 patients and were included in the study. Patients were divided into two groups as M694V (+) and M694V (-), and the demographic and clinical characteristics were compared.
Results. Of 113 patients, 91 (80.5%) were M694V (+), 22 (19.5%) were M694V (-), 45 (39.8%) were homozygous for M694V. In the M694V (+) group, symptom onset and diagnosis of both FMF and axSpA were at an earlier age compared to M694V (-) patients (p<0.05). The frequency of radiographically proven moderate to severe hip involvement (24.2% vs. 9.1%) and total hip replacement (11% vs. 4.5%) was higher in M694V (+) patients (p=0.12; p=0.36 respectively). In the homozygous M694V (+) group, symptom onset and diagnosis of both FMF and axSpA were significiantly at an earlier age than in the group homozygous M694V (-) (p<0.001). Erysipelas-like skin rash was more common in homozygous M694V (+) group (28.9% vs. 11.8% p=0.02), other symptoms and findings were similar in both groups (Table I).
Conclusions. FMF and SpA symptoms appear at an earlier age in M694V positive patients. The M694V mutation is associated with severe disease and early disease onset.

P33. Table I.

Features	M694V (+) (n=91)	M694V (-) (n=22)	P1	M694V Homo-zygous (n=45)	M694V Nonho-mozygous (n=68)	P2
Age at FMF symptom onset [years, med (25-75)]	11 (5-18)	21 (8-30)	**0.005**	7 (1-42)	18 (3-53)	**<0.001**
Age at FMF diagnosis [years, med (25-75)]	18 (10-27)	33 (27-38)	**<0.001**	12 (1-42)	28 (3-59)	**<0.001**
Age at AxSpA symptom onset [years, med (25-75)]	20 (15-25)	29 (24-38)	**<0.001**	20 (5-50)	22 (5-58)	0.43
Age at AxSpA diagnosis [years, med (25-75)]	24 (19-33)	37 (28-44)	**<0.001**	23 (11-51)	29 (7-59)	**0.039**
Fever n (%)	84 (92.3)	21 (95.5)	0.60	44 (97.8)	61 (89.7)	0.10
Abdominal pain n (%)	80 (87.9)	20 (90.9)	0.70	43 (95.6)	57 (83.8)	0.056
Peripheral arthritis n (%)	45 (49.5)	7 (31.8)	0.13	24 (53.3)	28 (41.2)	0.20
Erysipelas n (%)	19 (20.9)	2 (9.1)	20.2	13 (28.9)	8 (11.8)	**0.02**
Enthesitis n (%)	21 (23.1)	4 (18.2)	0.62	11 (24.4)	14 (20.6)	0.63
Uveitis n (%)	11 (12.1)	4 (18.2)	0.45	4 (8.9)	11 (16.2)	0.26
Psoriasis n (%)	6 (6.6)	1 (4.5)	0.72	2 (4.4)	5 (7.4)	0.82
HLA-B27 (+) n (%)	25 (27.3)	4 (18.2)	0.54	2/15 (13.3)	12/40 (30)	0.30
Syndesmophyte n (%)	20/82 (24.4)	6/19 (31.6)	0.52	7/43 (16.3)	19/59 (32.2)	0.07
Total ankylosis n (%)	4/83 (4.8)	1/19 (5.3)	0.94	1/43 (2.3)	4/59 (6.8)	0.39
Moderate to severe hip disease* n (%)	22 (24.2)	2 (9.1)	0.12	12/45 (26.7)	12 (17.6)	0.25
Total hip replacement n (%)	10 (11.0)	1 (4.5)	0.36	4 (8.9)	7 (10.3)	0.80

*BASRI-hip score ≥3 on any side.

P34

CO-EXPRESSION OF IL17F AND IL17A SECRETION BY ENTHESEAL RESIDENT T-CELLS AND CIRCULATING T-CELLS IS PREFERENTIALLY FROM THE CD4 T-CELL SUBSET

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Introduction. The IL17/IL23 axis has been implicated in many inflammatory diseases such as ankylosing spondylitits (AS), psoriatic arthritis (PsA), IBD and psoriasis, and has led to the development of a number of IL17 inhibitors. The enthesis is connective tissue where the tendon or ligament attaches to the bone. Enthesitis is the cardinal pathological process in SpA related diseases such as PsA. T-cell derived cytokines are thought to be central to SpA immunopathology, including IL-17A, IL17F and TNF. Clinical advances in the management of psoriasis have occurred from dual targeting of both IL-17A and IL-17F. However, the biology of IL-17F at the human enthesis is rudimentary.
Methods. Peripheral blood and spinal enthesis samples were processed to isolate the immune cell populations, for peripheral blood, the lymphocyte layer was isolated using lymphoprep and mechanical isolation of the immune cell populations was used for the enthesis samples. T-cells were

stimulated with αCD3 (100ng/ml) and soluble αCD28 (100ng/ml) for 72hrs in RPMI media. 3-4hrs before the end of the stimulation a golgi plug was added and the cells harvested for analysis of intracellular IL17A & IL17F via flow cytometry.
Results. IL17F is preferentially expressed by $CD4^+$ T-cells in peripheral blood and enthesis, with IL17F more strongly expressed over IL17A after 72hrs of inflammatory activation. IL17F expression was 2fold higher than IL17A expression. IL17A was not sustained by continuous activation of T-cells, whereas IL17F expression was elevated after 72hrs. Only a small percentage of cells were found to co-express IL17A and IL17F.
Conclusions. This is the first study looking at IL-17A and IL17F induction from normal entheses where biological differences between these two IL-17 family members has emerged.

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P35

RADIOGRAPHIC SPINAL DAMAGE IN PSORIATIC ARTHRITIS PATIENTS COMPARED TO SPA PATIENTS

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Background/objectives. There is an ongoing debate on axial involvement in psoriatic arthritis (PsA) patients. In this study the association between axial involvement, defined by different definitions, and the development of syndesmophytes in 2 years in PsA patients is described.
Methods. PsA patients originated from the Belgian Epidemiological Psoriatic Arthritis Study (BEPAS), a prospective multicentre cohort involving 17 Belgian rheumatology practices. Recruitment was from December 2012 until July 2014. Patients were included when patients fulfilled the Classification criteria for Psoriatic Arthritis (CASPAR). Radiographs of the spine were obtained at baseline and after 2 years. Two calibrated readers evaluated radiographic damage by assessing the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). When assessing the images, readers were blinded for time sequence, clinical data and information from other obtained images (radiographs of the hands and feet).
Results. In total 461 patients were included in BEPAS. Mean age was 52.79±12.29 years and 43.0% (n=198) were female; average disease duration was 8.5 ± 9.3 years and approximately 34% of the patients reported inflammatory axial pain. From 312 patients spinal radiographs were obtained. At baseline, the vast majority of PsA patients had an mSASSS of 0 (n=273, 87.5%), according to both readers. In 33 PsA patients (10.6%) mSASSS was 2 or more.

P35. Table. Spinal damage at baseline of patients from the BEPAS (PsA patients) and Be-Giant (SpA patients) cohorts.

	PsA patients (n=312)	SpA patients (n=260)
mSASSS ≥2, no of patients	33 (10.6%)	17 (7.9%)
mSASSS ≥1, no of patients	39 (12.5%)	19 (8.9%)
mean, (SD)	4.5 (4.24)	10.3 (14.91)
min, 0.25, median, 0.75, max	1-2-**3**-6-21	1-2-**5**-13-64
Erosions ≥1, no of patients	13 (4.2%)	4 (1.9%)
mean, (SD)	1.5 (1.39)	1 (0.0)
min, 0.25, median, 0.75, max	1-1-**1**-1-6	1-1-**1**-1-1
Squaring ≥1, no of patients	No obs.	4 (1.9%)
mean, (SD)	No obs	1.8 (0.96)
min, 0.25, median, 0.75, max	No obs	1-1-**1.5**-2.5-3
Sclerosis ≥1, no of patients	2 (0.6%)	6 (2.8%)
mean, (SD)	1.5 (0.71)	1.8 (1.33)
min, 0.25, median, 0.75, max	1-1-**1.5**-2-2	1-1-**1**-3-4
Syndesmophytes (total spine)	33 (10.6%)	14 (6.6%)
mean, (SD)	2.0 (1.45)	4.9 (5.78)
min, 0.25, median, 0.75, max	1-1-**2**-2-8	1-1-**3.5**-5-22
Syndesmophytes (cervical spine)	24 (7.7%)	9 (3.5%)
mean, (SD)	1.8 (1.32)	2.9 (2.89)
min, 0.25, median, 0.75, max	1-1-1-2-7	1-1-2-3-10
Syndesmophytes (lumbar spine)	11 (3.5%)	10 (4.7%)
mean, (SD)	1.9 (0.70)	4.2 (4.44)
min, 0.25, median, 0.75, max	1-1-**2**-2-3	1-1-**2**-6-12

For the SpA patients, percentages were lower but the trend was similar (see Figure 1). Though lesser patients showed abnormalities, the SpA patients with spinal damage show a higher mSASSS, therefore indicating more spinal damage then the PsA patients ($p<0.05$). Both patient groups show some outliers with high mSASSS, increasing the average mSASSS especially in the SpA cohort (mean mSASSS = 10.3±14.91) compared to the median of 5 (IQR 2-13) in the Be-Giant and 3 (IQR 2-6) in the BEPAS cohort.
Syndesmophytes are seen in 10.6% and 6.6% of the PsA and SpA patients, respectively. Similar to the mSASSS, SpA patients had more syndesmophytes (mean: 4.9±5.78) compared to PsA patients (mean 2.0±1.45); p<0.05. PsA patients had more often syndesmophytes located in the cervical spine; 24/33 patients (72.7%) compared to 11/33 (33.3%) patients with lumbar syndesmophytes. Syndesmophyte location was more evenly distributed in SpA patients; cervical 9/14 (64.3.9%) and lumbar 10/14 (71.4%). Percentages exceed 100%, as there were some patients with syndesmophytes in both spinal segments. Erosions and especially sclerosis and squaring are uncommon in both patient groups.
Conclusions. Spinal damage is seen in approximately 10% or less of both PsA and SpA patients in these cohorts. SpA patients show higher mSASSS values and more syndesmophytes as compared to the PsA patients. Syndesmophytes in PsA patients are more often located in the cervical spine while the location is more equally distributed in SpA patients.

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P36

ANTIBODIES TO TWO NOVEL PEPTIDES IN NEW ONSET AXIAL SPONDYLOARTHRITIS

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Introduction. Diagnosis of axial spondyloarthritis (axSpA) is challenging and a specific laboratory diagnostic test is lacking. Previously, we identified immunoglobulin G (IgG) antibodies to 3 Hasselt University (UH)-axSpA peptides (UH-axSpA-IgG 1, 4, 8) which could provide a novel tool for diagnosis of a subset of axSpA patients. Validation of antibody reactivity in plasma samples of early axSpA patients (disease duration < 5 years) from 2 independent cohorts revealed antibody reactivity against at least one of these 3 peptide targets in 14.2% of early axSpA patients (22/155) (1). Here we aim to validate the diagnostic potential of these 3 antibodies in a third independent cohort of new onset axSpA patients and controls.
Methods. Using ELISA, presence of antibodies to the 3 peptides was determined in 188 serum samples of the Belgian Inflammatory Arthritis and Spondylitis (Be-Giant) cohort, 74 controls with chronic low back pain (CLBP) and 112 age and gender-matched healthy controls (HC) from the UH cohort.
Results. The presence of antibodies against 2 of the 3 UH-axSpA peptides was confirmed in the Be-Giant cohort. Antibody reactivity against at least one of these 2 UH-axSpA peptides (UH-axSpA-IgG 4, 8) was found in 11.2% of newly diagnosed axSpA patients (21/188) compared to 3.6% (4/112, $p=0.0290$) in HC and 6.8% (5/74, $p=0.3619$) in CLBP.
Conclusions. The presence of antibodies to 2 UH-axSpA peptides was confirmed in the Be-Giant of newly diagnosed axSpA patients and could be of added value for axSpA diagnosis.

Reference

1. QUADEN D *et al.*: *Arthritis Rheumatol* 2020.

P37

ANTIBODIES OF DIFFERENT ISOTYPES TO NOVEL PEPTIDES IN EARLY AXIAL SPONDYLOARTHRITIS

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Background. There is an unmet need for biomarkers to identify patients with axial spondyloarthritis (axSpA). Previously, we identified immunoglobulin G (IgG) antibodies to 3 Hasselt University (UH)-axSpA peptides (UH-axSpA-IgG 1, 4 and 8) which could provide a novel tool for diagnosis of a subset of early axSpA patients (disease duration < 5 years) (1). Besides IgG antibodies, IgA isotype antibodies are of interest due to the strong link between gut inflammation and spondyloarthropathies. Therefore, an axSpA cDNA phage display library representing the antigenic repertoire from axSpA hip synovium was screened for reactivity with IgA antibodies in plasma of early axSpA patients, resulting in 3 UH-axSpA-IgA peptides (UH-axSpA-IgA.1, 3 and 10) with increased antibody reactivity in axSpA patients compared to healthy controls (HC). Here, we aimed to determine the added value of antibody reactivity to these UH-axSpA-IgA peptides, to that of our previously identified UH-axSpA-IgG peptides.
Methods. IgA antibody reactivity against UH-axSpA-IgA.1, 3 and 10 and IgG antibody reactivity against UH-axSpA-IgG.4 and 8 was determined using ELISA in individual plasma samples of 70 early axSpA patients, 67 chronic low back pain (CLBP) patients and 115 HC from the UH cohort.
Results. Antibodies to the 3 UH-axSpA-IgA peptides (UH-axSpA-IgA.1, 3 and 10) were more present in early axSpA patients from the UH-cohort (20.0% (14/70) compared to CLBP (14.9% (10/67) and HC (12.2% (14/115). When further investigating antibody reactivity against a combination of UH-axSpA-IgA and UH-axSpA-IgG, we found that a panel composed of 2 UH-axSpA-IgA (UH-axSpA-IgA.1 and 10) and 2 UH-axSpA-IgG peptides (UH-axSpA-IgG.4 and 8) resulted in a sensitivity of 24.3% (17/70) and a corresponding specificity of 98.5% (1/67) in CLBP patients.
Conclusions. Testing for different antibody isotypes to novel UH-axSpA peptides shows promising biomarker potential in a larger subset of early axSpA patients, but further validation is necessary in independent cohorts.

Reference

1. QUADEN D *et al.*: *Arthritis Rheumatol* 2020.

P38

EFFICACY AND SAFETY OF NON-PHARMACOLOGICAL AND NON-BIOLOGICAL THERAPY: A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2022 UPDATE OF THE ASAS-EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF AXIAL SPONDYLOARTHRITIS

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Objectives. To update the evidence for non-biological treatments of axial spondyloarthritis (axSpA), as a basis for the 2022 ASAS-EULAR recommendations for the management of axSpA.
Materials and methods. A systematic literature review (SLR) (2016-2021) on efficacy and safety for non-pharmacological and non-biological treatments, was performed, up to 1st January 2022 (PROSPERO registration CRD42021261959). The research question was formulated according to the PICOT format: Population: adult patients with r-axSpA and nr-axSpA; Intervention: non-pharmacological and non-biological treatments; Comparator: active comparator or placebo; Outcomes: all relevant efficacy and safety outcomes; Type of studies: randomised controlled trials (RCTs) and observational studies (the latter for efficacy of non-pharmacological treatments and safety only). Cohen's effect size (ES) was calculated for non-pharmacological and risk ratio (RR) for pharmacological treatments.
Results. 107 publications were included. Studies on non-pharmacological interventions addressed, among other, education (n=8), exercise (n=20) and physiotherapy (n=15). The ES for education was small to moderate for disease activity, function, mobility (ES range: 0.03-0.59, 0.04-0.58, 0-0.54 respectively). Exercise and physiotherapy had small to high ES on the same outcomes (ranges for exercise:0.22-1.36, 0.04-1.08, 0.06-1.14; ranges for physiotherapy: 0.23-1.96, 0.15-1.54, -0.04-1.40). Studies on conventional synthetic disease-modifying antirheumatic drugs (csDMARDs, n=3), non-steroidal anti-inflammatory drugs (NSAIDs, n=8) and other drugs (n=12) did not provide new relevant evidence on efficacy or safety (e.g., efficacy of NSAIDs confirmed, and limited efficacy of short-term glucocorticoids shown in one RCT: ASAS20 RR 1.80; 95%CI: 0.87-3.70; ASAS40 RR 2.47,

P38. Table. Effect of tsDMARDs on ASAS20, ASAS40.

Outcome drug	N	Population	Time point (weeks)	Dose	Response treatment (%)	Response placebo (%)	RR (95% CI)	NNT
ASAS20								
Apremilast	460	r-axSpA	16	20 mg	35	37	0.95 (0.75-1.27)	N/A
				30 mg	33		0.89 (0.66-1.20)	N/A
Filgotinib	116	r-axSpA	12	200 mg	76	40	1.91 (1.35-2.71)	2.8
Tofacitinib	207	r-axSpA	12	2 mg	56	40	2.16 (1.14-4.09)	6.3
				5 mg	63		2.35 (1.25-4.41)	4.4
				10 mg	67		1.96 (1.02-3.77)	3.7
Tofacitinib	269	r-axSpA	16	5 mg	56	29	3.10 (1.90-5.07)	3.7
Upadacitinib	187	r-axSpA	14	15 mg	65	40	2.02 (1.36-3.01)	4.0
Nilotinib	17	axSpA	12	400 mg	NR	NR	NR	N/A
ASAS40								
Apremilast	460	r-axSpA	16	20 mg	36	32	1.14 (0.84-1.55)	N/A
				30 mg	34		1.06 (0.78-1.45)	N/A
Filgotinib	116	r-axSpA	12	200 mg	38	19	2.00 (1.07-3.74)	5.3
Tofacitinib	207	r-axSpA	12	2 mg	42	19	2.16 (1.14-4.09)	4.4
				5 mg	46		2.35 (1.25-4.41)	3.8
				10 mg	38		1.96 (1.02-3.77)	5.3
Tofacitinib	269	r-axSpA	16	5 mg	41	12	3.10 (1.90-5.07)	3.6
Upadacitinib	187	r-axSpA	14	15 mg	52	26	2.02 (1.36-3.01)	3.8
Nilotinib	17	axSpA	12	400 mg	NR	NR	NR	N/A

RR: risk ratio; CI: confidence interval; NNT: number needed to treat; NR: not reported; N/A: not applicable (number needed to treat not calculated for ineffective treatments).

95%CI 0.98-6.22). Six RCTs on 5 targeted synthetic DMARDs showed efficacy of tofacitinib, upadacitinib and filgotinib, only in r-axSpA (Table). Two RCTs showed that apremilast (Table) and nilotinib are not efficacious in r-axSpA (BASDAI50 more often reached in placebo -33%- than nilotinib -0%).
Conclusions. Education, exercise, physiotherapy and NSAIDs confirmed to be efficacious in axSpA. Tofacitinib, upadacitinib and filgotinib were proved efficacious in r-axSpA

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P39

UPREGULATION OF INNATE INFLAMMATORY PATHWAYS IN PERIPHERAL BLOOD DURING THE PRECLINICAL PHASE OF AXIAL SPONDYLOARTHRITIS

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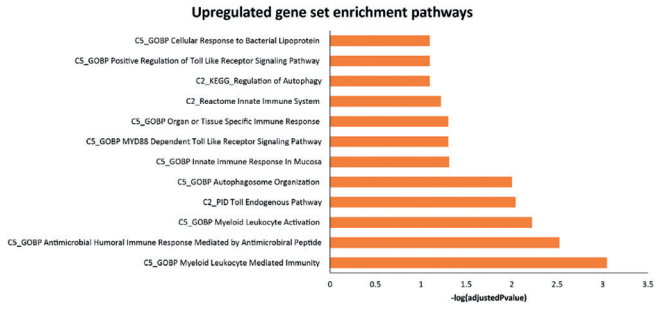
Introduction. The pathogenesis of spondyloarthritis (SpA) is incompletely understood. It is hypothesized that the clinical onset of SpA is preceded by a pre-clinical phase where specific molecular pathways are activated. This is supported by the presence of signs of subclinical inflammation on MRI of SI-joints in the Pre-SpA cohort of healthy first-degree relatives (FDR) of HLA-B27+ axial SpA patients and increased incidence of SpA in the first year of follow-up (1, 2).
Objectives. We aim to characterize the molecular pathways that are activated in the pre-clinical phase of SpA.
Methods. Whole blood bulk RNA sequencing (Illumina HiSeq 4000) was performed in four study groups (n=10, each) followed by gene set enrichment analysis of 21246 genes. The first group included baseline samples from participants of the Pre-SpA cohort who developed SpA during follow-up. The second group included baseline samples from participants of the Pre-SpA cohort who did not develop SpA. The third group included patients with established axSpA of the SPACE cohort (3). The fourth group included patients from the SPACE cohort with non-specific back pain**.**
Results. We observed an upregulation in innate inflammatory, autophagy related pathways and antimicrobial humoral immune response at baseline in FDRs who developed SpA (group 1) compared to those who did not (Fig. 1). An upregulation in innate inflammatory pathways and leukocyte transendothelial migration was seen in group 1 compared to patients with established axSpA. Moreover, an upregulation in innate inflammatory pathways, autophagy and unfolded protein responses was seen in group 1 compared to patients with non-specific back pain.



P39. Fig. 1. Upregulated gene set enrichment pathways. This figure shows a list of significantly upregulated gene sets in relation to molecular functions and canonical pathways at baseline in first degree relatives who developed the disease in comparison to those who did not. An upregulation of various pathways involved in innate immunity, humoral immune response and autophagy was observed.

Conclusions. Innate inflammatory, autophagy related pathways and humoral immune responses are specifically upregulated in at-risk individuals who later on develop axSpA, suggesting that these pathways are already active during the preclinical phase of disease. Future studies are required to investigate their potential as predictive biomarkers and targets for preventive therapy.

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P40

SPARCC, MASES, LEI AND MEI INDEXES CAPTURE DIFFERENT PATIENTS WITH ENTHESITIS IN AXIAL SPONDYLOARTHRITIS, PERIPHERAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS

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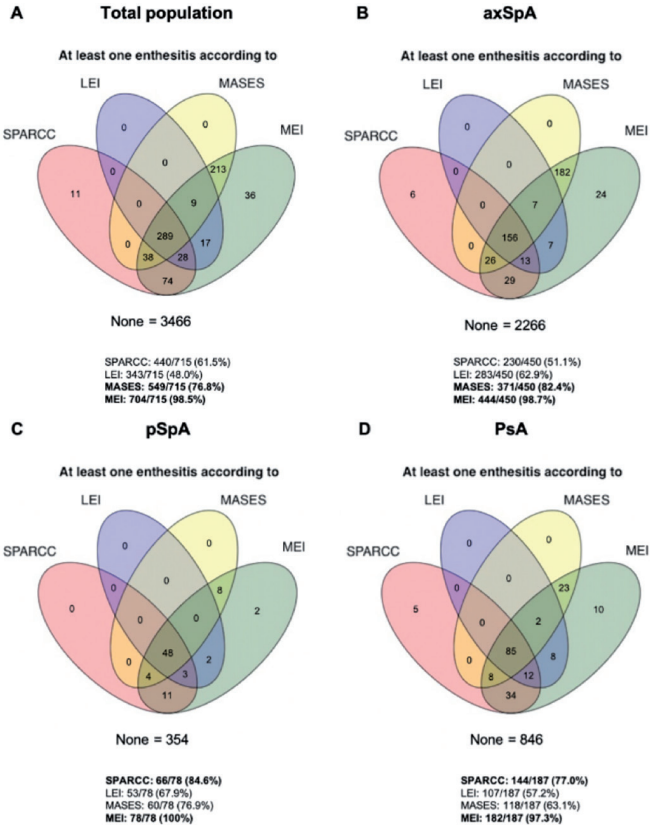
Introduction. Reliable clinical instruments have been developed to assess enthesitis in Spondyloarthritis (axial (axSpA), peripheral (pSpA) and psoriatic arthritis (PsA): SPARCC, LEI, MASES and MEI. The aim was to evaluate whether the prevalence of patients with at least one enthesitis across the three subtypes of SpA differs depending on the use of SPARCC, LEI, MASES and MEI indexes.



P40. Fig. 1. Prevalence of enthesitis captured by different indexes.

Methods. 4185 patients from the cross-sectional ASAS-PerSpA study with a diagnosis of axSpA (2719), pSpA (433) and PsA (1033) according to the Rheumatologist were included. The location of enthesitis during the study visit were evaluated according to the four indexes. The prevalence of patients with at least one enthesitis according to the different indexes were compared across the three diseases and pair-wise agreement between indexes were evaluated using the Cohen's kappa.
Results. In the overall population, 10.7%, 8.3%, 13.5% and 17.2% of patients showed at least one enthesitis according to the SPARCC, LEI, MASES and MEI indexes, respectively. Figure 1 shows that, among patients with axSpA, MEI and MASES indexes capture the majority of patients with at least one enthesitis (98.7% and 82.4%, respectively), while in pSpA and PsA, MEI and SPARCC are the indexes which capture the majority of patients with enthesitis (100% and 84.6% for MEI and SPARCC in pSpA, and 97.3% and 77% for MEI and SPARCC in PsA, respectively). In the total population, MASES and MEI showed the strongest agreement for patients with at least one enthesitis (absolute agreement 96.3%; Cohen's kappa: 0.86). Similarly results were found among axSpA patients (97.3%; 0.90). In pSpA patients, SPARCC and MEI showed the strongest agreement (97.2%; 0.90), as well as among PsA patients (95.4%; 0.82).
Conclusions. These results suggest that the prevalence of enthesitis across entities differs depending on the disease and on the use of the different index.

P41

TREATING SPONDYLOARTHRITIS EARLY: DOES IT MATTER? RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

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Objectives. To summarize the evidence on the relationship between symptom duration, disease duration or the presence of radiographic damage and treatment response in patients with axSpA treated with NSAIDs or b/tsDMARDs.
Methods. An SLR was conducted and supplemented by hand-searches. RCTs and cohort studies in axSpA addressing the impact of symptom/disease duration and presence of radiographic damage on treatment response were included. Based on the used cut-off of symptom/disease duration by each study or the presence of radiographic damage, groups of 'early' and 'established' disease were compared.
Two reviewers identified eligible studies and extracted the data. Relative risk (RR), relative risk ratio (RRR) and number needed to treat (NNT), and differences in differences were calculated.
Results. From the 8769 articles retrieved, 26 were included and 2 added by hand-search. Twenty-one studies (11 RCTs) compared groups based on symptom (n=6)/disease duration (n=15) and 7 (4 RCTs) based comparisons on absence/presence of radiographic damage.
When early axSpA was defined by symptom duration in RCTs (n=4), in nr-axSpA, early treatment was associated with higher RR and RRR and lower NNT for ASAS40 in two studies (Table I); a third study showed that patients with nr-axSpA achieving ASDAS-ID and ASAS-PR had shorter symptom duration than those not achieving this. Lastly, in one study including axSpA, no difference in treatment response was observed. When early axSpA was defined based on disease duration or radiographic damage, there was no difference in response to treatment between early and established axSpA.
Conclusions. When defining early axSpA based on symptom duration, in nr-axSpA, bDMARDs may lead to better outcomes compared to established disease whereas in one study on axSpA no difference is observed between early and established disease. When early axSpA is defined based on disease duration or radiographic damage no differences were found between the groups.

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P42

PLASMA EXOSOMAL MIRNAS IN ANKYLOSING SPONDYLITIS: PROSPECTS FOR BIOMARKERS

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Introduction. The cause of Ankylosing Spondylitis (AS) remains unclear. Among the genes associated with AS, HLA-B27 imparts the greatest risk and is present in 90% of patients. But there is one striking feature in this analysis: only 5% of B27-positive individuals develop AS. This has provided a compelling argument that epigenetic factors provide an important missing link in the genetic basis of AS. Micro RNAs (miRNA) are small non-coding RNAs that function as post-transcriptional regulators of gene expression by inhibiting the translation of messenger RNAs (mRNA). Pre-

P41. Table I. Assessment of treatment response in RCTs comparing patients with early vs established disease, with a stratification based on symptom duration.

Study	Population	Early vs established (years)	RR (early vs established)	RRR (95%IC)	NNTs (early vs established)
ASAS20					
Landewé 2014	axSpA	<5 vs ≥5	1.5 vs 1.5	0.96 (0.53-1.73)	5.5 vs 4.8
ASAS40					
Sieper 2012	nr-axSpA	<5 vs ≥5	8.2 vs 1.6	5.24 (1.12-24.41)	2.4 vs 9.1
Kay 2019	nr-axSpA	<5 vs ≥5	5.0 vs 3.3	1.52 (0.60-3.87)	2.1 vs 3.9
			3.6 vs 3.5	1.01 (0.46-2.20)	2.1 vs 2.9
ASDAS-MI					
Kay 2019	nr-axSpA	<5 vs ≥5	5.1 vs 6.5	0.78 (0.19-3.16)	2.7 vs 4.9
			7.1 vs 6.4	1.11 (0.34-3.66)	2.1 vs 3.0

Study	Population	Symptom duration		*p* value
		Responders	Non responders	
ASDAS-ID				
Sieper 2019	nr-axSpA	6.1±6.2	8.3±8.1	<0.001
ASAS-PR				
Sieper 2019	nr-axSpA	5.3±5.7	8.0±7.8	<0.001
Cell colours	In favor of early disease	In favor of established disease		Non significant

vious studies have revealed critical functions of miRNAs in the differentiation and function of helper T cells. Alterations of miRNAs in the circulation, inflammatory cell populations, or pathological samples of autoimmune diseases have also been documented. MiRNAs can be present in exosomes, which are extracellular vesicles smaller than 150 nm in diameter. Exosomes can affect the target cells via gene regulation, which is mediated by the transfer of miRNA. Gene regulation with exosomes, in which extrinsic miRNAs exert a direct effect on target genes in recipient cells, is regarded as a form of intercellular communication, which differs from conventional communication by cytokines and cell surface molecules. This study aims to demonstrate the critical involvement of exosomes in AS diseases.

Methods. To assess the value of exosomal miRNAs as biomarkers for AS, the expression of microRNAs was measured in a plasma fraction enriched in exosomes by differential centrifugation, using Illumina deep sequencing. Samples from 17 persons with a clinical diagnosis of AS dementia were compared to 10 controls. Although these samples contained less than 0.1 micrograms of total RNA, deep sequencing gave reliable and informative results.

Results. 18 miRNAs were identified to be differentially expressed in the exosomes in AS patients compared with HC. Of those, 2 miRNA were down-regulated (hsa-let-7b-5p, hsa-let-7c-5p) and 16 miRNA up-regulated (hsa-miR-1260b, hsa-miR-130a-5p, hsa-miR-140-3p, hsa-miR-145-3p, hsa-miR-22-5p, hsa-miR-2277-5p, hsa-miR-27a-3p, hsa-miR-29a-3p, hsa-miR-30c-5p, hsa-miR-330-5p, hsa-miR-345-5p, hsa-miR-4717-3p, hsa-miR-500a-3p, hsa-miR-502-3p, hsa-miR-598-3p, hsa-miR-6810-3p).

Conclusions. Circulating Exosomal miRNA with other data is likely to provide informative and robust Diagnostic Biomarkers in AS disease.

P43

ANKYLOSING SPONDYLITIS AND THE RISK OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASES: A TWO-SAMPLE MENDELIAN RANDOMIZATION STUDY

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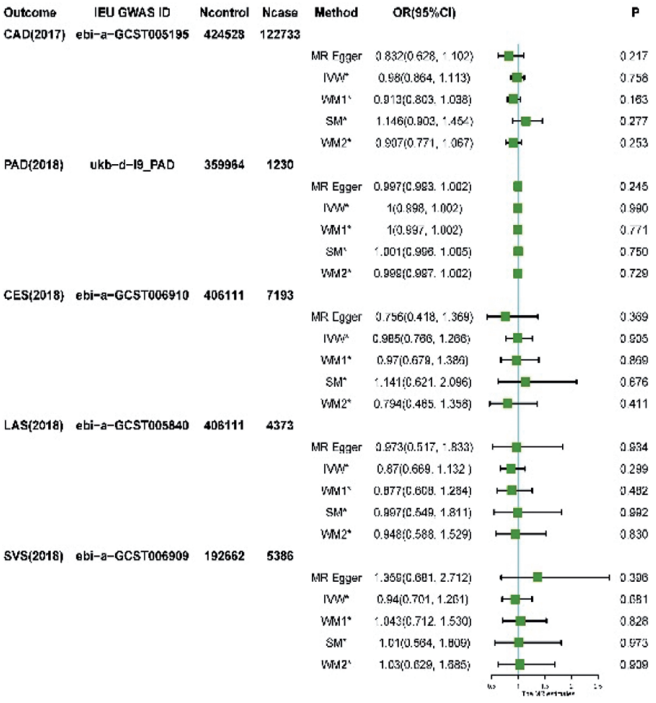
Introduction. In the past decades, observational studies have found atherosclerotic cardiovascular diseases (ASCVDs) as common comorbidities in ankylosing spondylitis (AS). However, the causal relationship between AS and ASCVDs has not yet been elucidated. Our aim was to infer the causality between them.

Methods. Two-sample Mendelian randomization analysis was implemented by integrating the genome-wide association (GWAS) summary datasets (listed in Table I) of AS and five kinds of ASCVDs [coronary artery diseases (CAD), peripheral artery diseases (PAD), large-artery stroke (LAS), small-vessel stroke (SVS), and cardioembolism stroke (CES)] to assess causality. To ensure the robustness of results, multiple sensitivity analyses were applied, including the heterogeneity test, the pleiotropy test and leave-one-out analysis.

Results. 19 AS-related SNPs were extracted as instrumented variables (IVs). The MR results were shown in Table II and Figure 1. The IVW method has indicated no causality between AS and the risk of CAD (OR=0.980, 95% CI: 0.863-1.112, p=0.76) or PAD (OR=1.000, 95% CI: 0.998-1.001, p=0.99), in line with other MR methods. Likewise, all MR methods have supported that the increasing risk of AS was not causally linked to any type of stroke (LAS: OR=0.870, 95% CI: 0.668-1.131, p=0.29; CES: OR=0.984, 95% CI: 0.766-1.266, p=0.90; SVS: OR=0.940, 95% CI: 0.701-1.261, p=0.68). The heterogeneity test has found no heterogeneity between IVs except for CAD (CAD: Cochrane's Q test: p<0.05). Leave-one-out analysis has demonstrated that the pooled MR effect estimates were not affected by any individual SNP. Overall, multiple complementary sensitivity analyses have proven the robustness of our MR results.

P43. Table I. The GWAS Summary datasets used for Mendelian analysis.

Phenotype	Year	nControl	nCase	nIVs	Ancestry	IEU GWAS ID
AS	2013	1550	9069	-	European	ebi-a-GCST005529
CAD	2017	424,528	122,733	19	European	ebi-a-GCST005195
PAD	2018	359,964	1,230	19	European	ukb-d-I9_PAD
LAS	2018	406,111	4,373	19	European	ebi-a-GCST005840
SVS	2018	192,662	5,386	19	European	ebi-a-GCST006909
CES	2018	406,111	7,193	19	European	ebi-a-GCST006910



P43. Fig. 1. The forest plot of Mendelian randomization analysis.

Conclusions. There was no proof that AS was a direct cause of ASCVD. Given the mediation of systemic inflammation and antirheumatic drugs, cardiovascular management in AS patients still warrants additional attention.

P44

A DEEP LEARNING FRAMEWORK FOR MRI DETECTION OF ACTIVE INFLAMMATORY AND STRUCTURAL CHANGES IN THE SACROILIAC JOINT CONSISTENT WITH AXIAL SPONDYLOARTHRITIS

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Background. Magnetic resonance tomography (MRI) plays a key role in the early diagnosis of axial spondyloarthritis (axSpA). However, the detection of changes indicative of axSpA requires specific expertise, which poses a challenge to non-specialized centers. Deep learning (an advanced machine learning method) based on training an artificial neural network may facilitate and support diagnostics in clinical practice.

Objective. To create a reliable deep learning tool for the detection of active inflammatory and structural changes indicative of axSpA on MRI of sacroiliac joints.

Methods. In this study, MRIs of sacroiliac joints from 477 patients from four cohorts (GESPIC-AS, GESPIC-Crohn, GESPIC-Uveitis and OptiRef comprising 266 patients with and 211 without axSpA) were used to develop a deep learning framework (randomly divided into training, n=404, and validation, n=73, datasets). MRIs from the ASAS cohort (n=116) were

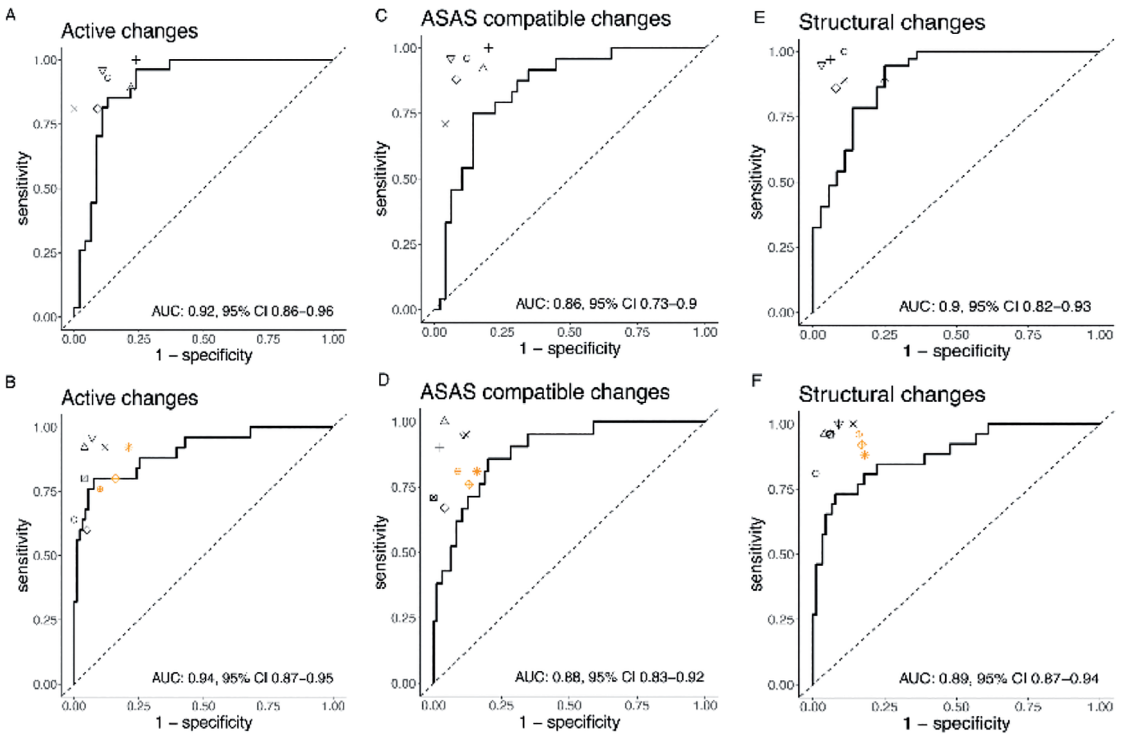
P43. Table II. The results of Mendelian randomization analysis.

Outcomes	Two-sample Mendelian analysis					Heterogeneity test			Pleiotropy test	
	Method	b	*p*-value	OR	95%CI	Q	Q_df	*p*-value	Intercept	*p*-value
CAD*	**MR Egger**	-0.184	0.217	0.832	0.628, 1.102	36.805	17	0.004	0.008	0.22
	IVW*	-0.020	0.758	0.980	0.864, 1.113	40.32	18	0.002		
	WM1*	-0.091	0.163	0.913	0.803, 1.038					
	SM*	0.136	0.277	1.146	0.903, 1.454					
	WM2*	-0.098	0.253	0.907	0.771, 1.067					
PAD*	**MR Egger**	-0.003	0.245	0.997	0.993, 1.002	20.944	17	0.229	0	0.194
	IVW	0.000	0.990	1.000	0.998, 1.002	23.193	18	0.183		
	WM1	0.000	0.771	1.000	0.997, 1.002					
	SM	0.001	0.750	1.001	0.996, 1.005					
	WM2	-0.001	0.729	0.999	0.997, 1.002					
CES*	**MR Egger**	-0.279	0.369	0.756	0.418, 1.369	17.793	17	0.402	0.012	0.349
	IVW	-0.015	0.905	0.985	0.766, 1.266	18.765	18	0.406		
	WM1	-0.030	0.869	0.970	0.679, 1.386					
	SM	0.132	0.676	1.141	0.621, 2.096					
	WM2	-0.230	0.411	0.794	0.465, 1.358					
LAS*	**MR Egger**	-0.027	0.934	0.973	0.517, 1.833	14.814	17	0.609	-0.005	0.707
	IVW	-0.139	0.299	0.870	0.669, 1.132	14.96	18	0.665		
	WM1	-0.131	0.482	0.877	0.608, 1.264					
	SM	-0.003	0.992	0.997	0.549, 1.811					
	WM2	-0.053	0.830	0.948	0.588, 1.529					
SVS*	**MR Egger**	0.307	0.396	1.359	0.681, 2.712	7.135	17	0.982	-0.017	0.264
	IVW	-0.061	0.681	0.940	0.701, 1.261	8.469	18	0.971		
	WM1	0.042	0.828	1.043	0.712, 1.530					
	SM	0.010	0.973	1.010	0.564, 1.809					
	WM2	0.029	0.909	1.030	0.629, 1.685					

*CAD: coronary artery disease; *PAD: peripheral artery disease; *CES: ischemic stroke (cardioembolic); *LAS: ischemic stroke (large artery atherosclerosis); *SVS: ischemic stroke (small-vessel); *IVW: inverse variance weighted; *WM1: weighted median; *SM: simple mode; *WM2: weighted mode.

used for independent testing (test dataset). Each examination in the training/validation dataset was evaluated for the presence of active inflammatory and structural changes indicative of SpA by six experienced, trained and calibrated readers and by seven expert readers in the test dataset. The presence of the changes was defined as the majority vote amongst readers. Discordant cases in the training/validation dataset underwent consensus reading. In addition, the test dataset was evaluated by three radiologists not specifically trained in SpA. Diagnostic performance was evaluated using the area under the receiver operating characteristic curve (AUC), accuracy, sensitivity and specificity.

Results. The prevalence of positive imaging findings for active inflammatory/structural changes indicative of axSpA was 41%/51% in the training/validation dataset and 22%/22% in the test dataset. The model for the detection of active inflammatory changes showed an AUC of 0.91 (0.83 – 0.97) – Figure 1 – and an accuracy of 84% on the validation dataset; the corresponding sensitivity and specificity were 96% and 76%, respectively. Despite a substantially lower prevalence of active inflammatory changes in the test dataset, the model showed good generalization with an AUC of 0.91 (0.84–0.97) and an accuracy of 75%; the sensitivity and specificity were 88% and 71%, respectively. The model demonstrated a similar perfor-



P44. Fig. 1. ROC curves and associated AUCs for model performance compared to the individual human experts.
A, **C** and **E** represent the ROC curves for diagnostic performance on the validation dataset, while the ROC curves for the test dataset are given in **B**, **D** and **F**.
The model performance did not exceed that of the trained experts (black symbols) but came close, especially for the detection of active inflammatory changes.
The performance of three board-certified radiologists who did not undergo specific training for axSpA imaging is indicated by the orange symbols in **B**, **D** and **F**.

mance on the validation and test datasets for the detection of active inflammatory changes fulfilling the ASAS definition. The model for the detection of structural changes indicative of axSpA showed good performance on the validation dataset with an AUC of 0.90 (0.82-0.96) for the detection of structural changes and an overall accuracy of 85%. The associated sensitivity and specificity were 95% and 75%, respectively. The model showed reasonable generalization to new data with an AUC of 0.89 (0.81–0.96) and an accuracy of 79%; the sensitivity and specificity were 85% and 78%, respectively. Overall, the model performed close to the individual human experts - Figure 1.

Conclusions. The developed framework allowed the detection of active inflammatory and structural changes indicative of axSpA on MRI. This approach may be used as an assistant tool in the diagnostic workflow.

P45

TREAT-TO-TARGET STRATEGY IMPLEMENTATION IN SPONDYLOARTHRITIS PATIENTS OF REAL-WORLD CLINICAL PRACTICE REMAINS LIMITED DESPITE HIGH DISEASE ACTIVITY LEVELS: A CROSS-SECTIONAL SINGLE-CENTER STUDY

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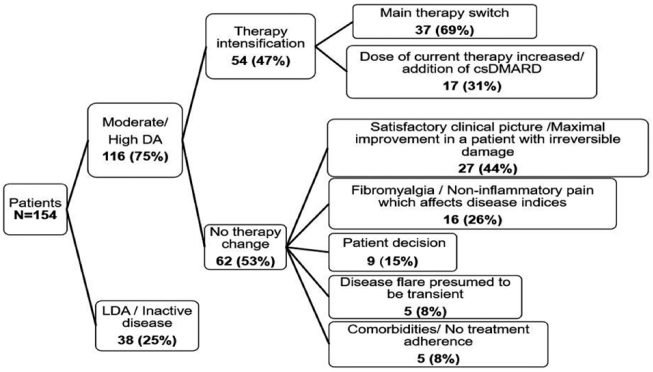
Introduction. The adoption of the treat-to-target (T2T) approach aiming at inactive disease (ID), or low disease activity (LDA) in axial (axSpA) and peripheral Spondyloarthritis (perSpA) is not well documented in clinical practice. Our aims were to assess the level of disease activity of SpA patients in real-world practice, the extent of T2T strategy implementation and the reasons of possible non-implementation.

Methods. Cross-sectional study in the University Hospital of Heraklion. All consecutive patients with SpA who visit the outpatient department or the one-day infusions' clinic during a 7-month period are included, after their consent. Detailed patient characteristics are collected, as well as questionnaires to physicians regarding treatment intensification or not (and reasons). For the present work, we analyzed patients included during the first 3 months of the study.

P45. Table. Patients' and disease characteristics, disease activity and patient function.

All patients, n	154	
Male gender, n (%)	92	(60)
Age (years), Median (IQR)	54	(43-63)
Disease duration from diagnosis (years), median (IQR)	3.2	(1.5 – 9.7)
Diagnosis: AxSpA, n (%)	112	(73)
with psoriasis, N	20	
with inflammatory Bowel Disease, n	13	
Peripheral SpA, n (%)	42	(27)
with psoriasis	28	
with inflammatory bowel disease	8	
Main therapy at current visit, n (%): csDMARDs	14	(9)
bDMARDs	117	(76)
NSAIDs only	13	(8)
No treatment	10	(7)
Nr of previous cs/bDMARDs, median (IQR)	1	(0-3)
Baseline total non-rheumatologic comorbidities, median (IQR)	3	(1-5)
Coexisting fibromyalgia, n (%)	41	(27)
Ever smokers, n (%)	95	(62)
BMI, Median (IQR)	29.5	(25 –33)
ASDAS-CRP, Median (IQR) *	2.5	(1.8-3.3)
ASDAS-CRP <2.1 (Low disease activity), n (%) *	36	(32)
ASDAS-CRP <1.3 (Remission), n (%) *	8	(7)
BASDAI, Median (IQR) *	4.6	(2.6-6.4)
BASFI, median (IQR) *	3.9	(1.8-6.3)
CRP (mg/dl), Median (IQR)	0.34	(0.2-0.6)
DAPSA Median (IQR) **	17.4	(9.3-28.8)
DAPSA <15 (Low disease activity), n (%) **	49	(43)
DAPSA <5 (Remission), N (%) **	11	(10)
PsA patients with Minimal Disease Activity (MDA), n (%) #	11	(18)
HAQ (0-3), Median (IQR)	0.6	(0.2-1)
ASAS-Health Index, Median (IQR)	7	(4-11)
PSAID, Median (IQR) #	3.8	(2.0-5.6)

*In patients with AxSpA, **In peripheral SpA and AxSpA patients with peripheral involvement, #In patients with psoriatic arthritis.



P45. Fig. 1. Level of disease activity, type of therapy intensifications and reasons of non-intensification if target not reached [n (%) of patients].

Results. We analyzed 154 patients (axSpA:112, perSpA:42), 76% of which were on a biologic (b-)DMARD therapy (Table). In axSpA, LDA and ID based on ASDAS-CRP was found in 32% and 7% of the patients respectively. However, when peripheral arthritis (DAPSA) and extraarticular manifestations were taken into account ("Complete" LDA or ID) the respective numbers were 25% and 7%. In perSpA, LDA and remission based on DAPSA was found in 29% and 12%, while "Complete" LDA and remission were seen in 24% and 12% respectively. Of the patients not having at least "Complete" LDA (N=116), 54(47%) had their treatment intensified. Physician-documented reasons of non-intensification are in Figure. In multivariable logistic regression analysis, the type of patients' main therapy [OR(95%CI) for non-bDMARD vs bDMARD:12.9 (3.7-44.4)] and physician's VAS [OR:1.10 (1.06-1.14)] were predicting therapy intensifications in patients not in target.

Conclusions. In this real-world study, the majority of SpA patients had high disease activity levels. T2T was implemented in less than half of those patients, especially those on non-biologic main therapy and high physician VAS score.

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P46

SAFETY OF GUSELKUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS WHO ARE BIO-NAIVE OR TNFI-EXPERIENCED: POOLED RESULTS FROM 4 RANDOMIZED CLINICAL TRIALS THROUGH 2 YEARS

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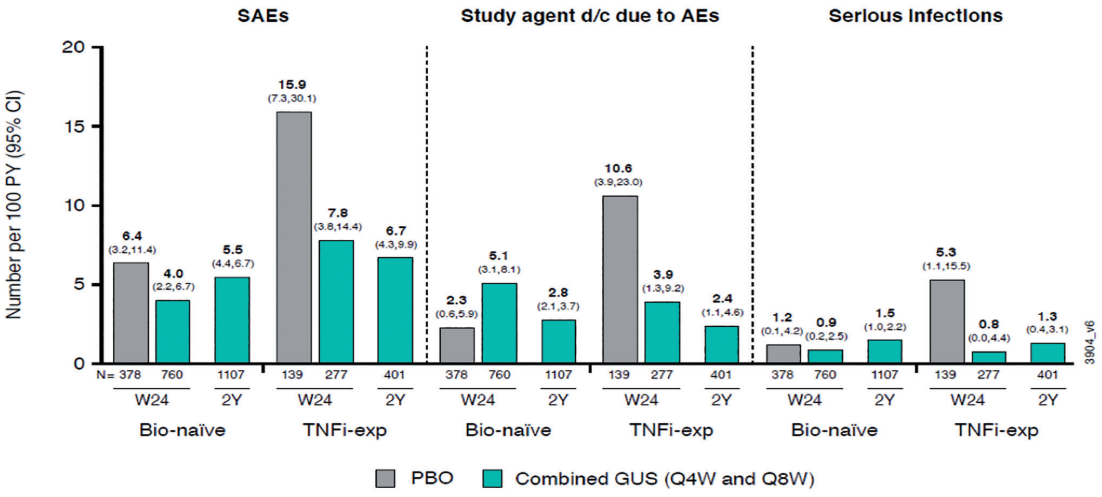
Introduction. Guselkumab (GUS), a selective IL-23p19 subunit inhibitor, demonstrated efficacy and a favorable safety profile in active psoriatic arthritis (PsA) in the phase-2, phase-3 (DISCOVER-1&2), and phase-3b COSMOS randomized controlled trials (RCTs). This study assessed GUS safety through 2-years in biologic-naive and tumor necrosis factor inhibitor (TNFi)-

P46. Table. Overall treatment-emergent AEs.

	PBO-controlled (W0-24)[a]				Through up to 2Y		
	PBO[b] (n=517)	GUS Q8W (n=664)	GUS Q4W (n=373)	Combined (n=1037)	GUSGUS Q8W (n=664)	GUS Q4W (n=373)	Combined GUS[c] (n=1508)
Total (median) PY	230 (0.5)	305 (0.5)	172 (0.5)	478 (0.5)	941 (1.1)	645 (2.1)	2125 (1.2)
Events/100 PY (95% CI)							
AEs	223 (204, 243)	233 (216, 250)	223 (201, 246)	229 (216, 243)	164 (156, 172)	139 (130, 148)	146 (141, 151)
SAEs	8.7 (5.3, 13)	4.9 (2.8, 8.1)	5.2 (2.4, 9.9)	5.0 (3.2, 7.5)	6.4 (4.9, 8.2)	4.7 (3.1, 6.6)	5.7 (4.7, 6.8)
AEs leading to study agent d/c	4.4 (2.1, 8.0)	3.6 (1.8, 6.5)	7.0 (3.6, 12.2)	4.8 (3.1, 7.2)	2.6 (1.6, 3.8)	2.9 (1.8, 4.6)	2.7 (2.1, 3.5)
Infections	59 (50, 70)	56 (48, 65)	57 (47, 70)	57 (50, 64)	43 (38, 47)	37 (33, 42)	39 (36, 42)
Serious infections	2.2 (0.71, 5.1)	0.33 (0.01, 1.8)	1.7 (0.36, 5.1)	0.84 (0.23, 2.1)	1.7 (0.97, 2.8)	0.77 (0.25, 1.8)	1.5 (1.0, 2.1)
Malignancy	0.44 (0.01, 2.4)	0.98 (0.20, 2.9)	0.00 (0.00, 1.7)	0.63 (0.13, 1.8)	0.42 (0.12, 1.1)	0.00 (0.00, 0.46)	0.28 (0.10, 0.61)
MACE	0.44 (0.01, 2.4)	0.33 (0.01, 1.8)	0.58 (0.01, 3.2)	0.42 (0.05, 1.5)	0.21 (0.03, 0.77)	0.46 (0.10, 1.4)	0.24 (0.08, 0.55)
GI-related SAEs	1.3 (0.27, 3.8)	0.33 (0.01, 1.8)	0.00 (0.00, 1.7)	0.21 (0.01, 1.2)	0.32 (0.07, 0.93)	0.46 (0.10, 1.4)	0.28 (0.10, 0.61)
OIs	0.00 (0.00, 1.3)	0.00 (0.00, 0.98)	0.00 (0.00, 1.7)	0.00(0.00, 0.63)	0.21 (0.03, 0.77)	0.00 (0.00, 0.46)	0.14 (0.03, 0.41)

MedDRA version 23.1. [a] Includes safety follow-up data through 2Y for pts who d/c study agent prior to W24 and did not receive any study agent at or after W24. [b] Includes data prior to GUS in PBO pts who switched from PBO to GUS. [c] Includes PBO to GUS cross-over at W24.
AEs, adverse events; CI, confidence interval; d/c, discontinuation; GI, gastrointestinal; GUS, guselkumab; MACE, major adverse cardiovascular events; OIs, opportunistic infections; PBO, placebo; PY, number of events/100 patient-years of follow-up; Q4W, every 4 weeks; Q8W, every 8 weeks; SAEs, serious adverse events; W, week; Y, year.



P46. Fig. 1. Summary of Select Treatment-emergent AEs Through 2Y: Bio-naive vs. TNFi-exp at Baseline.
AEs: adverse events; bio-naive: biologic-naive; CI: confidence interval; d/c: discontinuation; GUS: guselkumab; PBO: placebo; PY: number of events/100 patient-years of follow-up; Q4W: every 4 weeks; Q8W: every 8 weeks; SAEs: serious adverse events; TNFi-exp: tumor necrosis factor inhibitor-experienced;
W: week; Y: year.

experienced active PsA patients pooled across four RCTs (Week [W]56: phase-2 and COSMOS; W60: DISCOVER-1; W112: DISCOVER-2).
Methods. Patients in COSMOS had inadequate response to 1-2 prior TNFi; 9% of phase-2 patients and 30% of DISCOVER-1 patients had 1-2 prior TNFi; DISCOVER-2 patients were biologic-naive. Incidence rates of adverse events (AEs) were summarized among all treated patients for placebo-controlled (W0-24) and active treatment periods through 2-years (max exposure duration: 100W) according to actual treatment received, calculated as number of events/100 patient-year of follow-up (PY). Gastrointestinal-related serious AEs (SAEs) were identified using the MedDRA system-organ class; major adverse cardiovascular events (predefined as myocardial infarction/stroke/cardiovascular death) and opportunistic infections were identified through medical review.
Results. Across the four RCTs, 1508 patients with active PsA received GUS 100mg every 4-weeks or every 8-weeks and were followed for a median of 1.2-years, representing 2125 PY. In the overall population (N=1554), including placebo-treated patients that discontinued study agent before W24, 1138 patients were biologic-naive and 416 patients were TNFi-experienced. Among all treated patients, the overall GUS safety profile was generally consistent with that of placebo through W24; rates remained low through 2-years of GUS (Table). The GUS safety profile was similar to placebo within the biologic-naive and TNFi-experienced cohorts through W24. Incidence rates of AEs were generally consistent between cohorts in GUS-treated patients, whereas TNFi-experienced placebo-treated patients had more SAEs, study agent discontinuation due to AEs, and serious infections than biologic-naive placebo patients (Figure).
Conclusions. The favorable GUS safety profile demonstrated through W24 persisted through 2-years across biologic-naive and TNFi-experienced patients.

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P47

LOW RATES OF RADIOGRAPHIC PROGRESSION WITH 2 YEARS OF GUSELKUMAB, A SELECTIVE INHIBITOR OF THE INTERLEUKIN-23P19 SUBUNIT: RESULTS FROM A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF BIOLOGIC-NAIVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Introduction. Guselkumab (GUS, an IL-23p19-subunit inhibitor) 100mg every-4-weeks/every-8-weeks (Q4W/Q8W) significantly improved joint/skin symptoms in DISCOVER-2 patients with active psoriatic arthritis (PsA). We reported details of radiographic assessments comprising Reading Session 3 through W100 of DISCOVER-2, including relationships between radiographic changes and clinical outcomes.

Methods. Biologic-naive adults with active PsA (≥5 swollen joints/≥5 tender joints/CRP≥0.6mg/dL) were randomized (1:1:1) to GUS-100mg Q4W; GUS-100mg at W0/W4/Q8W; or placebo with crossover to GUS-100mg Q4W (placebo→Q4W) at W24, all through W100. Radiographic Reading Session 3 included assessments at W0/W24/W52/W100 (or at discontinuation after W52) from patients continuing treatment at W52; readers were blinded to treatment group/timepoint. Mean changes in total PsA-modified van der Heijde-Sharp (vdH-S)/joint space narrowing (JSN)/erosion scores were reported. Changes in total vdH-S scores from W0-100 were determined in patients who did/did not achieve clinical response at W100, assessed by ACR20/50/70/low disease activity (LDA) based on Disease Activity in PsA (DAPSA; ≤14)/PsA Disease Activity Score (PASDAS; ≤3.2)/minimal disease activity (MDA)/normalized HAQ-DI score (<0.5).

Results. Of 739 enrolled/treated patients, 664 had evaluable Reading Session 3 data/629 had evaluable data from W52-100. Mean baseline vdH-S scores were 28.0(Q4W)/23.9(Q8W)/25.6 (placebo→Q4W). Mean joint damage progression from W0-24 was numerically lower in GUS-treated than placebo-treated patients for erosion/JSN/vdH-S scores (Table), consistent with Reading Session 1 results. Mean radiographic score changes from W52-100 indicated low radiographic progression rates across GUS-groups. Among GUS-randomized patients, mean changes in vdH-S score from W0-100 were numerically lower for patients achieving clinical response (assessed by ACR20/50/70/DAPSA-LDA/PASDAS-LDA/MDA/HAQ-DI<0.5) versus nonresponders at W100 (Figure).

Conclusions. In biologic-naive patients with active PsA enriched for greater risk of radiographic progression, GUS-100mg (Q4W/Q8W) was associated with low rates of radiographic progression through 2-years. Patients achieving clinical response across several global measures of disease activity or normalized physical function at W100 had lower mean changes in total PsA-modified vdH-S scores versus nonresponders.

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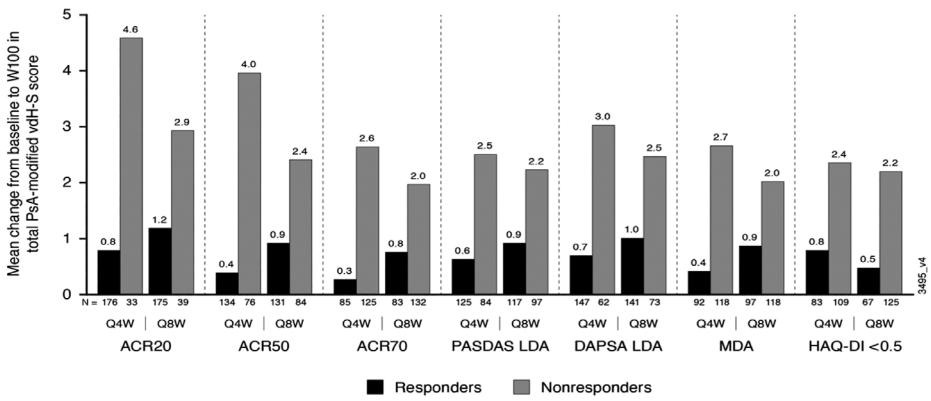
P47. Table. Observed erosion, joint space narrowing, and total PsA-modified vdH-S scores through W100 of DISCOVER-2.

	GUS Q4W			GUS Q8W			PBO→GUS Q4W		
Baseline PsA-modified vdH-S score, n	221			228			215		
Erosion	14.2 (23.3)			12.0 (21.9)			12.1 (21.9)		
Joint space narrowing	13.8 (21.8)			11.9 (19.5)			13.5 (21.6)		
Total	28.0 (43.6)			23.9 (40.4)			25.6 (42.4)		
Mean (SD) change in PsA-modified vdH-S score	**W0-24 n=221**	**W24-52 n=221**	**W52-100 n=211**	**W0-24 n=228**	**W24-52 n=228**	**W52-100 n=216**	**W0-24 n=215**	**W24-52 n=213**	**W52-100 n=202**
Erosion	0.27(1.91)	0.36(1.77)	0.45(2.90)	0.51(1.96)	0.20(1.24)	0.26(1.75)	0.73(2.20)	0.25(1.85)	0.09(1.98)
Joint space narrowing	0.21(1.17)	0.21(1.11)	0.30(1.32)	0.17(0.69)	0.12(0.66)	0.20(0.92)	0.39 1.72)	0.09(1.11)	0.04(1.90)
Total	0.48(2.70)	0.57(2.66)	0.75(4.02)	0.68(2.36)	0.31(1.57)	0.46(2.42)	1.12(3.80)	0.34(2.79)	0.13(3.74)

Data presented as mean (standard deviation).
GUS: guselkumab; PsA: psoriatic arthritis; Q4W: every 4 weeks; Q8W: every 8 weeks; SD: standard deviation; vdH-S: van der Heijde-Sharp; W: week.



P47. Fig. 1. Mean changes in PsA-modified total vdH-S score from W0-100 for patients who did and did not achieve select clinical responses at W100.
ACR20/50/70: American College of Rheumatology 20/50/70% improvement criteria; DAPSA: Disease Activity in Psoriatic Arthritis; HAQ-DI: Health Assessment Questionnaire-Disability Index; LDA: low disease activity; MDA: minimal disease activity; PASDAS: Psoriatic Arthritis Disease Activity Score; PsA: psoriatic arthritis; Q4W: every 4 weeks; Q8W: every 8 weeks; vdH-S: van der Heijde-Sharp; W: week.

Company, Janssen, and UCB; and consulting fees from AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB; **P. Rahman**: grants from Janssen and Novartis; personal fees from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Roche, and UCB; speakers bureau for AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB; **A.P. Kollmeier**, **X.L. Xu**, and **S. Sheng**: employees of Janssen Research & Development, LLC and may own stock or stock options in Johnson and Johnson; **Y. Jiang**: employee of Cytel, Inc. providing statistical support (funded by Janssen); **M. Shawi** and **F. Lavie**: employees of Janssen Global Services, LLC, and may own stock or stock options in Johnson & Johnson; **S.D. Chakravarty**: employee of Janssen Scientific Affairs, LLC may and own stock or stock options in Johnson & Johnson; **D. van der Heijde**: consulting fees from AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, and UCB Pharma; and serves as the director of Imaging and Rheumatology BV.

P48

CONSISTENT LONG-TERM GUSELKUMAB EFFICACY ACROSS PSORIATIC ARTHRITIS DOMAINS IRRESPECTIVE OF BASELINE PATIENT CHARACTERISTICS

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Introduction. In DISCOVER-1&2 studies, guselkumab (GUS) significantly improved joint symptoms/skin disease/enthesitis/dactylitis/physical function/quality-of-life through Week (W)52 in psoriatic arthritis (PsA) patients, regardless of baseline patient demographics/disease characteristics/conventional synthetic disease-modifying antirheumatic drug (csDMARD) use. This study assessed baseline predictors of, and by baseline patient subgroups, GUS efficacy across PsA disease domains through W100 of DISCOVER-2.

Methods. Biologic-naive adults with active PsA despite standard therapies (swollen/tender joint count [SJC/TJC]≥5, respectively, C-reactive protein [CRP]≥0.6mg/dL) were randomized 1:1:1 to GUS-100mg every-4-weeks (Q4W); GUS-100mg at W0/W4 then Q8W; or placebo. GUS effects on joint/skin/enthesitis/dactylitis/spinal pain/disease severity endpoints (change in Disease Activity in PsA [DAPSA]/SJC/TJC/Psoriasis Area Severity Index [PASI; baseline IGA≥2/BSA with psoriasis≥3%]/Leeds enthesitis index [LEI]/dactylitis/spinal pain/PsA Disease Activity Score [PASDAS], respectively) at W100 were evaluated for GUS-randomized patients by treatment group and by pooling patients across Q4W+Q8W. A multivariate linear model adjusting for baseline patient characteristics assessed associations between baseline predictors and changes in DAPSA/PASI/LEI scores, and least-squares mean changes in all continuous endpoints from baseline to W100 within patient subgroups defined by baseline sex/BMI/PsA duration/SJC/TJC/CRP/%BSA/PASI score/csDMARD use.

Results. 442(90%) GUS-randomized patients completed study treatment through W100. PsA duration (p=0.032)/SJC (p<0.001)/TJC (p<0.001) were significant predictors of long-term (baseline to W100) DAPSA score change; %BSA (p=0.002)/PASI (p<0.001)/SJC (p=0.008)/csDMARD use (p=0.014) were significant predictors of long-term PASI score change; none significantly predicted long-term LEI score change among pooled GUS patients (Fig.). Statistically significant improvements from baseline to W100 in DAPSA/PASI/ LEI scores were observed across all baseline strata, including those indicating more extensive/severe disease, in pooled GUS Q4W+Q8W patients (Fig, all p<0.001) and within each dosing group. Similar improvements were o.bserved for other continuous endpoints assessed (change in PASDAS/SJC/TJC/spinal pain/dactylitis score).

Conclusions. GUS significantly improved PsA signs and symptoms through W100 across all baseline patient subgroups evaluated, including patients with highly active disease, and regardless of dosing regimen.

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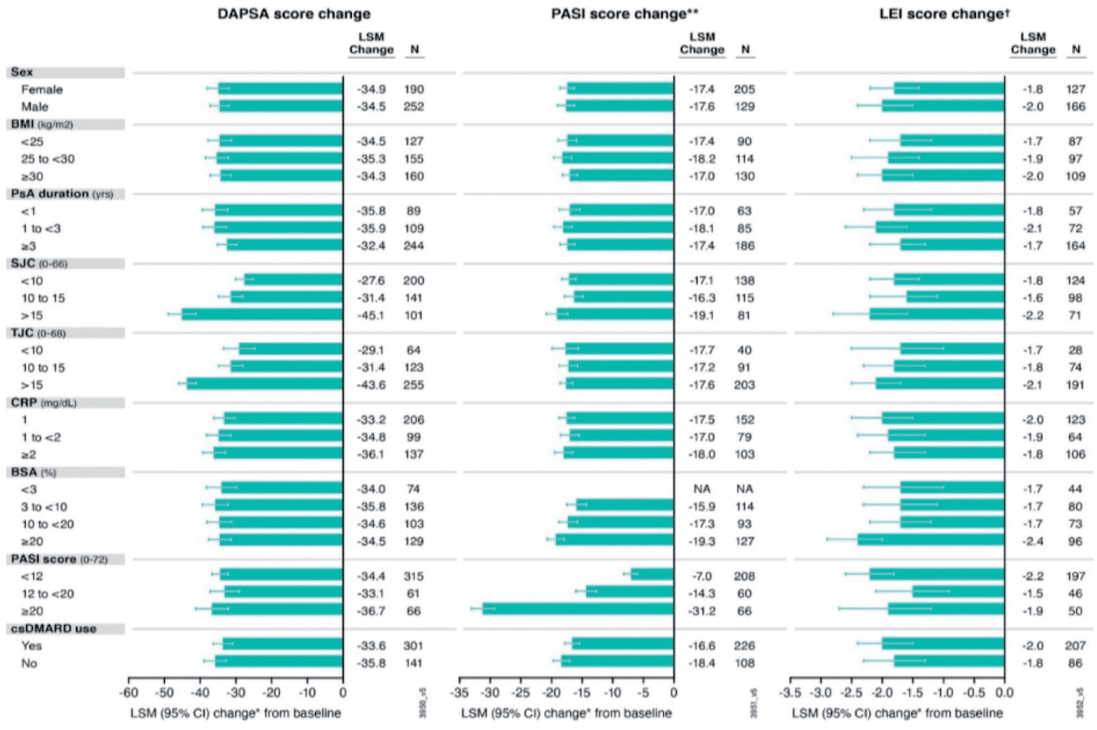

P48. Fig. 1. LSM (95% CI) Change* in DAPSA (0-4 [remission], 5-14 [low], 15-28 [moderate], >28 [high]), PASI (0-72)**, and LEI (0-6) A scores from BL at W100 by BL patient subgroups among pooled GUS patients.
*Derived from a multivariate linear model adjusting for BL subgroups; all p-values comparing LSM change from BL at W100 are p<0.001.
**Among pts with BL IGA ≥2 and BSA with PsO ≥3%.
†Among pts with enthesitis and an available LEI score at BL.
BL: baseline; BMI: body mass index; BSA: body surface area; CI: confidence interval; CRP: C-reactive protein; csDMARD: conventional synthetic disease-modifying antirheumatic drug; DAPSA: Disease Activity in PsA; GUS: guselkumab; IGA: Investigator's Global Assessment; LEI: Leeds Enthesitis Index; LSM: least-squares mean; PASI: Psoriasis Area Severity Index; PsA: psoriatic arthritis; PsO: psoriasis; SJC: swollen joint count; TJC: tender joint count; W: week.

Celgene, CoreVitas, Eli Lilly, Gilead, Janssen, Pfizer, and Sun Pharma; consulting fees from AbbVie, Eli Lilly, Janssen, Novartis, and Pfizer; speakers bureau fees from AbbVie, Amgen, BMS, Eli Lilly, Janssen and Pfizer; advisory board fees from BMS, Eli Lilly, Gilead, Janssen, Novartis, and Pfizer; **ES:** Consultant for Janssen; research grants from Janssen; **JFM:** Consultant and/or investigator for AbbVie, Arena, Biogen, Bristol Myers Squibb, Dermavant, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, and UCB; **SDC:** Employee of Janssen Scientific Affairs, LLC and may own stock or stock options in Johnson & Johnson; **ER:** Consultant for Janssen; employee of JSS Medical Research; **NJS:** Employee of Janssen Scientific Affairs, LLC and owns stock or stock options in Johnson & Johnson, AbbVie, and Gilead; **APK** and **XLX:** Employees of Janssen Research & Development, LLC, and may own stock or stock options in Johnson & Johnson; **MS** and **FL:** Employees of Janssen Pharmaceutical Companies of Johnson & Johnson, and may own stock or stock options in Johnson & Johnson; **PB:** Speaker honoraria from AbbVie, Eli Lilly, Gilead, Janssen, MSD, Pfizer, and UCB; advisor for Eli Lilly, Gilead, Janssen, Novartis, and Pfizer; **PJM:** Research support from AbbVie, Amgen, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Sun Pharma, and UCB; consultant fees from AbbVie, Aclaris, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GSK, Inmagene, Janssen, Novartis, Pfizer, Sun Pharma, and UCB; speaker fees from AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, Sun Pharma, and UCB

P49

EXAMINING THE IMPACT OF DISEASE ACTIVITY ON QUALITY OF LIFE IN WOMEN WITH AXIAL SPONDYLOARTHRITIS

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Introduction. Tools to assess disease activity and quality of life in axial spondyloarthritis (axSpA) were developed in ankylosing spondylitis cohorts biased towards male inclusion. It remains unclear how these tools capture disease experience in females. The Ankylosing Spondylitis Registry of Ireland (ASRI) is an epidemiological data source on patients with axSpA in Ireland. The aim was to examine and compare sex specific relationships between disease activity (assessed by BASDAI) and quality of life (assessed by ASQoL) in patients with axSpA.
Methods. IBM SPSS V.26 computed the analysis of BASDAI and ASQoL scores of the ASRI patients. Variables were assessed for presence of a monotonic relationship via inspection of a scatterplot. Records were split by sex and a Spearman's rank-order correlation was undertaken to assess strength of correlation of scores within each sex.
Results. Data on both BASDAI and ASQoL scores were available for analysis on 879 patients. For both outcomes means were significantly higher in females compared to males (BASDAI 4.57 vs 3.83, $p<0.01$; ASQoL 7.51 vs 6.12, $p<0.01$). There was a statistically significant, strong positive correlation between BASDAI and ASQoL scores in axSpA patients, $r_s=0.765$, $p<0.01$, translating clinically to higher BASDAI scores being associated with worse ASQoL scores. Analysis by sex showed the positive correlation becomes stronger if assessed within each sex for men but weaker for women (Males $r_s(644)=0.774$, $p<0.01$ vs Females $r_s(238)=0.728$, $p<0.01$).
Conclusions. There is a stronger relationship between disease activity and quality of life in men with axSpA than women. This raises the question, is the BASDAI fully capturing the impact of disease activity in axSpA women? Or are lower levels of disease activity resulting greater negative impact on quality of life in women compared to axSpA men? These insights are crucial to improving interpretation of patient outcomes between sexes in axSpA.

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P50

IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS SPINAL MOBILITY MEASURES CORRELATE WELL WITH THE WHOLE SPINE CT SYNDESMOPHYTE SCORE (CTSS)

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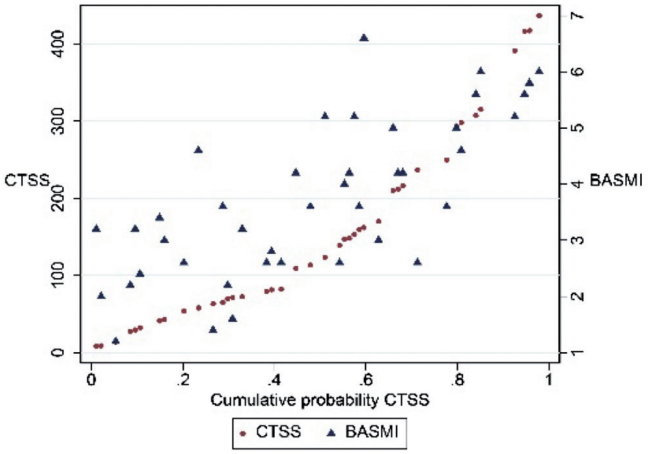
Introduction. The modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) is the best validated and widely used method for assessing radiographic progression in axial spondyloarthritis (axSpA) and is known to correlate with spinal mobility measures. The recently developed Computed Tomography Syndesmophyte Score (CTSS) assesses syndesmophyte presence and size on whole spine low dose CT but correlation with spinal mobility measures has not been investigated.
Methods. AxSpA patients from the SIAS cohort meet the Modified New York criteria and have ≥1 and <18 syndesmophytes on mSASSS at baseline. Correlations were tested for each of 8 spinal mobility measures (occiput to wall distance (OWD), tragus to wall distance (TWD) (calculated as OWD+11.1), lateral spinal flexion, mSchober, cervical rotation, chest expansion, intermalleolar distance (IMD) and Bath Ankylosing Spondylitis Metrology Index (BASMI) with CTSS and mSASSS using Spearman's rank correlation coefficients. A cumulative probability plot shows the relationship between BASMI and CTSS on the patient level.
Results. Forty-one patients (mean age 48 (SD 9), 83% male, 85% HLA-B27+) had scores for both CTSS and mSASSS and all spinal mobility measures. The CTSS showed substantial correlation with OWD/TWD ($r_s=0.68$), lateral spinal flexion ($r_s=-0.72$), cervical rotation ($r_s=-0.61$) and BASMI ($r_s=0.73$) (Figure 1). Patient level data is shown for BASMI with CTSS (Figure 2). CTSS correlated moderately with the mSchober ($r_s=-0.46$) and chest expansion ($r_s=-0.52$) but not with IMD ($r_s=-0.12$). The mSASSS also had significant correlations with all measures except IMD but all correlations were lower than with CTSS.

	CTSS $r_s(p)$	mSASSS $r_s(p)$
Occiput to wall distance	0.68	0.51
Tragus to wall distance	0.68	0.51
Lateral spinal flexion	-0.72	-0.64
mSchober	-0.46	-0.37
Cervical rotation	-0.61	-0.48
Chest expansion	-0.52	-0.34
Inter malleolar distance	-0.12	-0.29
BASMI	0.73	0.62

Legend Strength of association	
Low	0.00 – 0.20
Fair	0.21 – 0.40
Moderate	0.41 – 0.60
Substantial	0.61 – 0.80
Excellent	0.81 – 1.00

P50. Fig. 1. Spearman correlations for eight spinal mobility measures with the CTSS and mSASSS Correlations are colour codec according to the strengh of the association.



P50. Fig. 2. Cumulative probability plot showing patient-level data of the BASMI and the CTSS Patients are ordered on the X-axis according to their CTSS. The value of the CTSS is shown on the left Y-axis the value of the BASMI on the right Y-axis.

Conclusions. The CTSS correlates with 7 out of 8 spinal mobility measures. Lateral spinal flexion and total BASMI correlated best with both methods. The lack of correlation with IMD was expected since hip range of motion is not affected by spinal structural changes. These observed correlations compared favourably to mSASSS and support the construct validity of the CTSS.

P51

LOW DOSE COMPUTED TOMOGRAPHY HOUNSFIELD UNITS: A RELIABLE METHODOLOGY FOR ASSESSING CHANGES IN VERTEBRAL BONE DENSITY IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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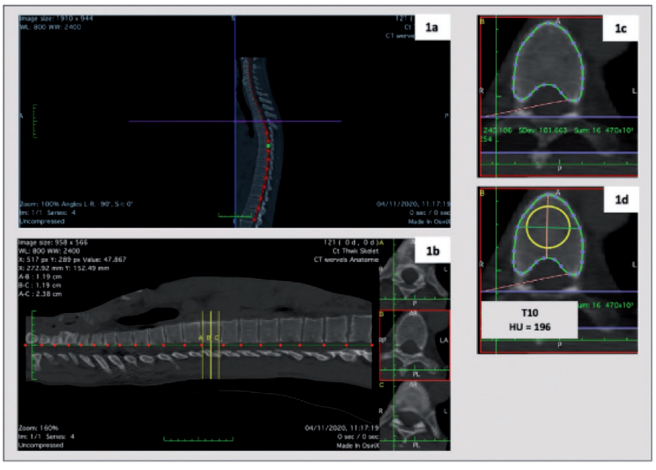
**Equally contributed*

Introduction. In radiographic axial Spondyloarthritis (r-axSpA), low dose Computed Tomography (ldCT) Hounsfield Units (HU) were shown to cross-sectionally reliably assess bone density at each vertebra from C3-L5 (1). HU change scores have never been studied.
Objectives. To describe ldCT HU 2-year change scores and analyse inter-reader reliability per vertebra.
Materials and methods. We used 49 patients with r-axSpA from the multicentre 2-year Sensitive Imaging in Ankylosing Spondylitis (SIAS) study. A standardized protocol and automatic exposure control calibration in ldCT imaging acquisition were used. HU measurements were independently assessed by two trained readers at baseline and two years (independent reading sessions ≥3 months apart) (Fig. 1). Mean (standard deviation, SD) for the change-from-baseline HU scores were provided per vertebra by reader. Intraclass correlation coefficients (ICC; absolute agreement, two-way random effects), Bland-Altman plots and smallest detectable change (SDC) were assessed. Percentages of vertebrae in which readers agreed on the direction of change and on change scores >|SDC| were computed.



P51. Fig. 1. Methodology of low dose Computed Tomography Hounsfield Units (HU) measurement.
1a: Using a three-dimensional curved-multiplanar reconstruction, the curve of the spine adjacent to the spinal canal was delimited. **1b**: On the obtained sagittal image, each vertebra (from C3 to L5) was identifiable. At each vertebra, two lines of reference were positioned at the superior (yellow line A) and inferior (yellow line C) limits of the vertebra. Equidistant to A and C, the yellow line B was automatically positioned by the software at the center of the vertebral body. **1c**: In the reconstructed cross-sectional slice, the vertebral body was manually delimited. **1d**: A region of interest was manually selected, having a diameter equal to 75% of the average of anteroposterior and transverse diameters. The density of the vertebra was displayed by the software as the average image intensity within the sample region, reported in HU.

Vertebra§	Mean change (SD)		Mean Difference (SD)	ICC	No agreement %	Agreement %	
	Reader 1	Reader 2				Change >|7|#	Change ≤|7|*
C3	18 (56)	17 (56)	0.2 (5.0)	0.97	5	84	11
C4	18 (53)	17 (52)	0.3 (5.5)	0.98	2	91	7
C5	28 (70)	29 (70)	-0.7 (5.0)	0.99	5	91	5
C6	23 (62)	23 (62)	0.4 (5.8)	0.99	7	84	9
C7	-3 (60)	-2 (59)	-0.7 (6.9)	0.98	12	86	2
T1	-6 (87)	-6 (88)	0.6 (5.0)	0.98	4	94	2
T2	3 (45)	3 (45)	0.7 (4.0)	0.97	10	76	14
T3	1 (43)	2 (43)	0.6 (4.4)	0.95	12	58	31
T4	-2 (48)	-1 (47)	0.2 (5.3)	0.94	6	80	14
T5	0.02 (48)	-0.3 (48)	0.3 (5.1)	0.91	6	78	16
T6	-3 (44)	-3 (45)	-0.1 (4.6)	0.95	8	78	14
T7	-4 (43)	-4 (43)	-0.1 (4.5)	0.99	8	76	16
T8	-1 (38)	-1 (40)	0.1 (4.6)	0.98	10	74	16
T9	-9 (50)	-9 (50)	0.02 (5.4)	0.99	20	75	4
T10	0.2 (59)	1 (59)	-0.4 (5.2)	0.96	16	70	14
T11	-8 (53)	-7 (53)	-0.6 (4.3)	0.94	10	70	20
T12	-23 (59)	-23 (60)	-0.3 (4.4)	0.99	6	84	10
L1	-9 (33)	-7 (33)	-1.9 (6.3)	0.97	20	68	12
L2	1 (46)	2 (45)	-1.1 (4.6)	0.98	10	64	27
L3	-4 (35)	-2 (34)	-1.2 (6.3)	0.92	14	64	22
L4	-2 (24)	1 (22)	-1.5 (5.4)	0.91	12	66	22
L5	8 (43)	9 (43)	-1.0 (6.0)	0.97	14	74	12

P51. Fig. 2. Change scores for each reader, mean differences between readers, intraclass correlation coefficients (ICC), and agreement on changes beyond measurement error, from C3 to L5.
§C3-C7: n=44; T1-L5: n=49. #Percentages of agreement on change beyond measurement error, *i.e.*, above the absolute value of the smallest detectable change (>|SDC|= >SDC and <-SDC). For consistency, the mean/median SDC of 7 was used as a cut-off to assess changes beyond measurement error in all vertebrae. *Percentages of agreement on change scores within measurement error (≤/SDC/= ≤SDC and ≥-SDC).

Results. Overall, 1,053 (98% of all possible) vertebrae were assessed at both time-points by each reader. Over two years, HU mean change values varied from -23 to 28 and 29 for reader 1 and 2, respectively (Fig. 2). Inter-reader reliability of the change scores per vertebra was excellent: ICC:0.91-0.99; SDC:6-10; Bland-Altman plots were homoscedastic, with negligible systematic error between readers. Readers agreed on the direction of change-score in 88-96% and on change-scores >|SDC| in 58-94% of vertebrae, per vertebral level, from C3 to L5. Overall, similar results were obtained across all vertebrae.
Conclusions. LdCT measurement of HU is a reliable method to assess changes in bone density at each vertebra from C3-L5. Being reliable across all vertebrae, this methodology can aid the study of bone loss in r-axSpA, a disease affecting the whole spine.

Reference
1. MARQUES ML *et al.*: *Arthritis Rheumatol* 2021; 73 (Suppl 10).

P52

IS INFLAMMATION-DRIVEN BONE LOSS ASSOCIATED WITH TWO-YEAR BONE FORMATION AT THE SAME VERTEBRA IN AXIAL SPONDYLOARTHRITIS? A MULTILEVEL ANALYSIS FROM THE SIAS COHORT

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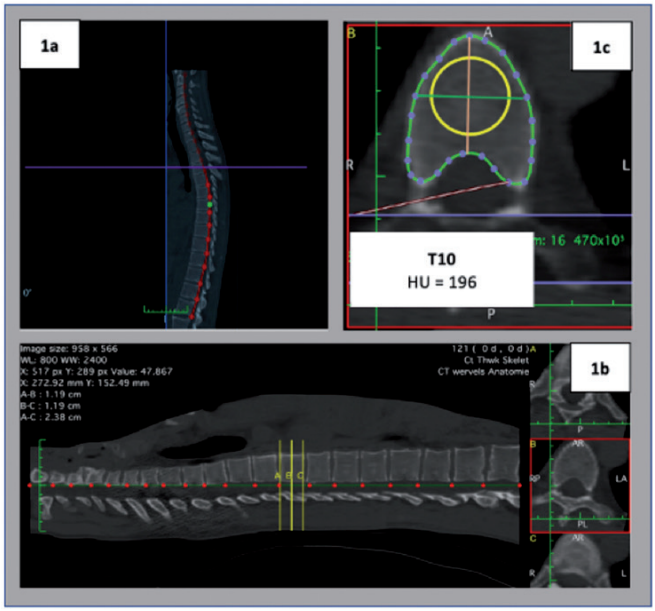
**Equally contributed*

Introduction. In r-axSpA, inflammation-driven trabecular bone loss is hypothesised to trigger bone repair at an anatomically distinct site of the same vertebra (the periosteum).
Objectives. To investigate whether inflammation is associated with lower bone density (surrogate of bone loss) and subsequently, if lower bone density is associated with a higher likelihood of 2-year bone formation at the same vertebra in r-axSpA.
Materials and methods. Data from the multicentre 2-year Sensitive Imaging in Ankylosing Spondylitis (SIAS) cohort was used. Baseline vertebral

bone density Hounsfield Units (HU) were assessed on low dose Computed Tomography (ldCT) by two readers (Fig. 1). Baseline magnetic resonance imaging bone marrow edema (MRI-BME) status-scores, and 2-year ldCT syndesmophyte formation or growth change-scores were assessed by three and two readers respectively. Inter-reader reliability was assessed by vertebra. Average of readers´ continuous scores (HU) or readers' agreement in binary scores (2/2 for syndesmophyte formation; 2/3 for MRI-BME) were used at the same vertebra (1-present in ≥1 quadrant/0-absent in all quadrants). Multilevel generalised estimating equations models were used, the unit of analysis being the vertebra.



P52. Fig. 1. Methodology of low dose Computed Tomography Hounsfield Units (HU) measurement.
1a: Using a three-dimensional curved-multiplanar reconstruction, the curve of the spine adjacent to the spinal canal was delimited. **1b**: On the obtained sagittal image, each vertebra (from C3 to L5) was identifiable. At each vertebra, two lines of reference were positioned at the superior (yellow line A) and inferior (yellow line C) limits of the vertebra. Equidistant to A and C, the yellow line B was automatically positioned by the software at the center of the vertebral body. **1c**: Vertebral HU measurements were taken from the reconstructed cross-sectional slice positioned at the center of the vertebra. A region of interest was manually selected, having a diameter equal to 75% of the average of anteroposterior and transverse diameters. The density of the vertebra was displayed by the software as the average image intensity within the sample region, reported in HU.

A.	**Independent variables**	**Bone density (ldCT Hounsfield Units)**	
		Univariable analysis Reg coeff. (95% CI) N = 910 to 985	Multivariable analysis Adj Reg coeff. (95% CI) N = 985
	MRI-BME (presence)	**-51 (-63 to -39)**	**-51 (-63 to -39)**
	Age (years)	-1 (-2 to 1)	-1 (-2 to 1)
	Gender (male)	21 (-20 to 63)	16 (-24 to 57)
	TNFi treatment (yes)	26 (-7 to 59)	27 (-6 to 61)
	Baseline syndesmophytes (presence)*	**-42 (-54 to -30)**	-
B.	**Independent variables**	**Syndesmophyte formation or growth§**	
		Univariable analysis OR (95% CI) N = 672 to 691	Multivariable analysis AdjOR (95% CI) N = 672
	Bone density (ldCT Hounsfield Units)	1.00 (0.99 to 1.00)	1.00 (0.99 to 1.00)
	Age (years)	1.02 (0.99 to 1.06)	1.02 (0.98 to 1.05)
	Gender (male)	0.44 (0.13 to 1.52)	0.56 (0.15 to 2.06)
	Smoking (current)	0.89 (0.40 to 1.97)	1.02 (0.42 to 2.44)
	Treatment with TNFi (yes)	1.34 (0.56 to 3.21)	1.30 (0.43 to 3.90)
	MRI-BME (presence)	**2.03 (1.23 to 3.71)**	**1.73 (1.06 to 3.34)**
	Baseline syndesmophytes (presence)*	**2.84 (1.83 to 4.41)**	-

P52. Fig. 2. Relationships at the same vertebra between (**A**) baseline MRI detected spinal inflammation (MRI-BME) and baseline bone density, and (**B**) baseline bone density and 2-year IdCT bone formation.
*Multicollinearity with MRI-BME. §Absolute agreement of readers. **adjOR**: adjusted odds ratio; **CI**: confidence interval; **BME**: bone marrow edema; **ldCT**: low dose computed tomography; **MRI**: magnetic resonance imaging; **TNFi**: Tumour necrosis factor inhibitors, Statistical significance highlighted in bold.

Results. We analysed 1,100 vertebrae in 50 patients with r-axSpA. Intra-class correlation coefficients for HU measurements:0.89-0.97, Fleiss-Kappa (MRI-BME status-scores):0.41-0.78, and Cohen's kappa (syndesmophyte formation/growth change-scores):0.36-0.74. Bone density HU decreased from cranial to caudal vertebrae. Baseline MRI-BME was present in 300/985 (30%) and syndesmophytes in 588/910 (65%) vertebrae, both most prevalent at the thoracolumbar region. Syndesmophyte formation or growth was observed in 18% of at-risk vertebrae (124/691). A cross-sectional significant confounder-adjusted association was found between inflammation and lower bone density (regression coefficient=-51;95%CI:-63;-39) (Fig. 2A). Bone density was not associated with 2-year syndesmophyte formation or growth (adjOR 1.00;95% CI:0.99;1.00) (Fig. 2B).
Conclusions. While in r-axSpA vertebral inflammation associates with low vertebral bone density, lower vertebral bone density itself does not increase the risk for subsequent bone formation at the same vertebra.

P53

INCREASED NEUTROPHIL FREQUENCY IN LYMPH NODES OF PATIENTS WITH PSORIATIC ARTHRITIS

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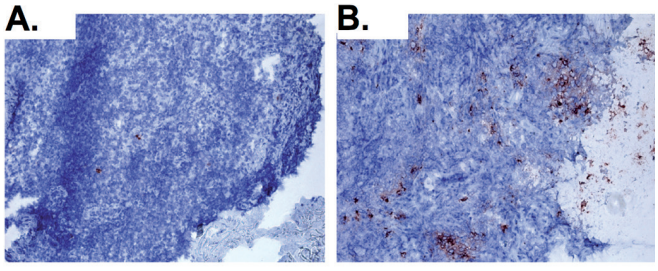
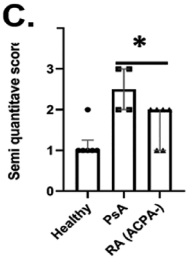
Introduction. An increased presence of neutrophils in the skin and synovium of patients with Psoriatic Arthritis (PsA) combined with neutrophil downregulation upon successful treatment, suggests a role for these cells in PsA pathogenesis. As neutrophils have been implicated in Th17 differentiation, gaining insight into the presence and function of neutrophils within lymph nodes, which are the epicentre of T cell activation and differentiation, could be important in unravelling disease pathogenesis. We hypothesize that activated neutrophils migrate from inflamed peripheral tissues to lymph nodes, where they steer inflammation by interacting with tissue resident cells and immune cells, ultimately resulting in activation of IL-17 producing T cells. To investigate this, we studied the presence of neutrophils in lymph node biopsies of patients with inflammatory arthritis, including PsA, and compared with controls.
Methods. Ten PsA patients, 34 seropositive individuals at risk of developing rheumatoid arthritis (RA-risk), 26 ACPA- RA patients and 10 healthy controls (HC) underwent ultrasound-guided inguinal lymph node biopsy. Whole lymph node biopsies were analysed using quantitative PCR and immunohistochemistry. Flow cytometry in fresh biopsies was used to determine cell frequencies in six active PsA patients (defined as arthritis in ≥1 joint) and two RA-risk individuals.





P53. Fig. 1. Immunohistochemistry staining of CD15 lymph nodes of HC (n=6), RA (n=6), and PsA (n=4) (all images magnification 200x).
A) Microscopy image of CD15 staining in a HC lymph node.
B) Microscopy image of CD15 staining in a PsA lymph node.
C) Semi-quantitative CD15 staining scores. CD15 staining was increased in PsA lymph nodes compared to HC (p=0.0079). HC; healthy controls, RA; rheumatoid arthritis, PsA; psoriatic arthritis.

Results. Lymph node biopsies of PsA patients showed significantly increased mRNA levels of Cathepsin G (CTSG), which is highly expressed by neutrophils, compared to healthy controls (p=0.020). Immunohistochemistry showed that neutrophil marker CD15 is significantly increased in lymph node tissue sections of PsA patients compared to HC (p=0.008) (Fig. 1). Preliminary flow cytometry analyses indicate a clear population of $CD45^+CD16^+CD66b^+$ neutrophils in lymph node biopsies of PsA patients while this was not observed in RA-risk individuals.
Conclusions. Overall, we show for the first time an increased presence of neutrophils in lymph nodes of PsA patients when compared to controls. Future studies are required to investigate their functional role in immune regulation within lymph node organs.
Acknowledgements. We would like to thank all participating patients and clinicians in Amsterdam UMC, Reade and the Flevoziekenhuis for patient referral.

P54

SIX YEARS TREATMENT WITH TNF-A INHIBITORS DOES NOT LEAD TO PROLONGED HYPERMINERALIZATION AS ASSESSED BY BONE TURNOVER MARKERS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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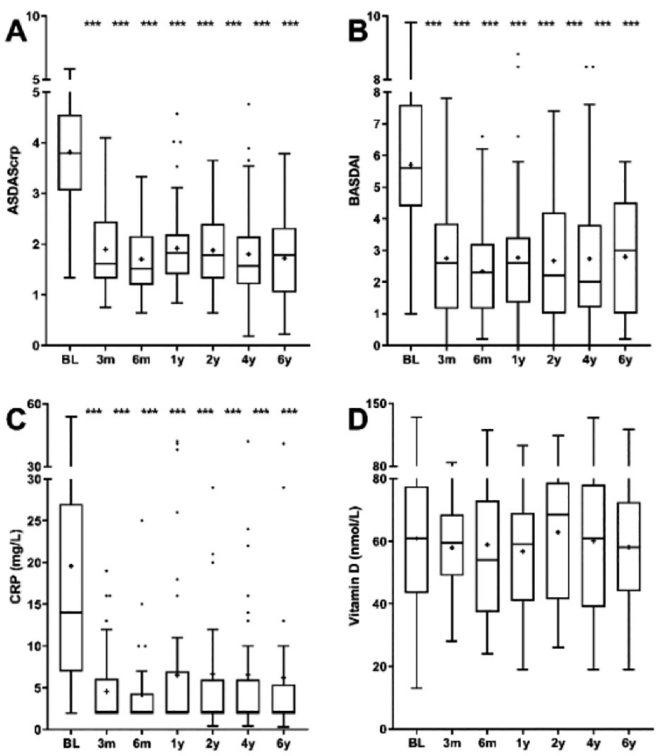
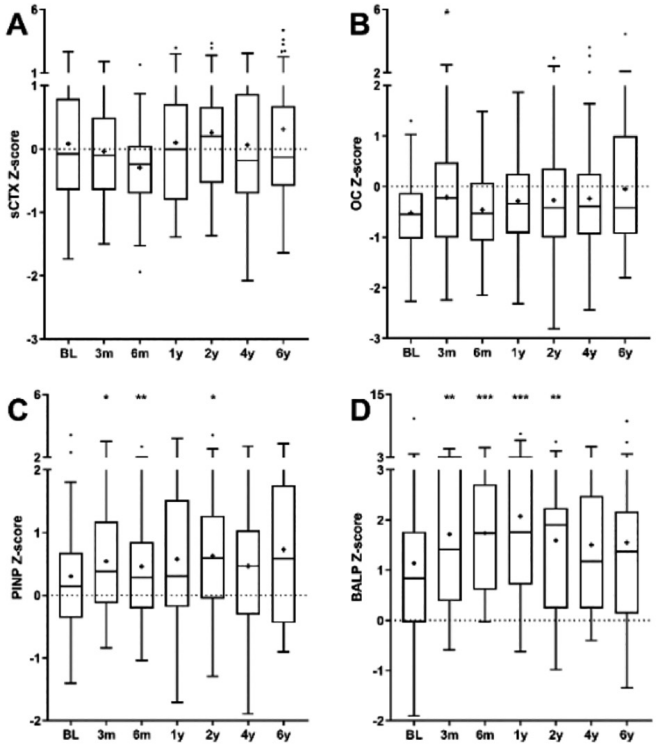
Background. In a previous study, we showed that the bone turnover balance favored bone formation, especially mineralization, during the first years of treatment with TNF-α inhibitors (TNFi) (1) in patients with ankylosing spondylitis (AS).
Objectives. To explore if this effect continues during more long-term TNFi treatment. Therefore our goal was to investigate the prolonged course of serum levels of bone turnover markers (BTM) during 6 years of TNFi treatment in patients with AS.
Methods. Included were consecutive AS outpatients from the UMCG GLAS cohort who were treated with TNFi for at least 6 years. Patients were excluded when they used bisphosphonates. Data for a specific visit was coded as missing when patients either had experienced a fracture or received systemic corticosteroids within 1 year from that particular visit regarding the possible effect on BTM. Standardized follow-up visits were performed at baseline (before start of TNFi), 3 and 6 months, 1, 2, 4 and 6 years. Serum markers of collagen resorption sCTX, bone regulation OC, collagen formation PINP, and bone mineralization BALP were measured. Z-scores were calculated to correct for the normal influence of age and gender using a healthy reference population. Generalized estimating equations were performed to analyze BTM Z-scores over time within patients.
Results. 53 AS patients were eligible for analyses (66% male, mean age 39 years). Disease activity showed rapid and sustained improvement after start of TNFi with a mean ASDAS change at 6 years of 2.0 (Fig. 1). sCTX did not significantly change during treatment. OC was only significantly increased at 3 months compared to baseline, with a change in Z-score of median +0.5. PINP showed significantly increased levels at 3 and 6 months and 2 years, with a maximum change in Z-score of median +0.3. BALP was significantly increased at all time points up to and including 2 years, with a maximum change in Z-score of median +1.2 and decreased thereafter (Fig. 2).
Conclusions. In AS patients receiving long-term TNFi, bone turnover balance favored collagen formation and mineralization during the first 2 years of treatment. Thereafter, at 4 and 6 years of follow-up, BTM Z-scores returned to levels not significantly different from baseline.

Reference
1. ARENDS *et al.*: *Arthritis Res Ther* 2012; 14(2): R98.



P54. Fig. 1. Disease activity index score ASDAScrp. (**A**) BASDAI (**B**) levels of acute phase reactant CRP (**C**) and levels of vitamin D (**D**) during 6 years of treatment with TNFi in patients with AS (n=53). Box-and-whisker plots (Tukey): boxes indicate medians with interquartile ranges, + indicates mean; whiskers indicate 1.5 times interquartile distances; •indicate cutliers.



P54. Fig. 2. Z-scores of collagen degradation marker sCTX (**A**) bone regulation marker OC (**B**), collagen formation marker PINP (**C**) and bone mineralization marker BALP (**D**) during 6 years of treatment with TNFi in patients with AS (n=53). Box-and-whiskers plots (Tukey): boxes indicate medians with interquartile ranges, + indicates mean; whiskers indicate 1.5 times interquartile distances; • indicate outliers.

P55

THE COURSE OF BONE MINERAL DENSITY DURING 8 YEARS OF TREATMENT WITH TNF-A INHIBITORS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background. Bone loss reflected by lower bone mineral density (BMD) compared to age and gender matched healthy controls is a common feature of ankylosing spondylitis (AS) and can already be observed at early stages of the disease (1). AS patients starting TNF-α inhibitors (TNFi) show overall a rapid increase in BMD (2). However, the course of BMD during long-term TNFi in these patients is not known.
Objective. To assess the course of BMD of the lumbar spine (LS) and hip in AS patients treated with TNFi during 8 years.
Methods. Patients from the GLAS cohort who received TNFi for at least 8 years were included. Patients were excluded when they used bisphosphonates. BMD of the LS (AP projection L1-L4) and hip (total proximal femur) was measured at baseline, 1 year, 2 years and then bi-annually using DEXA. Low BMD was defined as LS and/or hip BMD Z-score ≤1. Generalized estimating equations were used to analyze BMD Z-scores over time within subjects.
Results. 131 AS patients were included; 73% were male, mean ± SD age was 41.3±10.8 years, median (IQR) symptom duration was 14 (7-24) years, 83% were HLA-B27+, mean ASDAScrp was 3.8±0.8, median CRP level was 13 (6-22) mg/L, and median vitamin 25(OH)D3 was 61 (46-80) nmol/L at baseline. Disease activity showed rapid and sustained during TNFi treatment, with mean ASDAScrp of 2.1±0.9 and median CRP of 2 (2-5) at 8 years. Serum levels of vitamin D remained stable, with median vitamin 25(OH)D3 of 60 (47-81) at 8 years.
At baseline, mean LS and hip BMD Z-scores were -0.37±1.08 and -0.05±1.04, respectively. Low BMD at the LS and hip (Z-score ≤1) was present in 34% and 19% of patients, respectively. Overall, both LS and hip BMD Z-scores improved significantly during TNFi at all follow-up visits compared to baseline. Significant improvement of BMD Z-scores compared to the previous time point was found up to and including 4 years for LS and up to and including 2 years for hip. Thereafter, deflection of improvement was observed. Median percentage of improvement in absolute BMD after 8 years of TNFi compared to baseline was 7.1% (IQR 0.8-13.5) for LS and 1.6% (IQR -3.5-5.5) for hip (Fig. 1). At 8 years, low BMD at the LS and hip (Z-score ≤1) was present in 23% and 19% of patients, respectively.

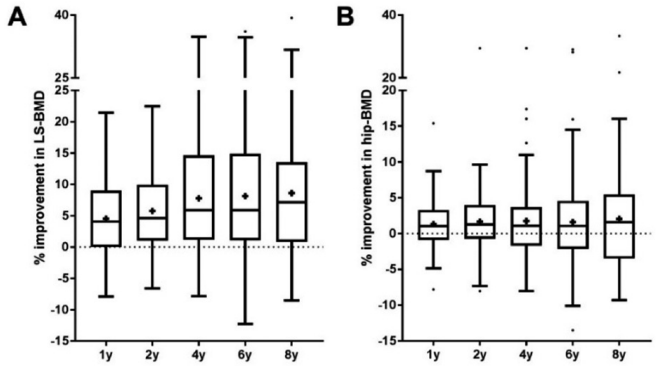

Fig. 1. Percentage improvement during 8 years of TNF-α blocking therapy on LS-BMD (**A**) and hip-BMD (**B**) in patients with AS (n=131). Box-and-whisker plots (Tukey): boxes indicate medians with interquartile renges, + indicates mean; whiskers indicate 1.5 times interquartile distances; • indicate outliers.

Conclusions. In AS patients treated long-term with TNFi, both hip and LS BMD significantly increased especially during the first 2-4 year of treatment and stabilized thereafter. This effect was most pronounced in the LS and small in the hip.

References
1. VAN DER WEIJDEN *et al.*: *Clin Rheumatol* 2012; 31(11): 1529-35.
2. ARENDS *et al.*: *Arthritis Res Ther* 2012; 14(2): R98.

P56

LONG-TERM FOLLOW-UP OF STARTING AND SWITCHING FROM ORIGINAL ADALIMUMAB TO ADALIMUMAB BIOSIMILAR: REAL-WORLD DATA IN AXIAL SPONDYLOARTHRITIS

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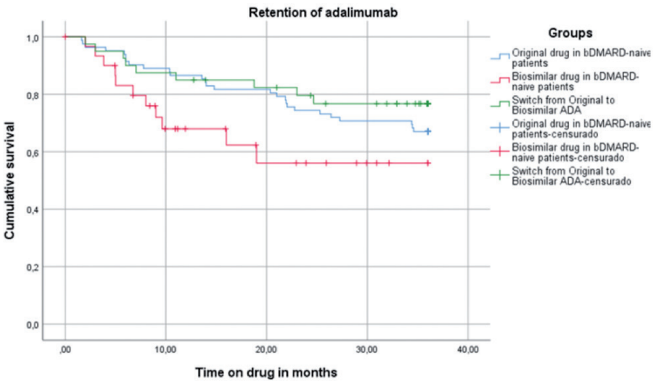
Introduction. Our aim was to compare the response to adalimumab (ADA) original and biosimilar in bDMARD-naive patients with axial spondyloarthritis (axSpA) and in patients who switched from originator to biosimilar; and to compare the effectiveness and safety of the originator and biosimilar in patients with axSpA, measured by persistence rates (PR) over three years.
Methods. Retrospective observational study in bDMARD-naive patients with a clinical diagnosis of axSpA who initiated treatment with ADA (original or biosimilar) and in patients who switched from originator to biosimilar. Disease activity at baseline and follow-up were compared using the chi-square test. The Kaplan-Meier estimator was used to calculate PR on biologic treatment.
Results. A total of 153 patients were included: 83 on original ADA, 31 on biosimilar ADA and 40 switched from original to biosimilar. Groups were similar, apart from disease duration, which was longer in the group that switched from original to biosimilar, and disease activity, which was lower in the group that switched from original to biosimilar. The 3-year PR (Fig. 1) was not significantly different between groups (p=0.080). In the original ADA group, the 3-year PR was 67.5% with a median time-on-drug (TOD) of 29.5 months; for the biosimilar, the 3-year PR was 64.5%, with a median TOD of 24.2 months. In patients who switched from original to biosimilar, the 3-year PR was 77.5% with a median TOD of 30.3 months. Response to treatment according to NICE guidelines was similar between groups (p>0.05). Overall, 47 (30.7%) patients stopped adalimumab. Discontinuations due to adverse events and inefficacy were the most frequent, without differences between groups.



P56. Fig. 1. Drug survival in the three adalimumab groups (original adalimumab – blue line, biosimilar adalimumab – red line, and switch from original to biosimilar adalimumab – green line).

Conclusions. Adalimumab original and biosimilar used as a first-line biological treatment showed similar effectiveness and safety in our long-term cohort of patients. The switch group showed to have a good PR after three years of follow-up (77.5%).

P57

PREDICTORS OF REMISSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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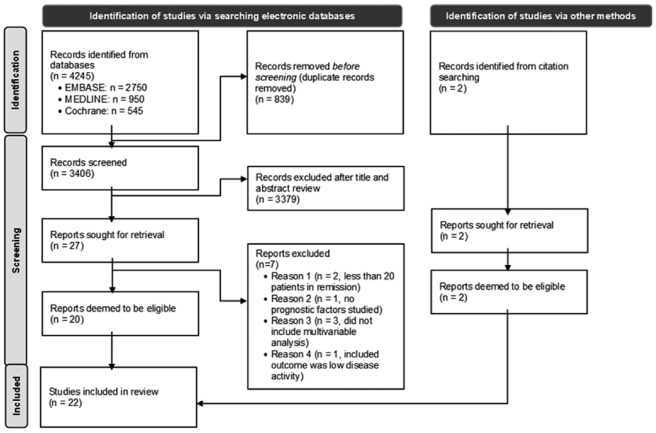
Introduction. Our aim was to systematically review and summarise predictors of remission in people with axial spondyloarthritis (axSpA).
Methods. Articles were identified in MEDLINE, EMBASE, Cochrane CENTRAL, and 2020-2021 ACR and EULAR meeting abstracts. Studies in which prognostic factors associated with remission were investigated by multivariable analysis were included.
Results. The systematic literature review (SLR) comprised 20 articles from 4245 citations (Fig. 1). Two studies investigated "sustained remission" (≥3 consecutive visits), while the others assessed "point remission" (at single points in time). The most used remission criteria were ASDAS inactive disease (13 studies) and ASAS partial remission criteria (11 studies). Younger age, HLA-B27 positivity, male gender, lower baseline BASDAI, lower baseline BASFI, and treatment with tumour necrosis factor inhibitors (TNFi), were the most consistent predictors of remission. Additionally, lower baseline ASDAS-CRP, lower body mass index, shorter disease duration, lower Health Assessment Questionnaire for the spondyloarthropathies, TNFi naivety, and concomitant use of conventional synthetic disease-modifying anti-rheumatic drugs, were predictors of remission in two studies. Other factors were found to be predictors of remission in one study only.



P57. Fig. 1. Flow diagram of study selection.

Conclusions. Our study summarised 31 predictors of remission in people with axSpA. Younger age, HLA-B27 positivity, male gender, lower baseline BASDAI, lower baseline BASFI, and treatment with TNFi were the most consistent factors predictive of remission. However, many of the predictors found were only identified in 1-2 studies. Considering the differences in study design, further well-designed prognostic studies are needed to confirm and allow generalisation of these predictors to the general axSpA population. Only two studies assessed sustained remission; axSpA is a disease characterised by fluctuating levels of inflammation and periods of flare, making sustained remission a particularly desirable outcome to investigate in future studies.

P58

DIFFERENTIATION BETWEEN IL-6 AND IL-17 PATHWAY INHIBITION IN RELATIONSHIP WITH CLINICAL OUTCOMES IN NON-BIOLOGICAL DMARD-IR AND BIOLOGICAL DMARD-IR PSORIATIC ARTHRITIS PATIENTS TREATED WITH UPADACITINIB IN SELECT-PSA 1 AND SELECT-PSA 2 STUDIES

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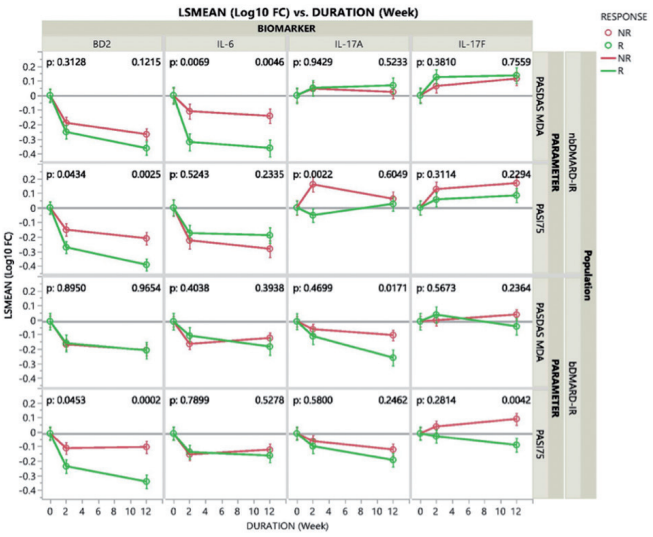
Objectives. We assessed the relationship between IL-6 and IL-17 pathway modulation and different clinical outcomes in upadacitinib (UPA) treated nbDMARD-IR and bDMARD-IR PsA patients.
Methods. A randomized, patient subset was selected from SELECT-PsA 1(n=74 of UPA 15 mg QD, n=74 of PBO) and PsA 2 studies (n=90 of UPA 15 mg QD, n=81 of PBO). Serum levels of IL-6, IL-17A, IL-17F, and beta-defensin 2(BD2) proteins were measured at baseline, week (Wk) 2, and Wk12 by validated immunoassays. A Repeated Measure Mixed Linear Model was used to compare UPA versus PBO effects in overall patients and between responders and non-responders defined by PASDAS score ≤3.6(Minimal Disease Activity, MDA) (4) and PASI75 at Wk12, respectively. Relationships between cytokines and clinical outcomes (PASI and DAS28-CRP) were assessed.
Results. In nbDMARD-IR PsA patients, UPA significantly decreased IL-6 and BD2 at Wk12. In bDMARD-IR PsA patients, reduction of IL-6 after UPA treatment was not different between responders and non-responders (PASDAS MDA or PASI75) and did not correlate with DAS28-CRP improvement, while reduction of BD2 remained significant in PASI75 responders and correlated with PASI improvement at Wk12. Further, UPA significantly reduced IL-17A in PASDAS MDA responders and IL-17F in PASI75 responders versus non-responders, respectively. Reduction of IL-17F correlated with PASI improvement at Wk12.



P58. Fig. 1. Biomarker inhibition effects in responders vs. non-responder subgroups differ between nbDMARD-IR and bDMARD-IR PsA patients treated with UPA (number annotations represent nominal p-values of the comparison between subgroups at week 2 and week 12, respectively).

Conclusions. IL-6 and IL-17 pathway inhibition after UPA treatment showed different profiles in relationship with clinical outcomes in nbDMARD-IR versus bDMARD-IR PsA patients. IL-6 decrease was more pronounced in nbDMARD-IR PsA patients and associated with joint manifestation improvement, while IL-17A and IL-17F decreases were only observed in bDMARD-IR PsA patients and associated with psoriasis improvement. BD2, a biomarker of Th17-associated skin pathology, significantly decreased after UPA treatment in both nbDMARD-IR and bDMARD-IR PsA studies, which likely contributed to UPA effects on psoriasis improvement in a broad range of PsA patients.

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P59

EFFECT OF GUSELKUMAB, A SELECTIVE IL-23P19 INHIBITOR, ON AXIAL-RELATED ENDPOINTS IN PATIENTS WITH ACTIVE PSA: RESULTS FROM A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY THROUGH 2 YEARS

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Introduction. Guselkumab (GUS) showed greater improvements in axial involvement symptoms/BASDAI scores vs placebo at Week (W)24 in patients with active PsA/investigator-confirmed sacroiliitis, which were maintained through 1-year. We assessed maintenance of GUS effect on axial involvement symptoms among biologic-naive PsA patients with investigator-confirmed sacroiliitis through 2-years of DISCOVER-2.

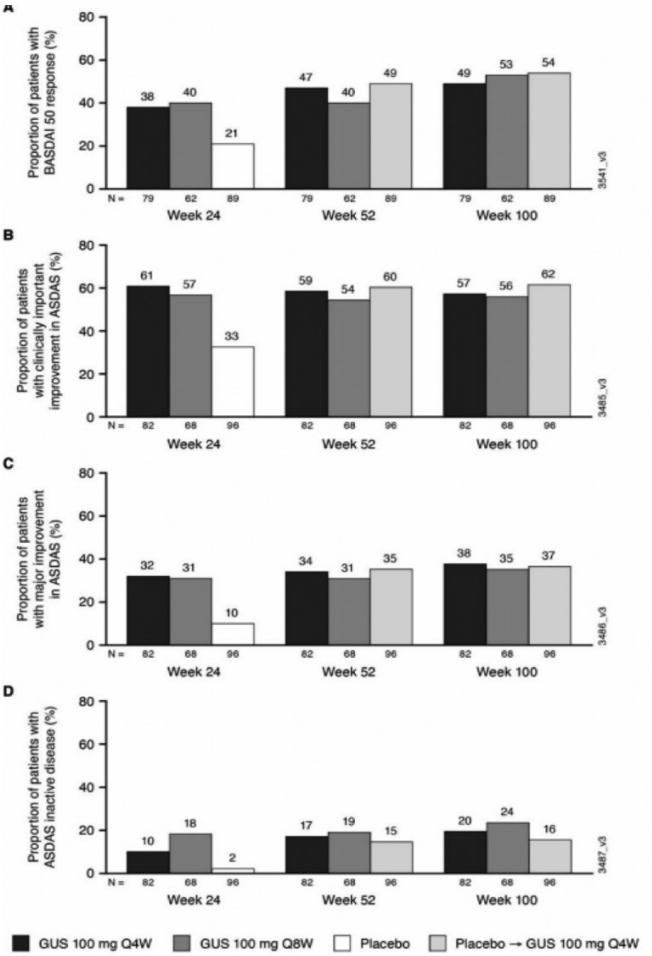
Methods. Biologic-naive patients (N=739) with active PsA (≥5 swollen joints/≥5 tender joints/CRP≥0.6mg/dL) and investigator-confirmed axial symptoms/sacroiliitis were randomized 1:1:1 to GUS-100mg every-4-weeks (Q4W; n=245); GUS-100mg at W0/W4, then Q8W (n=248); or placebo (n=246), with placeboàGUS-100mg Q4W at W24. Efficacy assessments included change in BASDAI/modified-BASDAI (mBASDAI, excluding Q3 [peripheral joint pain])/BASDAI Q2 (Spinal Pain) scores and proportions of patients achieving BASDAI50 response/Spinal Pain score ≤2/Ankylosing Spondylitis Disease Activity Score (ASDAS) responses through W100. Through W24, patients with treatment failure/missing data were considered nonresponders; after W24, missing data were imputed as nonresponse/no-change (nonresponder imputation [NRI]).

P59. Table. Axial symptom assessments through W100 in PsA patients with investigator-confirmed sacroiliitis in DISCOVER-2 (NRI).

	GUS Q4W n=82	GUS Q8W n=68	PBO→GUS Q4W n=96
Change in BASDAI score			
W24, LS mean (95% CI)	-2.5 (-2.9, -2.0)	-2.4 (-3.0, -1.8)	-1.2 (-1.7, -0.7)
Mean (SD)	-2.5 (2.0)	-2.6 (2.4)	-1.4 (2.4)
W52, mean (SD)	-2.9 (2.3)	-2.7 (2.5)	-2.9 (2.6)
W100, mean (SD)	-3.0 (2.3)	-3.1 (2.6)	-3.3 (2.6)
Change in mBASDAI (excludes Q#3) score			
W24, LS mean (95% CI)	-2.4 (-2.9, -1.9)	-2.4 (-2.9, -1.8)	-1.2 (-1.7, -0.7)
Mean (SD)	-2.5 (2.1)	-2.6 (2.5)	-1.3 (2.3)
W52, mean (SD)	-2.7 (2.6)	-2.6 (2.5)	-2.9 (2.4)
W100, mean (SD)	-3.3 (2.6)	-3.1 (2.6)	-3.0 (2.4)
Change in Spinal Pain (BASDAI Q#2) score			
W24, LS mean (95% CI)	-2.2 (-2.7, -1.7)	-2.3 (-2.9, -1.7)	-0.9 (-1.5, -0.4)
Mean (SD)	-2.3 (2.6)	-2.5 (2.8)	-1.1 (2.5)
W52, mean (SD)	-2.6 (2.7)	-2.5 (2.7)	-2.5 (2.7)
W100, mean (SD)	-2.8 (2.7)	-3.1 (2.8)	-3.0 (2.8)
Change in ASDAS score			
W24, LS mean (95% CI)	-1.3 (-1.6, -1.1)	-1.3 (-1.6, -1.1)	-0.6 (-0.8, -0.4)
Mean (SD)	-1.4 (1.0)	-1.5 (1.2)	-0.7 (1.1)
W52, mean (SD)	-1.5 (1.1)	-1.5 (1.3)	-1.5 (1.3)
W100, mean (SD)	-1.6 (1.2)	-1.7 (1.2)	-1.6 (1.2)

ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAIS: Bath Ankylosing Spondylitis Disease Activity Index; CIS: confidence interval; GUSS: guselkumab; LSS: least-squares; mBASDAIS: modified BASDAI; NRIS: nonresponder imputation; PBOS: placebo; PsAS: psoriatic arthritis; Q4WS: every 4 weeks; Q8WS: every 8 weeks; SDS: standard deviation; WS: week.

Results. 246 patients had investigator-confirmed sacroiliitis. Baseline characteristics were similar across treatment groups (62% male/mean age 44.4-years); mean BASDAI scores ranged from 6.5-6.6. At W24, least-squares mean/mean changes in BASDAI (-2.4/-2.6)/ASDAS (-1.3/-1.5) scores were greater in GUS- than placebo-treated patients. Mean changes from baseline were maintained through W100 in GUS-treated patients for BASDAI(-3.1)/Spinal Pain (-3.1)/mBASDAI (-3.1)/ASDAS (-1.7) scores (Table). Similar response patterns were observed for BASDAI50 response rates among GUS-treated patients (W24 38-40%/W100 49-54%). At W24, GUS-treated patients had higher response rates for achievement of ASDAS inactive disease/major improvement/clinically important improvement vs. placebo; response rates (NRI) were maintained, or further increased, at 2-years (Figure). Consistent results were observed for achievement of ASDAS LDA/Spinal Pain score ≤2. GUS-related improvements in axial symptoms through W100 were generally consistent across patients who were HLA-B27± (data not shown).



P59. Fig. 1. Proportion of PsA patients with investigator-confirmed sacroiliitis achieving BASDAI 50 response (A), and ASDAS clinically important improvement (decrease ≥1.1) (B), major improvement (decrease ≥2.0) (C), and inactive disease (<1.3) (D) through W100 (NRI).
ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; GUS: guselkumab; NRI: nonresponder imputation; PsA: psoriatic arthritis; Q4W: every 4 weeks; Q8W: every 8 weeks; W: week.

Conclusions. In bio-naive patients with active PsA and investigator-confirmed sacroiliitis, GUS provided durable improvements in axial symptoms through W100, with substantial proportions of patients achieving and maintaining clinically meaningful improvements.

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Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB; **DP:** consulting fees from AbbVie, Eli Lilly, GlaxoSmithKline, MSD, Novartis, Pfizer, and UCB; grants from AbbVie, Eli Lilly, MDS, Novartis, and Pfizer; **XB:** consulting fees, grant/research support/speaker's bureau support from AbbVie, Biocad, Chugai, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, and UCB; **SDC:** employee of Janssen Scientific Affairs, LLC and may own stock or stock options in Johnson & Johnson; **APK, XLX, SS, and SX:** employees of Janssen Research & Development, LLC and may own stock or stock options in Johnson & Johnson; **MS:** employee of Janssen Global Services, LLC and may own stock or stock options in Johnson & Johnson; **D. vd H:** consulting fees from AbbVie, Amgen, Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, and UCB Pharma; serves as the director of Imaging Rheumatology BV; **AD:** consulting fees from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, and UCB; grant/research support from AbbVie, Eli Lilly, Glaxo Smith & Kline, Novartis, Pfizer, and UCB; and speaker fees from AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, and UCB.

P60

EFFICACY AND SAFETY OF BIOLOGICAL DMARDS: A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2022 UPDATE OF THE ASAS-EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF AXIAL SPONDYLOARTHRITIS

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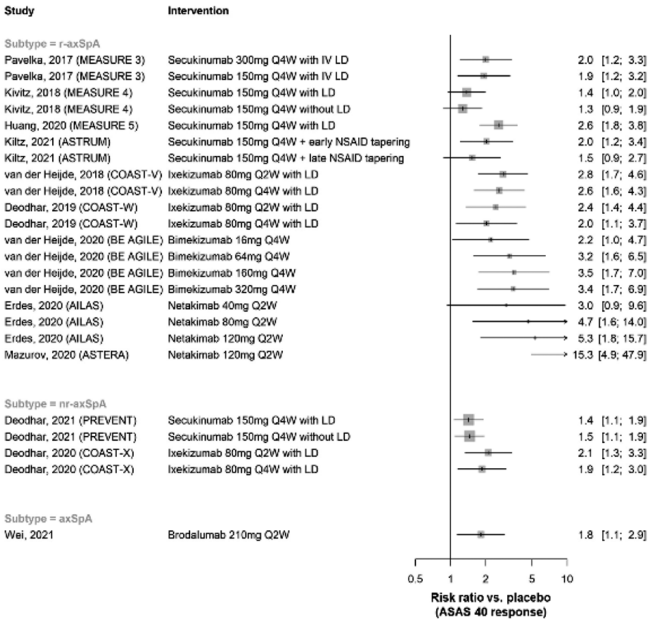
Objectives. To update the evidence on the efficacy and safety of biological disease-modifying antirheumatic drugs (bDMARDs) in patients with axial spondyloarthritis (axSpA) to inform the 2022 update of the ASAS-EULAR recommendations for the management of axSpA.

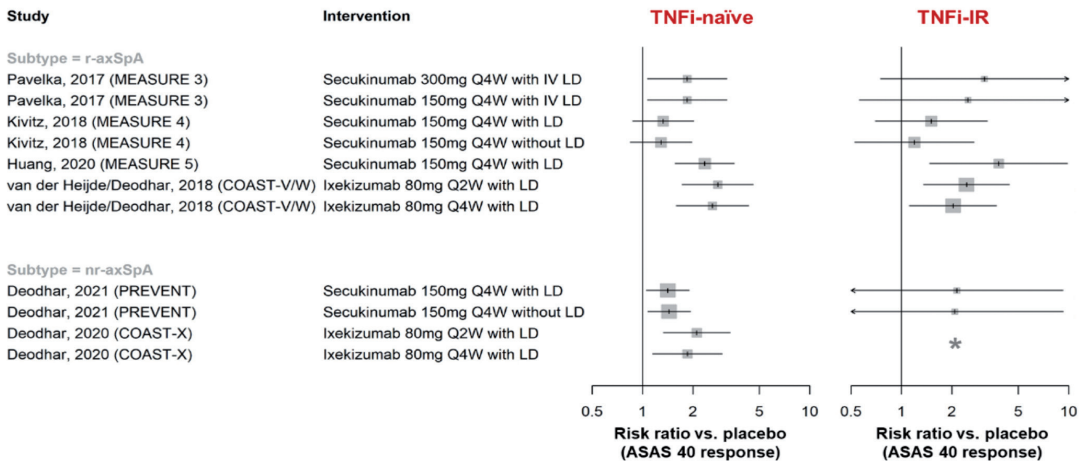
Materials and methods. Systematic literature review (2016-2021) of the efficacy and safety of bDMARDs in axSpA (including r-axSpA and nr-axSpA) (PROSPERO registration CRD42021257588). Eligible study designs included randomised controlled trials (RCTs), strategy trials and observational studies (the latter only for safety and extra-musculoskeletal manifestations). All relevant efficacy/safety outcomes were included. Risk ratios (RR) were used as effect measure.



P60. Fig. 1. ASAS 40 response in placebo-controlled RCTs of IL-17 inhibitors, by axSpA subtype. Risk ratios >1 favour the intervention. Only RCTs that reported ASAS 40 response rates are shown (12 out of 14 included). Numbers on the right are RR with 95% confidence interval. LD: loading dose.

Results. In total, 154 publications were included. Efficacy of golimumab and certolizumab was confirmed. Equivalence between adalimumab/etanercept biosimilars and originators was demonstrated (n=1 each). Fourteen placebo-controlled RCTs investigated efficacy of interleukin-17 inhibitors (IL-17i: secukinumab [n=7], ixekizumab [n=3], netakimab [n=2], brodalumab [n=1], bimekizumab [n=1]) and found clinically relevant effects (RR versus placebo to achieve ASAS40 response 1.3-15.3 [r-axSpA, n=9], 1.4-2.1 [nr-axSpA, n=2]; Fig. 1). Efficacy of secukinumab/ixekizumab was demonstrated both in TNFi-naive and TNFi-inadequate responders (Fig. 2). Trials of IL-23 inhibitors (IL-23i: ustekinumab [n=3], risankizumab [n=1]) failed to show relevant benefits compared to placebo and were stopped. Discontinuation of TNFi (n=3) and IL-17i (n=1) resulted in high rates of flare (45-80% within 48 weeks), while tapering of TNFi by spacing was non-inferior to standard-dose treatment (n=2). The first axSpA treat-to-target trial did not meet its primary endpoint (ASAS-HI 30% improvement), but showed improvements in secondary outcomes (ASAS20/40). No new risks with TNFi were found in observational studies (no data yet for IL-17i). Secukinumab and etanercept were associated with increased risk of uveitis compared to monoclonal TNFi in one and two observational studies, respectively.

Conclusions. New evidence supports the efficacy and safety of TNFi (originators/biosimilars) and IL-17i in r-axSpA and nr-axSpA, while IL-23i failed to show relevant effects.



P60. Fig. 2. ASAS 40 response in placebo-controlled RCTs of IL-17 inhibitors, by prior TNFi history and axSpA subtype. Risk ratios >1 favour the intervention. With the exception of PREVENT, all studies either stratified randomisation for prior TNFi treatment, or only included TNFI.naive or TNFi-IR patients (not both), *COAST-X only included TNFi-naive patients. LD: loading dose; TNFi-IR: inadequate responder to prior TNFi tratment

P61

FILGOTINIB TREATMENT RESULTS IN REDUCTION OF INFLAMMATORY AND MATRIX REMODELING BIOMARKERS ASSOCIATED WITH DISEASE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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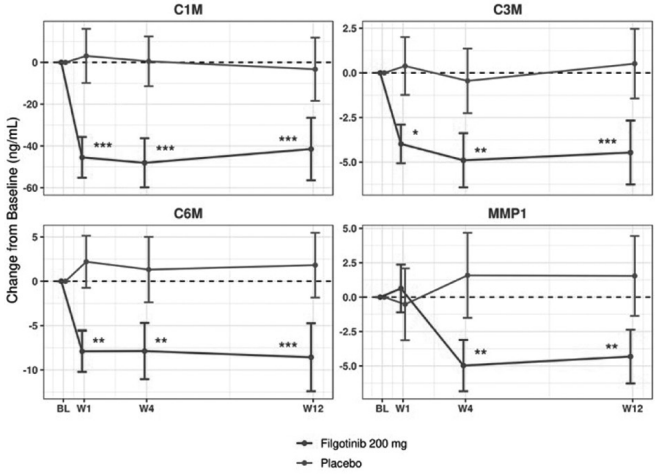
Introduction. Ankylosing spondylitis (AS) is a chronic inflammatory disease affecting the sacroiliac joints and spine. In TORTUGA, AS disease activity was significantly reduced following treatment with the preferential Janus kinase 1 (JAK1) inhibitor filgotinib (FIL) versus placebo (PBO). As JAK1 inhibition by FIL may block multiple inflammatory pathways, circulating biomarker concentrations from patients with active AS in TORTUGA were compared with healthy volunteers (HV). The impact of disease on circulating biomarkers and effect of FIL treatment was assessed.
Methods. TORTUGA (NCT03117270) was a 12-week, randomized, double-blind, placebo-controlled, phase 2 study. Patients were randomized 1:1 to FIL 200 mg (n=58) or PBO (n=58), once-daily. Samples (FIL: n=56, PBO: n=53) were collected at baseline (BL) and Weeks 1, 4 and 12, and analyzed using immunoassays. Change from BL in biomarker concentrations were analyzed and clustering analysis performed. Correlations between biomarkers and clinical scores were assessed. Change in biomarker levels were compared using PBO-adjusted estimates from a linear mixed effects model.
Results. Five clusters of biomarker response were identified based on the kinetics and magnitude of the change from BL following FIL. Compared to PBO, reductions in inflammatory biomarkers and matrix metalloproteinase-degraded collagen fragments C1M, C3M, C6M and MMP1 were observed (Fig. 1). The change in several biomarkers correlated with changes in clinical characteristics from BL to Week 12. Comparisons to HV were made; BL intercellular adhesion molecule 1 and vascular cell adhesion molecule 1 levels were elevated in patients with AS. Upon treatment, both were reduced to levels comparable to HV, remaining low.



P61. Fig. 1. Circulating levels of matrix remodeling biomarkers are reduced with FIL treatment. The change from baseline resulting from PBO or FIL treatment on tissue metabolites of type 1, 3 and 6 collagen (C1M, C3M, C6M) and matrix metalloproteinase-1 (MMP1) levels at BL and Weeks 1, 4 and 12 was calculated using a linear mixed effects model (adjusted for age, sex, body mass index, BLAS disease activity score and BL spine Spondyloarthritis Research Consortium of Canada MRI scores) including a treatment by visit multiplicative interaction. The data are presented as the mean and 95% confidence interval. False discovery rate-corrected p-values: *Adj.p<0.05; **Adj.p<10^{-3}; ***Adj.p<10^{-6}.

Conclusions. In patients with active AS, FIL treatment reduced levels of inflammatory cytokines, matrix remodeling biomarkers and cellular adhesion molecules associated with disease. This is consistent with reduced disease activity reported in TORTUGA, suggesting that FIL treatment can rapidly reduce inflammatory cytokines involved in AS pathobiology.

Funding. Gilead.

P62

SERUM GRANULOCYTE-MONOCYTE COLONY STIMULATING FACTOR (GM-CSF) IS INCREASED IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS (AS) AND PERSISTS DESPITE ANTI-TNF TREATMENT

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Introduction. Granulocyte-Monocyte Colony-Stimulating-Factor (GM-CSF) is a growth factor for both myeloid lineages and a potent pro-inflammatory cytokine activating myeloid cells. It signals through the JAK-STAT pathway. We measured serum GM-CSF together with markers of bone metabolism in AS patients before and after anti-TNF treatment.
Methods. The study included AS patients with increased disease activity, all being eligible for treatment with a bDMARD. Healthy donors were sampled as controls. Serum was collected before (baseline, BL) and after 4-6 months (follow-up, FU) of anti-TNF treatment and the following molecules were measured using ELISA: GM-CSF, Sclerostin (SOST) and Dickkopf-1 (Dkk-1).
Results. Twelve patients with AS (7 males, median age 37 years (22-52)) with a median disease duration of 1 year (0.5-25) and 16 age- and sex-matched controls were included. At BL, patients had mean BASDAI 6.3±2 and ASDAS 3.2±0.7. At FU the mean BASDAI decreased to 4.1±1.7 and ASDAS to 2.2±0.6. At BL, AS patients had significantly higher mean serum levels of GM-CSF (150 vs 62pg/ml, p=0.049), significantly lower Dkk-1 (1228 vs 3052pg/ml, p=0.001), but similar levels of SOST (369 vs 544pg/ml, p=0.144) compared to controls. Anti-TNF treatment did not significantly affect GM-CSF, Dkk-1 or SOST levels (p>0.05 for all comparisons at FU vs BL). Spearman correlation analysis showed that GM-CSF correlated positively with ASDAS at BL (r=0.61, p=0.039), negatively with age (r=-0.68, p=0.018), but not with disease duration (r=-0.27, p=0.400). No correlations were identified between bone markers (Dkk-1, SOST) and GM-CSF or disease activity indices.
Conclusions. GM-CSF is increased in active AS, particularly in younger ages, and strongly correlates with disease activity, but not with duration. In contrast, TNF-inhibition does not affect GM-SCF levels, despite improving disease activity. GM-CSF may represent an important pathway in AS that could be responsible for residual inflammation during TNF-blockade, but also explain the efficacy pathway of treatment with JAK-inhibitors.

P63

EARLIER CLINICAL RESPONSE PREDICT LOW RATES OF RADIOGRAPHIC PROGRESSION IN BIO-NAIVE ACTIVE PSORIATIC ARTHRITIS PATIENTS RECEIVING GUSELKUMAB TREATMENT

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Introduction. Guselkumab (GUS), an IL-23p19-subunit inhibitor, demonstrated efficacy and a favorable safety profile in patients with psoriasis and psoriatic arthritis (PsA). In the Phase-3, DISCOVER-2 study, GUS 100mg every-4-weeks/every-8-weeks (Q4W/Q8W) significantly improved joint and skin symptoms. Low rates of radiographic progression (RP) were ob-

served, regardless of dosing regimen. This study determined whether earlier clinical improvement predicts long-term RP through 2 years in DISCOVER-2.

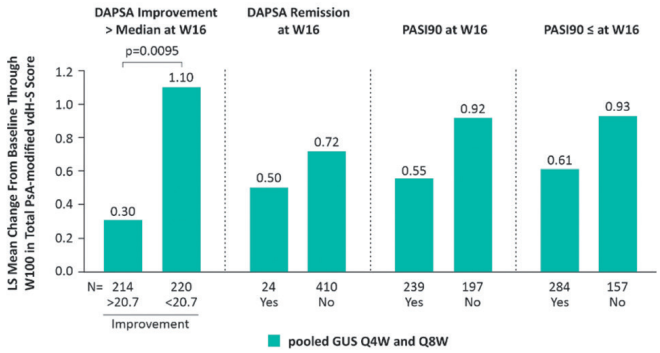
Methods. Biologic-naive patients with active PsA (≥5 swollen and ≥5 tender joint counts [SJC/TJC]; CRP ≥0.6 mg/dL) were randomized (1:1:1) to GUS 100mg Q4W; GUS 100mg at W0,W4,then Q8W; or placebo with crossover to GUS 100mg Q4W at W24. For patients randomized to GUS Q4W/Q8W, predictive models (mixed linear) were developed post-hoc to assess the associations of earlier (at W16) improvement in disease activity (DAPSA remission/DAPSA Improvement/DAPSA Improvement >20.7) or skin improvement (PASI90/PASI≤1) with changes in total PsAmodified van der Heijde-Sharp (vdH-S) score through W100, after adjusting for known baseline determinants of RP (vdH-S score/age/gender/CRP).

Results. PsA duration, CRP, and SJC at baseline weakly correlated with baseline vdH-S score. No correlation was seen between baseline PASI and baseline vdH-S score (Table). Greater improvement in DAPSA score (β [95%CI]: -0.03 [-0.04, -0.01]) and improvement >20.7 in DAPSA from baseline to W16 was associated with significantly less RP through W100 after adjusting for baseline DAPSA score, vdH-S score, age, gender, and CRP level. Achievement of PASI90, PASI≤1, and DAPSA remission at W16 was associated with numerically less RP through W100 after adjusting for baseline PASI, vdH-S score, age, gender, and CRP (Figure).

P63. Table. Correlation of select baseline disease characteristics with baseline vdH-S score among GUS randomized patients.

Baseline determinants	Spearman's correlation coefficient	*p*-value
Age	0.27335	<.0001
CRP	0.28181	<.0001
PASI score	0.03078	0.5153
PsA duration	0.37070	<.0001
PsO duration	0.20509	<.0001
SJC (66)	0.26321	<.0001

CRP: C-reactive protein; GUS: guselkumab; PASI: Psoriasis Area and Severity Index; PsA: psoriatic arthritis; PsO: psoriasis; SJC: swollen joint count; vdH-S: van der Heijde-Sharp.



P63. Fig. 1. LS Mean Change in Total PsA-modified vdH-S Score from BL at W100 by Achievement of Ealier DAPSA Improvement/Remission or Skin improvement.
BL: baseline; DAPSA: Disease Activity in Psoriatic Arthritis; GUS: guselkumab; LS: least squares; PASI: Psoriasis Area and Severity Index; PsA: psoriatic arthritis, Q4W: every 4 weeks; Q8W: every 8 weeks; vdH-S: van der Heijde-Sharp; W: week.

Conclusions. In GUS-treated biologic-naive patients with active PsA, following adjustment for known baseline determinants of RP, earlier (W16) DAPSA improvement was a significant predictor of less RP through W100; DAPSA remission and skin improvement at W16 each showed a numerical trend toward less RP through W100.

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P64

SPINAL RADIOGRAPHIC PROGRESSION AND ITS ASSOCIATION WITH PROGRESSION TO ANKYLOSING SPONDYLITIS IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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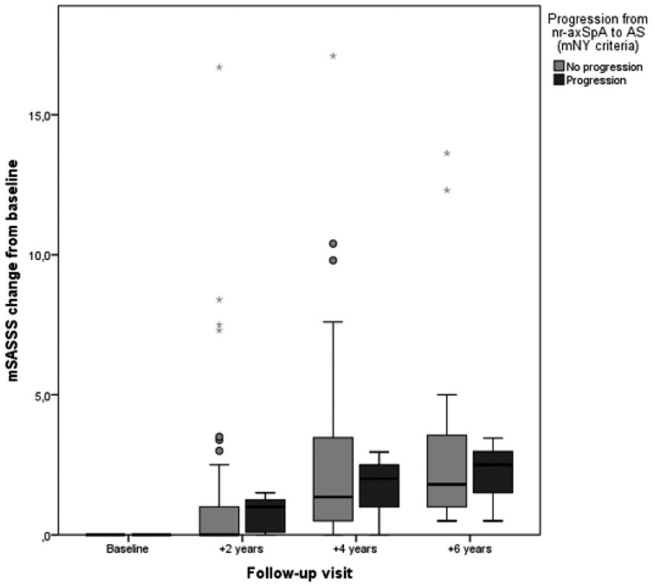
Introduction. In two years, approximately 10% of patients with nr-axSpA progresses to AS. There is little data available of more long-term follow-up or its relation to spinal radiographic progression. Our aim was to assess the association between spinal radiographic progression and sacroiliac progression in patients with up to six years of follow-up.

Methods. Patients enrolled in the ongoing Groningen Leeuwarden Axial SpA (GLAS) cohort, classified as nr-axSpA at baseline with a baseline pelvic radiograph and follow-up radiographs up to 6 years were selected for analyses. Radiographs were randomized with radiographs of AS patients and scored with known time sequence according to the mNY criteria by three trained readers. Spinal radiographs were scored by two trained readers using the mSASSS, and the mean of both scores was calculated. In case of >5 points discrepancy between both readers, the mSASSS of a third independent reader was used to calculate the mean with the closest mSASSS of the two primary readers.

Results. 85 patients were classified as nr-axSpA at baseline. After 2, 4 and 6 years, 9/85 (10.6%), 4/47 (8.5%) and 2/24 (8.3%) had progressed to AS. At baseline mean age was 39±11 years, 52% was male, median symptom duration was 6 (IQR 3-17) years, mean ASDAS was 2.7±1.1, and 75% was HLA-B27+.

Median mSASSS at baseline was 1.8 (IQR 0.5–5.1; mean 6.1). Median mSASSS change from baseline was 0.1 (IQR 0.0–1.0; mean 1.2) at 2 years; 1.1 (IQR 0.0–3.0; mean 2.2) at 4 years; and 1.8 (IQR 0.6–3.4; mean 2.8) at 6 years. mSASSS change did not differ significantly between patients with sacroiliac progression and those without.

Conclusions. In our observational cohort with up to 6 years of follow-up, mSASSS progression was low and did not differ between patients who did and did not progress to AS.



P64. Fig. 1. LS Comparison of mSASSS progression between patients with and without progression to AS during the first 6 years of follow-up.

P65

PLATELET-DERIVED GROWTH FACTOR B IS A KEY ELEMENT IN THE PATHOLOGICAL BONE FORMATION OF ANKYLOSING SPONDYLITIS

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Introduction. Enthesophyte formation plays a crucial role in the development of spinal ankylosis in ankylosing spondylitis (AS). We aimed to investigate the role of platelet-derived growth factor B (PDGFB) in enthesophyte formation of AS using in vitro and in vivo models, and to determine the association between PDGFB and spinal progression in AS.
Methods. Serum PDGFB levels were measured in AS patients and healthy controls (HC). Human entheseal tissues attached to facet joints or spinous processes were harvested at the time of surgery and investigated for bone-forming activity. The impact of a pharmacological agonist and antagonist of PDGFRB were investigated respectively in curdlan-treated SKG mice.
Results. PDGFB levels were elevated in AS sera and correlated with radiographic progression of AS in the spine. Mature osteoclasts secreting PDGFB proteins were increased in the AS group compared to HC and were observed in bony ankylosis tissues of AS. Expression of PDGFRB was significantly elevated in the spinous enthesis and facet joints of AS compared to controls. Moreover, recombinant PDGFB treatment accelerated bone mineralization of enthesis cells, which was pronounced in AS, whereas PDGFRB inhibition efficiently reduced the PDGFB-induced bone mineralization. Also, PDGFRB inhibition attenuated the severity of arthritis and enthesophyte formation at the joints of curdlan-treated SKG mice.
Conclusions. This study suggests that regulating PDGFB/PDGFRB signaling could be a novel therapeutic strategy to block key pathophysiological processes of AS.

P66

IMMUNOGLOBULINS ARE UPREGULATED IN PSORIATIC ARTHRITIS SKIN LESIONS BUT NOT IN PSORIASIS SKIN LESIONS

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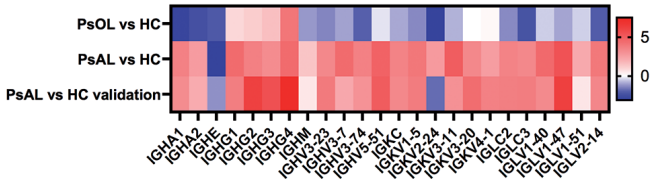
Introduction. Up to 30% of patients with psoriasis develop psoriatic arthritis (PsA). A previous proteomic analysis challenged the assumption that the skin disease is the same in both conditions. This project compared the skin transcriptome in PsA and psoriasis.
Methods. RNA sequencing data from full thickness skin biopsies from healthy controls (HC) and paired lesional and uninvolved skin samples from patients with PsA were analysed using Searchlight2. The findings were compared to the analysis of published skin sequencing data from patients with psoriasis without PsA compared to HC (GSE121212). Participants with PsA in the GSE121212 dataset were analysed as a validation cohort.
Results. HC and paired uninvolved and lesional skin biopsies were included from 9 participants in the main PsA study, 16 participants in the psoriasis study and 4 participants in the PsA validation cohort. There were more differentially expressed genes in uninvolved skin in psoriasis than in PsA. Although most transcriptomic changes in psoriasis and PsA skin lesions (PsAL) were shared, immunoglobulin genes were upregulated in PsAL specifically (Figure). This was confirmed in the PsA validation cohort. Moreover, the transcription factor POU2F1, which regulates immunoglobulin gene expression, was enriched in PsAL.



P66. Fig. 1. Log2fold changes in immunoglobulin gene expression in skin lesions compared to healthy control.

Conclusions. These data suggest involvement of immunoglobulin genes in the skin disease in PsA but not in psoriasis without arthritis. Others have identified autoantibodies to skin antigens in PsA serum and synovial fluid, and the findings of this study further suggests a role of the B cell compartment in PsA. Future studies are required to determine if a differential immune response within skin lesions with generation of autoantibodies leads to the spread of inflammation from the skin to joints in PsA.

P67

UTILITY OF THE SUBCHONDRAL BONE ATTENUATION COEFFICIENT OF THE SACROILIAC MARGINS TO DIFFERENTIATE SPONDYLOARTHRITIS AND OSTEITIS CONDENSANS ILII

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Introduction. Differentiating ankylosing spondylitis (AS) from osteitis condensans ilii (OCI) remains challenging. The aim of this study was to determine whether Subchondral Bone Attenuation Coefficient of the SacroIliac margins (SBAC-SI) is different in AS, OCI and diffuse idiopathic skeletal hyperostosis (DISH).
Methods. A monocentric retrospective observational study was performed. Patients included were followed for AS, DISH or OCI and underwent CT scan including sacroiliac joint. Patients with tumor lesion of bone or a history of pelvic radiotherapy were excluded. AS and OCI patients were matched with a control of the same age and sex. All scans were acquired on the same CT-scan unit (Somatom 64 definition AS+, Siemens Healthineers, Erlangen, Germany), with a slice thickness of 0.625 mm. In the coronal

oblique plane of the SIJ, three slices (anterior, middle and posterior) and four quadrants per joint were defined. Twenty-four identical circular regions of interest (ROIs) (30 mm2), 8 per slice, were manually placed separately subcortical to the SIJ, four on the sacral side and four on the iliac side. The distance between the circle of the ROI and the cortical bone was 2 to 3 mm. An overall score was obtained from the sum of all ROIs. For every ROI, an Attenuation Coefficient was measured and expressed in Hounsfield Unit. The total SBAC-SI score was the sum of the 24 ROI. The sacral and iliac SBAC-SI scores were the sum of the sacral or the iliac ROI.
Results. Thirty AS and AS controls, 31 DISH, 29 OCI and OCI controls were included. SBAC-SI score was 9727 (±2430) in the OCI group (p<0.01) and HLA B27 is associated with lower SBAC-SI (6523 [5198; 7137] VS 2809 [1568; 3371]; p<0.001).
Conclusions. SBAC-SI is significantly different between AS and OCI and could help to distinguish these two diseases.

P68

WHOLE BLOOD TRANSCRIPTIONAL CHANGES FOLLOWING TREATMENT WITH FILGOTINIB IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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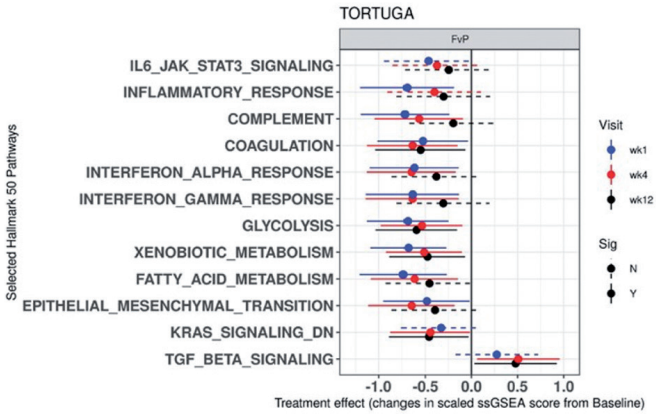
Introduction. Ankylosing spondylitis (AS) is a chronic inflammatory disease affecting the sacroiliac joints and spine. Inhibition of Janus kinase 1 (JAK1) can block multiple inflammatory pathways and lessen AS disease severity. In the TORTUGA study, the preferential JAK1 inhibitor filgotinib (FIL) significantly reduced AS disease activity versus placebo (PBO). Here, the impact of FIL on transcriptional biomarkers in TORTUGA patients with AS from was evaluated.
Methods. TORTUGA (NCT03117270) was a phase 2, double-blind, PBO-controlled study in patients with AS and an inadequate response to >1 nonsteroidal anti-inflammatory drugs. Patients were randomized 1:1 to oral FIL 200 mg (FIL200) or PBO once daily for 12 weeks. Whole blood samples were collected at baseline and Weeks 1, 4 and 12. Illumina TruSeqStranded mRNA was generated for 414 samples from 96 patients; FIL200 (n=49) and PBO (n=47). Gene-level quantification of RNAseq counts and transcripts/million was conducted. Pathway analysis was performed using single sample gene set enrichment analysis (ssGSEA) based on Hallmark 50 pathways.
Results. The JAK-STAT, inflammatory response, complement and coagulation Hallmark 50 pathways were significantly correlated with C-reactive protein (CRP) levels at baseline. AS disease activity score correlated with inflammatory response and coagulation pathways. FIL treatment decreased several metabolic pathways, immune pathways at Week 1, and increased the TGF-β signaling pathway at Weeks 4 and 12 (Fig. 1). FIL downregulated CRP-associated and JAK-STAT pathway genes. A decrease in circulating neutrophils and monocytes (Weeks 1, 4) occurred following FIL treatment, with an increase in B cells (Weeks 4, 12) and lymphocytes (Weeks 1, 4). These fluctuations accounted for some of the gene expression changes observed.
Conclusions. In patients with active AS, FIL treatment decreased inflammatory pathways and genes associated with disease activity. TGF-β signaling pathways increased as a result of changes in inflammatory gene expression and alterations in circulating cellular composition.



P68. Fig. 1. FIL treatment effect on selected Hallmark 50 pathways. Whole blood transcriptomic analysis of PBO-subtracted FIL gene expression changes at Weeks 1, 4 and 12 compared to baseline. Center dots represent the mean changes of the pathway single sample gene set enrichment analysis scores from baseline and the horizontal bar indicate the 95% confidence interval. Treatment effect significance at each time point is indicated by a solid line and is based on the nominal p-value generated by Limma. IL6: interleukin 6; KRAS: Kirsten rat sarcoma virus; Sig: significance; STAT: signal transducer and activator protein; TGF: transforming growth factors; wk: week.

Funding. Gilead.

Disclosures. D Poddubnyy has received consultancy and speakers fees from AbbVie, Eli Lilly and Company, MSD, Novartis, Pfizer, UCB, BMS, and Roche, and grant/research support from AbbVie, Eli Lilly and Company, MSD, Novartis, and Pfizer; **Y Liu** is an employee and patent holder at Gilead Sciences; **W Barchuk** is an employee and patent holder at Gilead Sciences**; R Besuyen** is an employee and shareholder of Galapagos; **R Galien** is an employee and patent holder at Galapagos NV and has received other financial or material support from Galapagos NV; **Y Tian** is an employee and patent holder at Gilead Sciences; **V Malkov** is an employee and patent holder at Gilead Sciences; **A Hertz** is an employee and patent holder at Gilead Sciences.

P69

WHAT DOES IT MEAN – A GOOD RESPONSE TO NSAIDS? A SYSTEMATIC COMPARISON OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND CONTROLS WITH CHRONIC BACK PAIN

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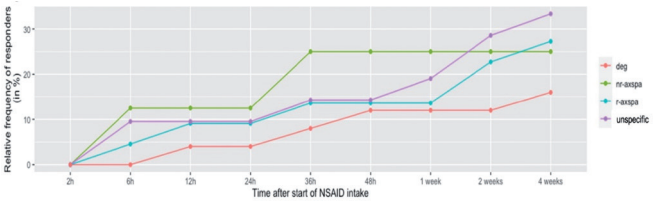
Introduction. We aimed to study the differences in the velocity and magnitude of NSAID response in patients with established bDMARD-naive axSpA vs. patients with other, non-inflammatory reasons of back pain.
Methods. Patients with axSpA or with degenerative or unspecific back pain with high levels of back pain (NRS≥4/10) were consecutively recruited. Upon study inclusion, patients were treated with the maximum possible dose of an NSAID. Assessment of response was performed using a standardized questionnaire after 2, 6, 12, 24, 36, 48 hours and after 1, 2 and 4 weeks. Any NSAID response was defined as improvement of pain >2/10 points and a good response to NSAIDs as an improvement >50% from the initial status.

P69. Table. Demographic data of the included patients.

	proportion of males	mean age, years	main symptom duration, years
axSpA, n=68	57.4%	42.7±10.7	15.1±11.1
Degenerative, n=107	19.6%	51.2±11.3	16.1±12.6
unspecific back pain, n=58	19.0%	45.8±10.0	11.9 ±10.1



P69. Fig. 1.

Results. A total of 68 axSpA patients, 107 with degenerative and 58 with unspecific back pain were included (Table). Inflammatory back pain was reported by 42 (75%), 48 (57.8%), and 29 (60.4%) patients and the mean pain score was 6.2±2.3, 6.7±1.8, and 6.2±1.8, respectively. In axSpA, the mean BASDAI score was 5.5±1.8 and BASFI 4.5±2.5. There was no difference in the cumulative response to NSAIDs between all three diagnoses, with an overall proportion of 27%-30% of patients showing improvement. However, better but not faster responses were found for the nr-axSpA patients (Fig. 1) and for the male patients in the entire axSpA group, while axSpA patients

with increased CRP value showed lower rates of response as compared to non-inflammatory back pain. All other subanalyses did not reveal any differences between axSpA and other non-inflammatory reasons of back pain.
Conclusions. In this evaluation, the generally proposed better response of axSpA patients to treatment with NSAIDs as compared with non-inflammatory back pain was not confirmed, although the overall rate of responders was similar to previously reported rates. On the other hand, better responses were found in nr-axSpA patients and in male patients.

P70

GUSELKUMAB MAINTAINS RESOLUTION OF DACTYLITIS AND ENTHESITIS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS THROUGH 2 YEARS FROM A PHASE 3 STUDY

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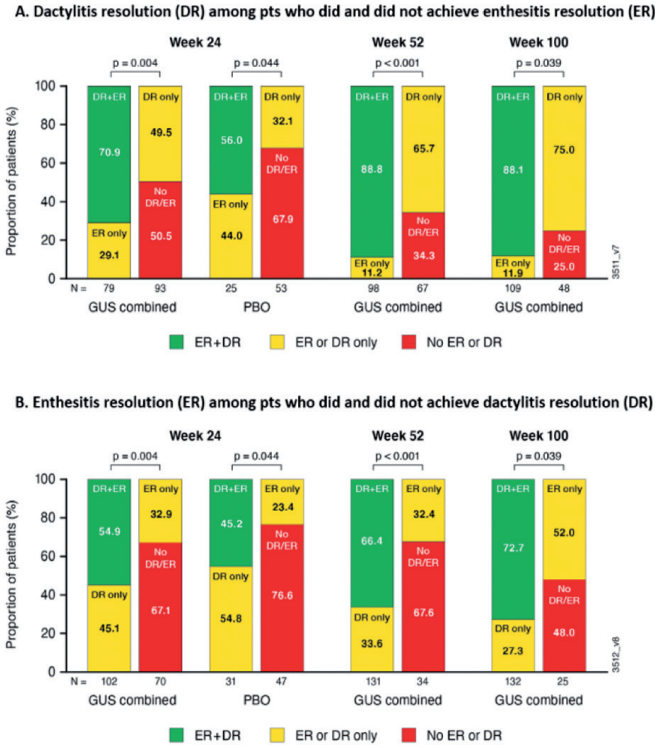
Introduction. Guselkumab (GUS) significantly improved diverse manifestations of active psoriatic arthritis (PsA), including dactylitis/enthesitis, in DISCOVER-1&2 patients with active PsA, with response rates maintained through 1-year. This study evaluated GUS ability to provide long-term resolution of dactylitis/enthesitis in PsA patients through 2-years of DISCOVER-2.
Methods. DISCOVER-2 biologic-naive patients with active PsA were randomized 1:1:1 to GUS-100mg every-4-weeks (Q4W); GUS-100mg at W0/W4/Q8W; or placebo (with crossover to GUS-Q4W at W24). Independent assessors evaluated dactylitis (total score:0-60)/enthesitis (Leeds Enthesitis Index [LEI]; total score:0-6). These post-hoc analyses assessed baseline frequency/severity of enthesitis in dactylitis patients and dactylitis frequency in enthesitis patients. Post-baseline changes in dactylitis/LEI scores over time (least-squares mean/analysis of covariance) and dactylitis/enthesitis resolution rates (Chi-square correlation test) were determined.

P70. Table. LS mean change from baseline over time in dactylitis and LEI scores in patients with manifestation at baseline.

	GUS 100 mg Q4W	GUS 100 mg Q8W	PBO → GUS 100 mg Q4W
Dactylitis score (0-60)			
Pts, N	121	111	99
Week 24[a]	-5.9 (-6.7, -5.0)	-6.0 (-6.8, -5.1)	-4.0 (-5.0, -3.1)
Week 52[a]	-6.5 (-7.2, -5.8)	-7.2 (-7.9, -6.5)	-6.9 (-7.6, -6.2)
Week 100[a]	-6.5 (-7.1, -5.8)	-7.5 (-8.1, -6.8)	-6.9 (-7.6, -6.2)
LEI Score (1-6)			
Pts, N	170	158	178
Week 24[a]	-1.5 (-1.8, -1.3)	-1.6 (-1.8, -1.4)	-1.0 (-1.3, -0.8)
Week 52[a]	-1.8 (-2.0, -1.6)	-1.9 (-2.1, -1.7)	-2.0 (-2.2, -1.8)
Week 100[a]	-1.9 (-2.1, -1.7)	-2.1 (-2.3, -1.8)	-2.1 (-2.3, -1.9)

*Results are LS Mean (95% confidence interval {CI}) change; LS: mean change determined by ANCOVA; missing data was imputed as no change for pts who discontinued treatment abd using multiple imputation for remaining missing data ANCOVA, Analysis of Covariance; GUS: guselkumab; LEI: Leeds Entheisitis Index; LS: least-squares; PBO: placebo; Pts: patients; Q4W: every 4 weeks; Q8W: every 8 weeks.

Results. At baseline, more DISCOVER-2 patients had enthesitis (68%) than dactylitis (45%); patients with (78%) vs without (61%) dactylitis had enthesitis; patients with (51%) vs without (32%) enthesitis had dactylitis. Among patients with enthesitis at baseline, higher percentage of patients with (52%) vs without (44%) dactylitis had severe enthesitis (LEI≥3); resolution rates of dactylitis (57%-Q4W/64%-Q8W) and enthesitis (44%-Q4W/54%-Q8W) at W24 increased through W52 (dactylitis, 74%-Q4W/78%-Q8W; enthesitis, 57%-Q4W/61%-Q8W) and were maintained at W100 (dactylitis, 72%-Q4W/83%-Q8W; enthesitis, 62%-Q4W/70%-Q8W). Consistent results were observed when evaluating mean changes in dactylitis/LEI scores, including patients who crossed over from placebo to GUS-Q4W at W24 (Table). In patients with dactylitis/enthesitis at baseline, GUS-treated patients showed significant correlations between resolution of enthesitis/dactylitis at W24 (p=0.004), W52 (p<0.001) and W100 (p=0.039), with ~90% of patients with enthesitis resolution also achieving dactylitis resolution at W52 and W100 (Figure).



P70. Fig. 1. Correlation analysis between resolution of enthesitis and dactylitis over time among pts with enthesiris and dactylitis at baseline.
p-value was calculated using Chi square test.
ER: enthesitis resolution; DR: dactylitis resolution; GUS: guseljumab; PBO: placebo; pts: patients.

Conclusions. Patients with PsA often present with concurrent enthesitis and dactylitis, both of which can be recalcitrant to treatment. GUS resolved enthesitis/dactylitis in substantial proportions of patients through W100. GUS-treated patients achieving enthesitis resolution were more likely to achieve dactylitis resolution and vice versa.

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P71

SCREENING FOR THE EARLY IDENTIFICATION OF PSORIATIC ARTHRITIS WITH AXIAL INVOLVEMENT (AXPSA) IN A COHORT OF ITALIAN PATIENTS AFFECTED BY PSORIASIS (ATTRACT): PRELIMINARY RESULTS OF A CROSS-SECTIONAL STUDY

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Introduction. There is growing interest towards the early identification of patients with axial involvement in PsA (axPsA) with adequate screening tools. Herein we report preliminary results of a study aiming to evaluate whether a screening strategy focused on the dermatologic setting may improve diagnosis and classification of axPsA patients.

Methods. In this cross-sectional study, patients with psoriasis are enrolled consecutively if they fulfil the following inclusion criteria: 1. age > 18 years; 2. diagnosis of psoriasis (Pso) by a dermatologist; 3. be able to sign the informed consent. Patients will be considered eligible for referral after the completion of the Italian version of the on-line referral tool (OSR). The patients giving a positive answer to both the 2 question of the entry criteria of the chronic back pain features (duration >3 months and age of onset <45 years) will be referred to the rheumatologist for clinical, laboratory and radiological assessment if they answered Yes to at least another question (Table I).

P71. Table I. Questions of the OSR with proportion of "Yes" responses.

QUESTION	YES % in 205
Does your back pain last 3 month or longer?	59,6
Did your back pain start prior to 45 years of age?	49.8
What are the characteristics of your back pain?	**YES % in 125**
The back pain onset was rather slow and was not related to a trauma	86.3
I suffer from stiffness in my back of 30 minutes or longer upon getting up in the morning	69.4
Movement or exercise (but not rest) improve my back pain	78.9
I wake up sometimes in the night (especially 2nd half) because of my back pain	46.0
I have or I had alternating (flipping from side to side) pain in my buttocks	53.2
Other signs and symptoms which might indicate an inflammatory nature of the back pain	
I took a nonsteroidal anti-inflammatory drug (such as Diclofenac or Ibuprofen) because of back pain, and pain was completely relieved or was much better after the drug intake	57.7
I have / had joint pain with swelling and/or inflammation in the areas of tendons insertion to the bone (*e.g.*, heels).	80.6
The genetic marker HLA-B27 has been tested in my blood already and the result was positive	2.4
I have / had elevated markers of inflammation in the blood (C-reactive protein or erythrocyte sedimentation rate), which are unlikely to be explained by other reasons (such as infections)	36.1
I suffer from psoriasis	92.7
I suffer from inflammatory bowel disease (Crohn's disease or ulcerative colitis)	3.2
I suffer / suffered from iritis	2.1
One or several of my direct relatives suffer /suffered from ankylosing spondylitis, psoriasis or inflammatory bowel disease (Crohn's disease or ulcerative colitis)	60.5

Results. From February 15th to April 29th, 256 patients (121 F, mean age 53.04±15.81y) have been evaluated jointly in a dermo-rheumatologic clinic and 253 completed the questionnaire. With regard to Pso, mean BSA was 3.59±6.04, mean PASI 3.25±5.1, 103 (57.2%) patients presented onychopathy with a mean NAPSI score of 1.7±1.3. A total of 123 patients (48.6%) answered Yes to both questions of chronic back pain (Table I).

After rheumatologic evaluation, 29 patients among 65 who have been re-evaluated received a diagnosis of PsA. Among them, actually axPsA has been diagnosed in 18 patients (62%) (among them, 8 also with peripheral involvement).

Conclusions. In this study we report that chronic back pain is present in more than half of the outpatients with psoriasis and the easily applicable screening by the OSR resulted in a high proportion of patients diagnosed with axPsA.

P72

NO CHANGE IN SERUM LEVELS OF BONE TURNOVER MARKERS CORRECTED FOR AGE AND GENDER DURING THE FIRST YEAR OF SECUKINUMAB TREATMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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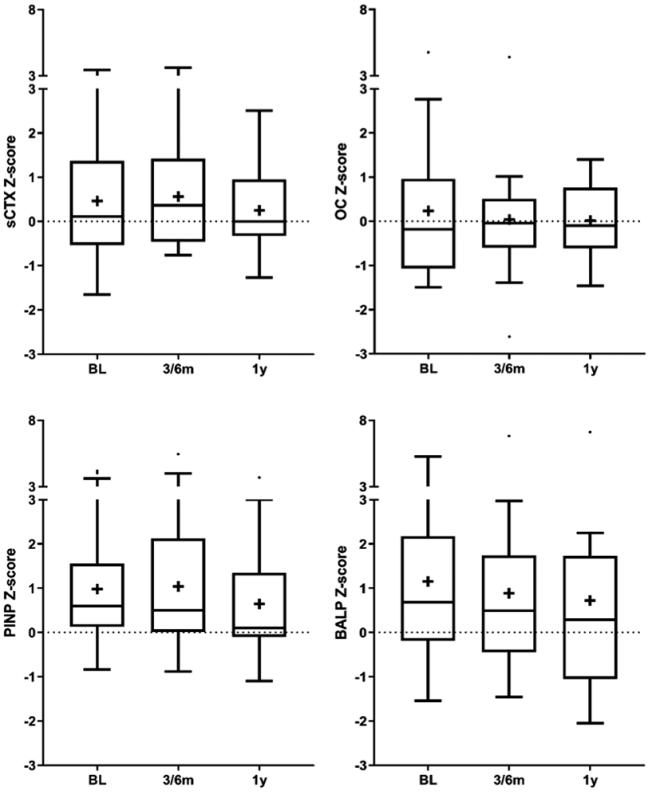
Background. In patients with ankylosing spondylitis (AS), TNF-α inhibitors influence the course of serum bone turnover markers (BTM), favoring an increase in mineralization during the first years (1). Little is known about the effect of IL-17 inhibitors on these serum BTM levels.

Objective. To evaluate serum markers of bone resorption, formation, and mineralization during 1 year of secukinumab treatment in AS patients in daily clinical practice.

Material and methods. Included were consecutive outpatients from the GLAS cohort with a clinical diagnosis of AS who started treatment with secukinumab between April 2016 and June 2020, and had available serum samples at ≥1 visit. Standardized follow-up visits were performed at baseline (before start of secukinumab) and after 3 or 6 months and 1 year of treatment. BTM were measured in serum: osteocalcin (OC; regulation marker), serum type 1 collagen C-telopeptide (sCTX; collagen resorption marker), procollagen type 1 N-terminal peptide (PINP; collagen formation



P.72. Fig. 1. Z-scores of collagen degradation marker sCTX, bone regulation marker OC, collagen formation marker PINP and bone mineralization marker BALP in AS patients during 1 year of secukinumab treatment.
Box-and-whisker plots (Tukey): boxes indicate medians with interquartile ranges, + indicates mean; whiskers indicate 1.5 times interquartile distances.

marker) and bone-specific alkaline phosphatase (BALP; bone mineralization marker). BTM Z-scores were calculated using a healthy reference population to correct for the normal influence of age and gender. Patients using bisphosphonates were excluded from analyses. Data was coded missing if patients experienced a fracture or received systemic corticosteroids within 1 year of a study visit. Generalized estimating equations were used to analyze BTM Z-scores over time within patients.

Results. In total, data of 26 AS patients were eligible for analyses; 50% were male, mean age was 46.0±14.6 years, 81% were HLA-B27 positive, mean ASDAS at baseline was 3.7±1.0, and 50% was TNFi naive. Before secukinumab treatment, median PINP and BALP Z-scores were +0.6 and +0.7 SD, respectively, compared to age and gender matched healthy controls, however, the large majority remained within the normal range of ±2 SD. Overall, BTM Z-scores of OC, sCTX, PINP and BALP did not change significantly compared to baseline during the 1st year of secukinumab treatment (Fig. 1).

Conclusions. In daily clinical practice, serum BTM levels including mineralization corrected for the normal influence of age and gender did not change during the 1st year of secukinumab treatment in patients with AS. Our data confirm recent findings of stable BTM levels at group level during 2 years of secukinumab treatment in posthoc analysis of MEASURE 1 (2).

Acknowledgements. This study was supported by an investigator initiated research grant from Novartis.

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P73

THE ASAS CORE OUTCOME SET FOR AXIAL SPONDYLOARTHRITIS

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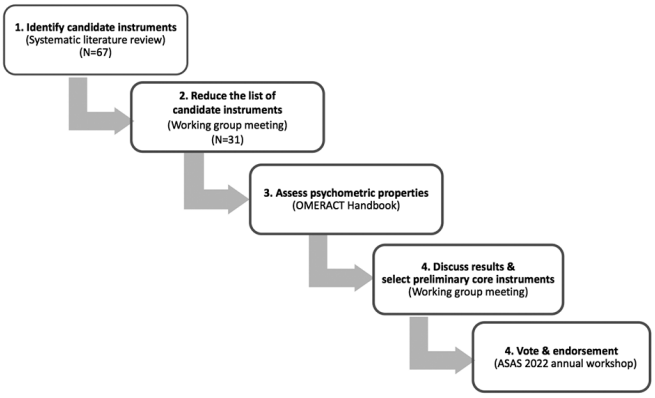
Background. Recently, the core domains of the 20-year-old core outcome set for ankylosing spondylitis were updated.[1] The next step is to define the measurement core set, which includes at least one instrument for each domain.

Objectives. To define the instruments for the ASAS-OMERACT core domain set for axial spondyloarthritis (axSpA).

Methods. An international working group representing key stakeholders selected the core outcome instruments following a predefined process: i) Identifying candidate instruments using a systematic literature review; ii) Reducing the list of candidate instruments by the working group, iii) Assessing the instruments' psychometric properties following OMERACT Filter 2.2, iv) Selection of the core instruments by the working group; v) Voting and endorsement by ASAS (Fig. 1).

Results. The updated core set for axSpA includes seven instruments for six domains that are mandatory for all trials: ASDAS and NRS patient global assessment of disease activity; NRS total back pain; average NRS of duration and severity of morning stiffness; NRS fatigue; BASFI; and ASAS health index. There are 9 additional instruments considered mandatory for disease modifying drugs (DMARDs) trials: MRI activity SPARCC sacroiliac joints and SPARCC spine, uveitis, IBD and psoriasis assessed as recommended by ASAS, 44 swollen joint count, MASES, dactylitis count, and mSASSS. The imaging outcomes are considered mandatory to be included in at least one trial for a drug tested for DMARD-properties. Table I. Furthermore, 11 additional instruments were also endorsed by ASAS to be used in axSpA trials on top of the core instruments: BASDAI, CRP, Berlin MRI-SIJ and MRI-spine activity scores for disease activity, NRS back pain at night for pain, severity (BASDAI Q5) and duration (BASDAI Q6) for morning stiffness, SF-36 for overall functioning and health, 66 swollen joint count and SPARCC enthesitis for peripheral manifestations and MRI-SIJ erosions scores (SPARCC SSS) for structural damage.

Conclusions. The previous core measurement set has been updated and endorsed by ASAS for the use in all axSpA trials.



P73. Fig. 1. Development process to determine the instruments of the core outcome set.

P73. Table I. Instruments for updated COS for axial spondyloarthritis.

Mandatory instruments for all trials	
Domain	**Instrument**
Disease activity	ASDAS Patient global assessment of disease activity (NRS)
Pain	NRS total back pain (BASDAI Q2)
Morning stiffness	Severity and duration of stiffness (BASDAI (Q5+Q6)/2))
Fatigue	NRS fatigue (BASDAI Q1)
Physical function	BASFI
Overall functioning & health	ASAS-HI
Additional mandatory instruments for disease modifying drugs trials	
Domain	**Instrument**
Disease activity	SPARCC MRI-SIJ* SPARCC MRI-spine*
Extra-musculoskeletal manifestations	Acute anterior uveitis†‡ Psoriasis†§ Inflammatory bowel disease†‖
Peripheral manifestations	44 swollen joint count MASES Dactylitis count (including active fingers and/or toes)
Structural damage	mSASSS*

*Needs to be assessed at least once in a disease-modifying drug programme;
†According to ASAS recommendations: diagnosis has never been made, was known at the preceding visit or has been made since the last visit; ‡ In case of diagnosis: the number of episodes since the last visit and corresponding treatment; § In case of diagnosis: percentage of skin area with psoriasis and treatment yes/no; ‖In case of diagnosis: subtype and treatment yes/no.
ASDAS: Ankylosing Spondylitis Disease Activity Score; NRS: Numerical Rate Scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; Q: question; BASFI: Bath Ankylosing Spondylitis Functional Index; SPARCC: SpondyloArthritis Research Consortium of Canada Scoring System; MRI: Magnetic Resonance Imaging; SIJ: Sacroiliac Joint; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score.

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P74

IMPACT OF SPINE ANKYLOSIS ON BONE FRAGILITY EVALUATED ON CT-SCAN IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Introduction. To assess the association between bone fragility threshold through scanographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1) and spine ankylosis evaluated on opportunistic CT scan in patients with ankylosing spondylitis (AS).
Materials and methods. Spondyloarthritis patients who met the New York criteria for AS and explored during their follow-up by a thoraco-abdomino-pelvic CT (TAP-CT) were included. Spine ankylosis on CT was evaluated for the anterior and posterior parts from C7 to S1. The score of ankylosis ranged from 0 to 36 corresponding to the sum of anterior disco-vertebral units (n=18) and facet joints (n= 18). Bone fragility was measured through the SBAC-L1. A SBAC-L1 ≤145HU defined the fracture threshold.
Results. 67 AS patients were included (median age: 61.2 years, 89% men, 63.5% HLA-B27+), 38 presented spine ankylosis with a median ankylosis scoring of 2 [0;35]. The mean SBAC-L1 was significantly different between ankylosed and non-ankylosed patients (119.3HU (±47.9) versus 158.5HU (±40.8). 40 patients were under the fracture threshold (SBAC-L1≤145HU). Patients with spine ankylosis had an OR=3.9 (CI95%: 1.43-10.9) to present a SBAC-L1≤145HU. The score of ankylosis was more severe in patients with a SBAC-L1≤145HU (19.0 (± 21) versus 8.7 (±13.1) (p=0.014). In multivariate analysis, spine ankylosis was associated with a SBAC-L1≤145HU (p=0.007) and biological inflammation (CRP>5mg/l) (p=0.034).
Conclusions. SBAC-L1 and spine ankylosis were inversely correlated. AS patients with spine ankylosis were more frequently under the fracture threshold for SBAC-L1.

P75

ARE α4β7+ γδ T CELLS PRONE FOR THE IL-17 AND IL-22 SECRETION IN SPONDYLOARTHRITIS?

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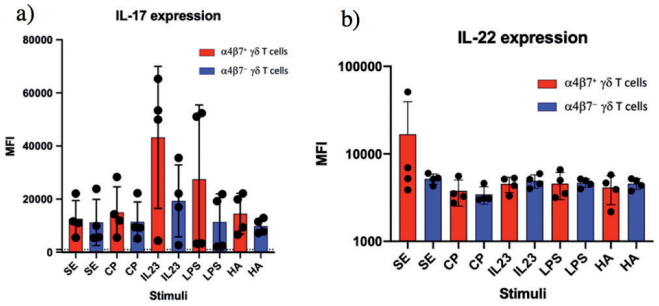
Introduction. Spondyloarthritis (SpA) is a heterogeneous group of inflammatory diseases of unknown cause that share clinical characteristics. Several proposals have intended to elucidate the genesis of the disease, but none of them can entirely explain it. Besides the relationship of HLA-B27, genome-wide association studies (GWAS) have already identified genes that increase the risk for SpA and relate it with Inflammatory Bowel Disease (IBD). The γδ T cell subset, typically found in the epithelial barriers, contributes to barrier homeostasis and microbe clearance. Recently, our group described a novel population of γδ T cells in SpA patients that overexpress the α4β7 integrin, along with Toll-like Receptor (TLR) 2 and TLR 4.
Methods. The objective of this work is to characterize the α4β7-positive γδ T cell subset and to determine the secretion of interleukin (IL)-17 and IL-22 upon lipopolysaccharide (LPS), low molecular weight hyaluronan (HA) and IL-23 stimuli. We will recruit 15 patients formerly classified with ASAS criteria and clinical evaluation and take a 40 ml blood sample for peripheral mononuclear cell obtention; afterward, we will stimulate 4x10^6 cells per stimulus using a 24 wells plate. The assessment of the α4β7 integrin, IL-17, and IL-22 expression will be approached by antibodies and flow cytometry.
Results. A total of four healthy controls agreed to participate in our study. We found a global tendency for the α4β7-positive γδ T cell, in healthy controls, to secrete more IL-17 upon LPS, HA, or IL-23 (p=0.82) (Fig. 1).



P75. Fig. 1. (a) Global tendency of secretion of IL-17 α4β7 γδ T cells upon IL-23, LPS, HA, commercial stimulation cocktail and without stimulus (Kruskal-Wallis p=0.82). **(b)** Secretion of IL-22 apparently is not augmented upon stimuli in healthy controls (Kruskal-Wallis p=0.24).

Conclusions. Expression of the integrin α4β7 in γδ T cell subset indicate both their intestinal activation and their designation for migration. Once activated, these cells can secrete IL-17 even in healthy persons upon bacterial, immunological, and mechanical stress stimuli that could encourage them to migrate and exert their immune functions in the enthesis in SpA patients.

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P76

INCREASED EXPRESSION OF B CELL RECEPTOR SIGNALLING GENES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Introduction. Studies into B cell involvement in ankylosing spondylitis (AS) have demonstrated the presence of B cells at inflammatory sites, imbalances of peripheral B cell subsets and presence of autoantibodies, such as anti-CD74/CLIP. Our objective was to compare gene expression profiles of B cells isolated from AS patients, healthy donors (HD) and patients with primary Sjögren syndrome (pSS), a typical B-cell-associated autoimmune disease.
Methods. To analyse gene expression, we isolated RNA from sorted CD19+ B cells of 8 AS patients (mean age 48.0±9.7 years, 63% male, mean ASDAS 2.5±0.7) compared to 8 age-matched pSS patients and 8 sex and age-matched HDs. Next, characterization of differentially expressed genes was performed using transcriptomic analysis by the NanoString nCounter® Autoimmune Profiling Panel, which utilizes a direct hybridization technique without PCR amplification. Pathway scores were calculated based on overall mean expression of z-scores from genes belonging to a particular pathway.
Results. Analysis of differential gene expression revealed upregulation of 8 genes in B cells from AS patients, such as *MAPK14*, *KMT2A* and *PKM* (p<0.05) and downregulation of only the *DDIT4* gene. The B cell receptor signalling pathway (n=60 genes) showed a higher mean pathway score in B cells from AS patients compared to HDs (p=0.02), but not to pSS patients (p=0.68).
Conclusions. In this cross-sectional study, we observed upregulation of genes associated with B cell receptor signalling in AS patients, compared to HDs. The increased expression of genes involved in downstream B cell receptor signalling is suggestive for enhanced B cell activation in AS.

P77

REAL-WORLD PERSISTENCE AND TREATMENT PATTERNS IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH ANTI-IL17 THERAPY: THE PERFIL-17 STUDY

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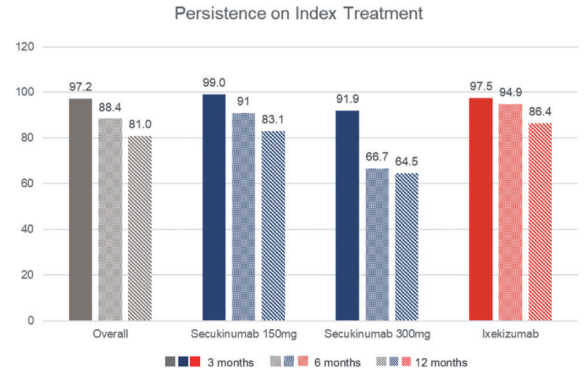
Introduction/objectives. Interleukin-17 inhibitors (Anti-IL17) have provided an additional treatment option in psoriatic arthritis (PsA). This study aims to describe the patient profile, treatment patterns and persistence in PsA patients treated with ixekizumab and secukinumab in real-life setting.
Material and methods. A multicenter retrospective study was conducted at 8 Spanish hospitals. Three cohorts of adult PsA patients, newly initiating treatment with an anti-IL 17A (secukinumab 150mg [SECU150], secukinumab 300mg [SECU300], ixekizumab [IXE]), between January-2019 and March-2020 were included. Data of patients exposed to anti IL-17 drugs with a follow-up visit were collected until March-2021. Demographic and clinical characteristics, treatment patterns, and persistence were analyzed descriptively. Continuous data were presented as mean (Standard Deviation (SD) and categorical variables as frequencies with percentage. Persistence rates at 3/6/12 months were calculated.
Results. A total of 221 PsA patients were analysed (SECU150: 103 [46.6%], SECU300: 38 [17.2%] and IXE: 80 [36.2%]). Treatment patterns differed by clinical characteristics: SECU150 patients presented more moderate PsA and less peripheral joint damage, while SECU300 patients included higher rate with enthesitis and active psoriasis and IXE patients showed longer time since PsA diagnosis, more frequent comorbidities, joint damage and psoriasis diagnosed (Table I). 77.8% of patients were previously treated with csDMARDs in monotherapy and 72.9% with bDMARDs/tsDMARDs (93.8% IXE, 68.4% SECU300 and 58.3% SECU150). Mean number of previous bDMARDS/tsDMARDS were 2.4 (1.5), 1.7 (0.9) and 1.6 (1.0), respectively. Anti-IL-17 persistence is shown in Figure 1. Most frequent reason for discontinuation was lack of effectiveness (13.8%).



P77. Fig. 1. Anti-IL17 persistence, overall and by study cohorts over one year follow-up.

Conclusions. Most of PsA patients treated with Anti-IL-17 in Spain had a moderate to severe disease, high peripheral joint damage and skin involvement and had received at least 1 previous bDMARDS/tsDMARDS. More than 80% of patients with one year follow-up were persistent to Anti-IL-17 treatments, observing the highest rate with IXE, followed by SECU150 and SECU300.

P77. Table I. Demographic and clinical patient characteristics at baseline.

	Overall n (%)	SECU150 n (%)	SECU300 n (%)	IXE* n (%)
Patients	221 (100.0)	103 (100.0)	38 (100.0)	80 (100.0)
Age at index treatment (years), mean (SD)	51.5 (11.6)	51.8 (12.4)	46.1 (10.3)	53.7 (10.4)
Male, n (%)	114 (51.6)	54 (52.4)	18 (47.4)	42 (52.5)
BMI (kg/m2), mean (SD); n	28.6 (6.3); 90	29.0 (6.8); 32	29.0 (6.7); 21	28.1 (5.9); 37
Duration of PsA since diagnosis (years), mean (SD)	8.1 (7.7)	6.9 (7.3)	6.5 (6.8)	10.5 (8.2)
Duration of PsO since diagnosis (years), mean (SD); n	15.2 (13.9); 114	13.0 (13.3); 49	16.7 (13.6); 17	16.9 (14.6); 48
Comorbidities, n (%)	183 (82.8)	82 (79.6)	30 (78.9)	71 (88.8)
Diagnosed psoriasis				
Yes	191 (86.4)	82 (79.6)	33 (86.8)	76 (95.0)
Unknown	9 (4.1)	6 (5.8)	2 (5.3)	1 (1.3)
Active Psoriasis				
Yes	133 (69.6)	56 (68.3)	28 (84.8)	49 (64.5)
Unknown	26 (13.6)	9 (11.0)	2 (6.1)	15 (19.7)
PASI, mean (SD); n	7.9 (6.0); 25	3.9 (3.2); 4	8.3 (6.5); 9	9.0 (6.2); 12
Psoriatic arthritis severity[a]				
Mild	46 (20.8)	18 (17.5)	13 (34.2)	15 (18.8)
Moderate	119 (53.8)	59 (57.3)	17 (44.7)	43 (53.8)
Severe	36 (16.3)	12 (11.7)	7 (18.4)	17 (21.3)
Unknown	20 (9.0)	14 (13.6)	1 (2.6)	5 (6.3)
Joint damage				
Yes	206 (93.2)	92 (89.3)	35 (92.1)	79 (98.8)
Peripheral	180 (87.4)	72 (78.3)	33 (94.3)	75 (94.9)
Axial	92 (44.7)	43 (46.7)	14 (40.0)	35 (44.3)
Dactylitis				
Yes	41 (18.6)	20 (19.4)	7 (18.4)	14 (17.5)
Unknown	11 (5.0)	8 (7.8)	0 (0.0)	3 (3.8)
Enthesitis				
Yes	56 (25.3)	20 (19.4)	15 (39.5)	21 (26.3)
Unknown	14 (6.3)	9 (8.7)	1 (2.6)	4 (5.0)

If specific N values are not provided by variable, data correspond to the full sample per cohort. * 160 mg as starting dose allowing a subsequent maintenance dose of 80 mg as per SmPC. [a] Disease remission (DAS28 < 2.6, DAPSA ≤4), Mild (DAS28 >= 2.6 <= 3.2, DAPSA >4 and ≤14), Moderate (DAS28 > 3.2 y <= 5.1, DAPSA >14 y≤28), Severe (DAS28 > 5.1, DAPSA >28). BMI: Body Mass Index; PASI: Psoriasis Area and Severity Index.

P78

TREATMENT WITH UPADACINITIB IN REFRACTORY PSORIATIC ARTHRITIS. MULTICENTER STUDY OF 51 PATIENTS OF CLINICAL PRACTICE

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Background. Upadacitinib (UPA) is an inhibitor of JAK kinases recently approved by EMA for the treatment of psoriatic arthritis (PsA) in Europe (January 2021) (1). UPA has shown efficacy in refractory patients to anti-TNF (2).
Objectives. A) to assess efficacy and safety of UPA in the first cases in Spain in clinical practice (CP). B) to compare the profile of clinical practice patients with clinical trial (CT) of UPA in PsA refractory to biologics (2).
Methods. Study of 51 patients of clinical practice with PsA treated with UPA in Spain. The diagnosis of PsA was made using CASPAR criteria. Patients who received at least one dose of UPA were included.
Patients with refractory PsA from 16 National Rheumatology Services (January 2021-January 2022) who had received at least one dose of UPA (15 mg/day) were included. Refractory PsA was defined if low clinical activity or remission was not achieved with biological (b) and/or targeted synthetic (ts) disease modifying drugs (DMARDs). The outcomes were efficacy, safety, and corticosteroid sparing. A comparative study was carried out between this CP cohort and those of the SELECT-PsA 2 CT (PsA refractory to antiTNF (2).
The results are expressed as percentages, mean±SD or median [IQR] depending on the distribution of the variable.
Results. 51 patients (37 women) were studied, mean age 52.3±10.6 years (Table I). The joint pattern was: peripheral (n=27; 52.9%), mixed (n=20; 39.2%) and axial (n=4; 7.8%). During the evolution of PsA, they also presented enthesitis (n=26; 51%), dactylitis (n=16; 31.4%), skin involvement (n=40; 78.4%) and onychopathy (n=12; 23.5%).

P78. Table I.

	CLINICAL PRACTICE N=51	CLINICAL TRIAL N=211	p
Baseline demographic parameters			
Age, years (mean±SD)	52.3 ± 10.65	53.0 ± 12.0	0.703
Sex, n (%) female	37(72.5)	113 (53.6)	**0.014**
Disease Characteristics			
Duration of psoriatic arthritis, year (mean±SD)	11.99±9.40	9.5 ± 8.4	0.067
HAQ-DI	1.23±6.23	1.10 ± 0.6	0.778
Swollen joint count, mean±SD	5.7±6.8	11.3 ± 8.2	0.001
Painful joint count, mean±SD	7.70±7.54	24.9 ± 17.3	0.001
Enthesitis, n (%)	17(33.3) (MASES)	172 (81.5) SPARCC	
Dactylitis, n (%)	4 (7.8)	55(26.1)	0.005
PASI score, mean±SD	2.51±1.93	10.1 ± 9.2	0.031
CRP (mg/L)	10.67±17.89	11.2 ± 18.5	0.858
Oral glucocorticoid use, n (%)	25(49)	22 (10.4)	**0.001**
Concomitant synthetic DMARDs, n (%)		98 (46,4)	
Previous use of biological DMARDs, n (%)	50 (98.03)	195 (92.4)	0.143
Number of prior failed biologic DMARDs, n(%) *0 1 2 ≥3	 1 (2) 5 (9.8) 5 (9.8) 40 (78.4)	 18 (8.5) 135 (63.7) 35 (16.5) 24 (11.3)	 **0.001**
UPA week0			
Monotherapy, n (%)	32 (62.75)	113 (53.6)	0.539
Combined with conventional DMARDs, n (%)	19 (37.3)	98 (46.4)	0.113

*Patients with intolerance but not inadequate response to a biologic DMARD, HAQ-DI Health Assessment Questionnaire-Disability Index, PASI Psoriasis Area Severity Index, CRP C-reactive protein, DMARD disease-modifying antirheumatic drug.

Prior to UPA, they received oral corticosteroids (64.7%) (maximum dose of prednisone; median [IQR] 7.5 [0.0-15.0] and a mean per patient of conventional synthetic DMARDs (1.9±1.0) and b-DMARDs (4.4±2.3) The bDMARDs were: etanercept (n=34), adalimumab (36), infliximab (14), golimumab (20), certolizumab (18), secukinumab (37), ixekizumab (21), ustekinumab (26), abatacept (2) and brodalumab (1) In addition, they received the following tsDMARDs: apremilast (n=13), tofacitinib (15) and filgotinib (1).
UPA at baseline was associated with a) prednisone (n=25; 49%; mean dose 6.9±3.1 mg/d). b) conventional DMARDs (n=19; 37.3%); methotrexate (n=11), leflunomide (5), and sulfasalazine (3); or in monotherapy (n=32; 62.75%). At the start of the UPA they had peripheral arthritis (76%), axial activity (21.57%), skin involvement (25.5%), onychopathy (7.8%), enthesitis (33.3%) and dactylitis (7.8%). After a mean follow-up of 3.7±2.6 months, a rapid improvement was observed in a) activity indices (DAS28, DAPSA) (table 2) and b) laboratory tests (CPR). At the 6th month, an improvement in extra-articular manifestations was observed; dactylitis (50%), enthesitis (11.8%) and skin involvement (23.12%) and a corticosteroid-sparing effect (p; NS) (Table II).

P78. Table II.

	Baseline (N=51)	1st month (N=26)	3th month (N=28)	6th month (N=16)
Prednisone, n (%) Dose (mean±SD)	25 (49) 6.88±3.06	14 (53.8) 7.14±3.51 p=0.785	11 (39.2%) 5.45±2.45 p=0.238	6 (37.5) 4.58±2.92 p=0.102
N. Patients: Skin involvement, n (%) *Improvement* **n (%)**	13 (100)	5 (38.5)	4 (30.8)	3 (23.12)
N. Patients: Nail involvement, n (%) *Improvement* **n (%)**	4 (100)	1 (25)	2 (50)	
Joint Count: Swollen joint count, median IQR]	4 [1.00;7.75]	2 [0.00; 4.00] **p 0.001**	1 [0.00; 2.75] **p 0.007**	0.50 [0.00; 2.25] **p 0.014**
Painful joint count, median [IQR] *P (vs baseline)*	6 [3.00; 9.75]	3 [2.00; 4.00] **p 0.002**	2 [0.50; .00] **p 0.001**	1 [0.00; 2.25] **p 0.001**
N. Patients: enthesitis, n (%) *Improvement* **n (%)**	17 (100)	7 (41.2)	7 (41.2)	2 (11.8)
N. Patients: dactylitis, n (%) *Improvement* **n (%)**	4 (100)	-	1(25%)	2 (50%)
CRP mg/dl, median [IQR] *P (vs baseline)*	3.80 [1.00; 10.00]	4 [0.40; 11.10] p=0.423	2.75 [0.40; 5.87] p=0.809	0.50 [0.32; 4.75] p=0.099
DAS28, median [IQR] *P (vs baseline)*	4.7 [4.1; 5.2]	3.8 [3.25; 4.66] **p 0.007**	3.46 [2.76; 4.00] **p 0.002**	2.09 [1.35; 3.68] **p 0.043**
DAPSA, median [IQR] *P (vs baseline)*	26.4 [20.5;30.3]	17.53 [11.58;19.25] **p 0.001**	16.30 [10.10;22.02] **p 0.003**	12.01 [10.76;13.25] **p 0.005**

CP patients compared to RCT patients have a higher proportion of women, duration of PsA and prior b-DMARDs (Table I).
No serious adverse effects (AEs) were observed. One or more minor AEs were reported in 6 (11.8%) patients. UPA was suspended in 12 (23.5%) in the majority due to inefficacy. 1 event of thrombophlebitis was observed. Analytical parameters (lymphocytes, neutrophils, cholesterol and transaminases) remained stable.
Conclusions. The UPA seems effective, fast and relatively safe in refractory PsA in CP, despite being patients with a longer duration of PsA and a greater number of previous b-DMARDs than those of the CT.

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P79

IMPACT OF PATIENT AND DISEASE CHARACTERISTICS ON GLOBAL FUNCTIONING AND HEALTH IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A BAYESIAN NETWORK ANALYSIS OF DATA FROM AN EARLY AXSPA COHORT

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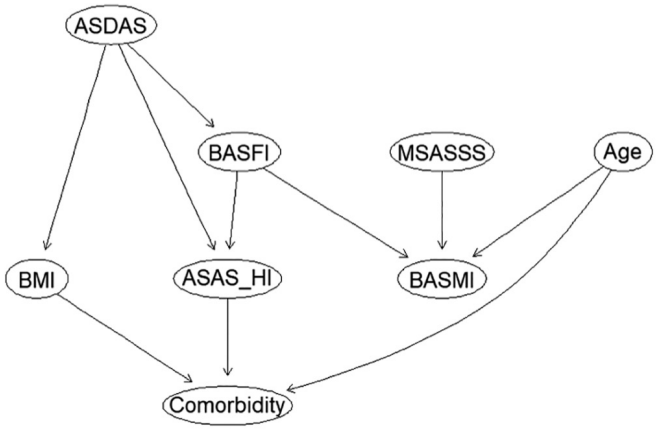
Objectives. To build a structural model that visualizes interrelationships of different patient- and disease characteristics with global functioning and health in pts. with early axSpA.
Methods. Data from the DESIR cohort was analyzed. Information on patient- and disease characteristics was retrieved from the 72-month visit after inclusion, which was the first time point of ASAS HI collection. A Bayesian network (BN) was used to obtain insight of the underlying structural model.

BNs are capable of capturing complex relationships between variables and allow the incorporation of existing (prior) knowledge from previous studies.
Results. In total 398 patients had ASAS-HI available at month 72 and could be included (Table I). The mean ASAS HI was 5.7 with 51% in 'good', 40% in 'moderate' global functioning and 9% in 'bad' global functioning. The structural model that was constructed from combining data and prior expert knowledge is visualized in Figure 1. It suggests that ASDAS and BASFI have a direct impact on ASAS HI and that ASDAS has also an indirect impact via BASFI. Moreover, the model suggests that ASDAS has an impact on the number of comorbidities via BMI and that BASFI determines BASMI, which is in turn also influenced by age and mSASSS. It suggests a direct effect of age, BMI and ASAS HI on the comorbidity count. The model denies a relationship between BASMI or mSASSS and ASAS HI.

P79. Table I. Patient and disease characteristics at month 72.

	N=398
Gender (male), N (%)	181 (45%)
Age (years)	40.7 (8.7)
Symptom duration (years)	7.5 (0.9)
BMI (kg/m^2)	25.0 (4.6)
ASDAS	2.0 (1.0)
BASFI (0–10)	2.3 (2.1)
BASMI (0–10)	2.5 (1.0)
mSASSS (0-72)	1.0 (3.6)
ASAS HI (0-17)	5.7 (3.9)
good global functioning: ASAS HI ≤5, N (%)	201 (51%)
moderate global functioning: 5< ASAS HI <12, N (%)	160 (40%)
bad global functioning: ASAS HI ≥12, N (%)	37 (9%)
Comorbidity count	1.4 (0.7)



P79. Fig. 1. Structural model on interrelationships of different patient- and disease characteristics with global functioning and health (ASAS HI) in patients with early axSpA.

Discussion. The BN-analysis approach serves to better understand the construct of global functioning and health in pts. with early axSpA. Our model shows that ASAS-HI is determined both by patient-reported physical function (BASFI) and by disease activity (ASDAS), which confirms the hierarchical model once proposed by Machado *et al*. The observed directional relationship between ASAS HI and comorbidity count is counterintuitive and requires further investigation.

P80

DEVELOPMENT THROUGH CO-CREATION OF A PERSONALIZED, MULTIMODAL, PHYSIOTHERAPIST-LED, WORK-ORIENTED INTERVENTION TO INCREASE WORKABILITY IN WORKING PEOPLE WITH AXIAL SPONDYLOARTHRITIS OR RHEUMATOID ARTHRITIS

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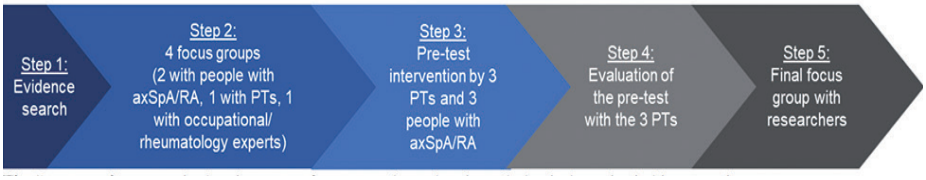
Introduction. Work is underexposed in current treatment of people with axial SpondyloArthritis (axSpA) and Rheumatoid Arthritis (RA). Physiotherapists (PT) might play an important role in optimizing workability of people with axSpA/RA.
Objectives. Developing a personalized, multimodal, PT-led, work-oriented intervention for working people with axSpA/RA and reduced workability.
Materials and methods. A systematic co-creation process was conducted (see Figure). In step 1, a concept intervention was developed based on literature. In step 2, barriers and facilitators of work-oriented treatments and adaptations to the draft intervention were discussed in focus groups with people with axSpA/RA, PTs and occupational/rheumatology experts. In step 3, the intervention was tested in a primary physiotherapy setting and evaluated with participating PTs in step 4. In step 5, necessary adaptations for the final intervention were discussed in a focus group with researchers.
Results. After developing the concept intervention, two focus groups with people with axSpA/RA (n=16), one focus group with PTs (n=12) and one focus group with occupational/rheumatology experts (n=9) were conducted. People with axSpA/RA emphasized three aspects: i) PTs should have expertise in axSpA/RA, ii) high potential for a 'buddy' role by PTs in support of work-related problems, and iii) most PTs lack expertise on work-related problems. PTs and experts underlined the importance of extensive training of PTs on work-related legislation and interprofessional collaboration. A test in three PTs and three working people with axSpA/RA indicated that the intervention was feasible and facilitated PTs to support people in optimizing workability. Adequate training on providing this intervention was recognized to be essential. In a focus group with researchers (n=6), consensus was reached on minor adjustments to the intervention.
Conclusions. Through a systematic co-creation process, we developed a personalized, multimodal, PT-led, work-oriented intervention for working people with axSpA/RA and a reduced workability, which will be evaluated in a RCT.
Acknowledgements. This study is funded by the Dutch Arthritis Society (ReumaNederland) and the Scientific College of Physical Therapy (WCF) of the Royal Dutch Society for Physical Therapy (KNGF). This study is registered in The Netherlands Trial Register under number NL9343.

P80. Fig. 1. Process of systematic development of co-created, work-oriented physiotherapist-led intervention.



P81

PREDICTORS OF SUSTAINED REMISSION IN PEOPLE WITH AXIAL SPONDYLOARTHRITIS TREATED WITH BIOLOGIC DRUGS

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Introduction/objectives. To determine predictors of sustained remission in people with axial spondyloarthritis (axSpA) after treatment with their first biological DMARD (bDMARD).
Methods. Hacettepe University Rheumatology Biologic Registry (HURBIO) is a prospective, single center registry of rheumatic disease patients treated with bDMARDs. AxSpA patients were selected, and sustained remission defined as attainment of ASAS-Partial Remission (ASAS-PR) and/or ASDAS-Inactive Disease (ASDAS-ID) status for ≥2 consecutive visits spanning ≥6 months during follow-up. Multivariable logistic regression analysis was performed to determine independent factors predictive of sustained remission. Two separate multivariable models were built, one with and one without the covariate "achievement of remission at 3-6 months", to assess consistency of findings and to account for missing information regarding remission status between 3-6 months.
Results. Data on 990 patients with sustained remission data were available. Of these, 299 (30%) were in sustained remission, while 691 (70%) were not. Patients in sustained remission were younger, had earlier disease onset, were more frequently male, had lower BMI and were more frequently HLA-B27 positive, compared to patients not in sustained remission (Table I). Furthermore, at the start of bDMARD treatment, BASDAI, BASFI, and patient global assessment (PGA, 0-10 scale) were lower, while ESR and CRP were higher, in the sustained remission group.
In multivariable analysis, male gender, concomitant conventional synthetic DMARD (csDMARD) use, and early achievement (between 3-6 months) of remission were independently associated with sustained remission (Table II-model 1). In the model without the variable early achievement of remission (Table II-model 2), similar and additional associations were described: age at diagnosis, male gender, concomitant csDMARD use, PGA, BASDAI, and baseline symptom duration.
Conclusions. These data can be used to aid clinical and personalized management of axSpA, and to facilitate better communication between health care professionals and patients regarding the course and prognosis of their condition.

P81. Table I. Demographic and clinical characteristics of patients in sustained remission by ASAS PR and/or ASDAS-ID.

	All (n= 990)	Sustained remission (n= 299)	Non-remission (n= 691)	*p*-value
Age*, years	45.1 ± 11.5	43.6 ± 10.9	45.7 ± 11.7	**0.008**
Age at disease diagnosis*, years	34.1 ± 11	31.8 ± 10.1	35.1 ± 11.3	**<0.001**
Age at symptom onset*, years	29.9 ± 10.9	28.3 ± 9.8	30.5 ± 11.3	**0.002**
Male*, n (%)	556 (56.2)	224 (74.9)	332 (48)	**<0.001**
Disease duration*, years	11 ± 6.7	11.8 ± 6.1	10.7 ± 6.9	**0.011**
Delay in diagnosis*, years	4.2 ± 5.9	3.5 ± 5.2	4.5 ± 6.1	**0.006**
Duration between onset of disease and bDMARDs*, years	8.2 ± 7.7	7 ± 6.7	8.8 ± 8	**<0.001**
HLA B27 (n= 607), n (%)	303 (49.9)	110 (59.8)	193 (45.6)	**0.001**
BMI*	27.7 ± 10.9	26.7 ± 10.3	28.2 ± 11.2	**0.048**
Smoking (n= 988), n (%)				
-Never	358 (36.2)	104 (34.9)	254 (36.8)	
-Ex-smoker	209 (21.2)	71 (23.8)	138 (20)	
-Current smoker	421 (42.6)	123 (41.3)	298 (43.2)	0.4
Uveitis (n= 989), n (%)	122 (12.3)	37 (12.4)	85 (12.3)	0.98
Swollen joints (n= 635), n (%)	70 (11)	23 (13.3)	47 (10.2)	0.26
Tenderness joints (n= 630), n (%)	125 (19.8)	37 (21.5)	88 (19.2)	0.52
Concomitant csDMARDs (n= 934), n (%)				
-Sulphasalazine	137 (14.7)	56 (19.2)	81 (12.6)	**0.009**
-Methotrexate	57 (6.1)	20 (6.8)	37 (5.8)	0.52
Baseline BASDAI (n= 810)	5.6 ± 2.1	4.9 ± 2.1	5.9 ± 2	**< 0.001**
Baseline BASFI (n= 630)	4.4 ± 2.4	3.6 ± 2.4	4.6 ± 2.4	**<0.001**
VAS-PGA (n= 816)	61.1 ± 20.6	53.1 ± 21.7	64.3 ± 19.4	**<0.001**
VAS-pain (n= 624)	65.3 ± 23	57.9 ± 23.8	67.8 ± 22.2	**<0.001**
VAS-fatigue (n= 619)	55.6 ± 28.3	41.6 ± 28.6	60.4 ± 26.6	**<0.001**
Baseline ASDAS-CRP (n= 600)	3.32 ± 0.87	3.24 ± 0.95	3.35 ± 0.84	0.19
Baseline ESR (mm-h) (n= 913)	27.04 ± 22.5	30.9 ± 24.6	25.3 ± 21.3	**0.001**
Baseline CRP (mg/L) (n= 901)	25.1 ± 36.4	34.9 ± 45.9	20.8 ± 30.3	**<0.001**

***n=990** patients. Baseline refers to start of bDMARDs treatment.
ASAS PR: Assessment in Ankylosing Spondylitis Partial Remission; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score C-reactive protein; ASDAS-ID: Ankylosing Spondylitis Disease Activity Score Inactive Disease; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; bDMARDs: biological disease-modifying anti-rheumatic drugs; BMI: Body mass index; CRP: C-reactive protein; csDMARDs: Conventional synthetic disease-modifying anti-rheumatic drugs; ESR: Erythrocyte sedimentation rate; HLA: Human leukocyte antigen; VAS-PGA: Visual analogue scale patient global assessments; VAS: Visual analogue scale.

P81. Table II. Multivariable analysis (best-fit model) of predictors of sustained remission.

Covariates	**Model 1** Multivariable Analysis (n= 541)		**Model 2** Multivariable Analysis (n=739)	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age at diagnosis	NS	NS	0.97 (0.96-0.99)	0.006
Male sex	2.84 (1.71-4.70)	<0.001	2.31 (1.60-3.35)	<0.001
Concomitant csDMARD use (at baseline or follow-up)	2.94 (1.57-5.51)	0.001	1.88 (1.23-2.86)	0.003
Baseline PGA	0.97 (0.96-0.98)	<0.001	0.98 (0.97-0.99)	0.002
Baseline BASDAI	NS	NS	0.87 (0.78-0.96)	0.009
Baseline symptom duration	NS	NS	0.97 (0.94-0.99)	0.021
Achievement of remission at 3-6 months after baseline	11.70 (7.11-19.23)	<0.001	NA	NA

Baseline refers to start of bDMARD treatment. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; csDMARDs: Conventional synthetic disease-modifying anti-rheumatic drugs; NA: not applicable; NS: not selected (not contributing to the model); OR: Odds ratio; VAS-PGA: Visual analogue scale patient global assessments.

P82

MULTI-BIOLOGIC RESISTANT ANTERIOR UVEITIS IN THE CONTEXT OF SPONDYLOARTHRITIS

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Introduction. Uveitis is a common extraskeletal manifestation of axial and peripheral spondyloarthritis (SpA). It can be the presenting symptom of the disease and sometimes drives the therapeutic decision. While in the majority of cases, uveitis responds well to local or systemic treatment, it can be refractory requiring multiple immunosuppressive agents
Objectives. To identify patients with diagnosis of SpA that received multiple biological treatments (≥2) due to resistant anterior uveitis (RAU). To describe patients' characteristics, biologics switching and outcome of the ocular involvement.
Methods. We reviewed medical records from two tertiary referral centers in Greece. All patients with diagnosis of SpA who received (≥2) biologics due to RAU were identified.
Results. We identified eight patients, (50%) females. Duration of follow-up (years), median, (range) 9(5-14), 5/8(62%) of patients were diagnosed with Axial SpA (all with Ankylosing Spondylitis) and 3(38%) with Peripheral SpA (one associated with psoriasis). 5/8 (62%) were HLA-B27 positive and 7/8 (87%) had bilateral involvement. The median age (years) at the first episode of uveitis was 30 (19-45). All patients had received concomitant methotrexate, 6/8 (75%) of patients have failed to 2 consecutive biologics and 2/8 (25%) to 3 and all patients had developed damage: 1/8(12%) blindness from one eye, 1/8(12%) band keratopathy and the rest 6/8 (76%) posterior synechiae and/or cataract (Table I).

P82. Table I. Previous and current biologic treatments of reported cases and type of ocular damage.

Patients/sex	Previous biologics	Current biologic	Ocular damage
1/ Male	Etanercept, Infliximab	Adalimumab	Cataract
2/ Female	Adalimumab, Golimumab	Certolizumab	Band keratopathy
3/ Male	Ustekinumab, Secukinumab	Infliximab	Posterior synechiae
4/ Male	Etanercept, Adalimumab	Certolizumab	Posterior synechiae
5/ Female	Etanercept, Adalimumab	Certolizumab	Cataract
6/ Female	Etanercept, Adalimumab, Golimimab	Infliximab	Cataract, posterior synechiae
7/ Male	Etanercept, Adalimumab	Infliximab	Blindness(left) eye
8/ Female	Etanercept, Adalimumab, Golimumab	Infliximab	Cataract, posterior synechiae

Conclusions. In our case series all patients with RAU despite treatment with multiple-biologics have developed ocular damage, suggesting the existence of small group of patients with(SpA in which AU follows independent and aggressive course.

P83

KOREAN TREATMENT RECOMMENDATIONS FOR THE PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Objectives. To develop evidence-based recommendations for treating axial spondylarthritis (axSpA) in the context of Korea.
Methods. A committee for developing the recommendations was assembled and included rheumatologists from the Korean Society of Spondyloarthritis Research, a methodologist, a nurse, and two patients from patient organizations. They selected eighty-eight key clinical questions, for which evidence was searched among Korean or English articles published between 1990 and 2021 from MEDLINE, EMBASE, Cochrane databases, KoreaMed, and Kmbase. Systemic literature reviews were conducted, quality of evidence was determined, and draft recommendations were formulated according to GRADE methodology. Extended panels voted on each statement to finalize the recommendations.
Results. Three principles and 21 recommendations were established based on at least 80% agreement among the voting panels. Principles are regarding the definition of axSpA, treatment goals, shared decision, and multidiscipline approach. Recommendations 1 and 2 are for treatment strategies; individualized therapy, regular assessments of disease status and activity, and rheumatologist-steered collaboration with other relevant specialists. Patient education, exercise, and smoking cessation are strongly recommended (recommendations 3 and 4). Recommendations 5 to 12 are for pharmacologic treatment for the active disease using NSAIDs, glucocorticoids, sulfasalazine, biologics, and JAK inhibitors. Recommendations 13 to 16 are for on-demand NSAID and alternative biosimilar for stable disease, biologic tapering in the patients with long-term remission, and analgesics for residual pain. We suggest against spa and acupuncture (recommendation 17). Recommendations 18 and 19 refer to the surgical indication of total hip arthroplasty and spinal surgery. Monitoring of comorbidities and drug toxicities is recommended weakly and strongly, respectively (recommendations 20 and 21).
Conclusions. These treatment recommendations were developed based on comprehensive clinical questions and evidence so far for applying to a Korean context. We hope that it will be a guide for the best care in the treatment of axSpA.

P84

DISTRIBUTION OF INFLAMMATORY/DEGENERATIVE/ AMBIGUOUS LESIONS ON CONVENTIONAL LUMBAR LATERAL RADIOGRAPHS IN PSORIATIC ARTHRITIS PATIENTS

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Introduction. The aim of this study is to determine the distribution and the relation of different type of lesions on the lumbar radiographs of Psoriatic arthritis (PsA) patients receiving bDMARD therapy.
Methods. The upper-lower regions of each vertebra were evaluated between T12-S1. Lesions were determined according to mSSASS. Osteophytes (O) were grade between 0-3. Lesions without clear distinction were defined as ambiguous. For patients with follow-up radiographs, the change of lesions defined as ambiguous was also recorded. All of the assessments were done by an experienced rheumatologist (UK) and (LK) reviewed the cases with suspicion and a consensus was reached.
Results. The mean (SD) age of 182 PsA (69.2% female) patients was 47.6 (12.7), the age at diagnosis of PsA was 39.7 (12.7). Of the patients, 112 (61.5%) met the criteria for mNY. O was the most frequently detected lesions (42.3%). While syndesmophyte (SP) was present in 24.2% of all patients, ambiguous lesions were detected in 13 (4.7%) patients. O were most frequently grouped between L2-L4 regions, SPs were distributed in a similar ratio between T12-L4 regions, ambiguous lesions were anywhere between T12 -L5. Patients with ambiguous lesions were older (p=0.017), lumbar mSSASS score was higher (p=0.002) SPs (p=0.013) and bridging SPs (p=0.006) were more common, while no difference was found in terms of O grade 2 (p=0.63). Changes were observed in 5 ambiguous as, 4 of them transformed into SP, and one was evaluated as osteophyte grade 2.
Conclusions. Approximately one-fifth of patients presenting with O ≥ grade 2 and SP was found in one fourth. Around 5% of all patients, lesions were ambiguous. The frequency of SPs in other vertebral areas are more prominent in patients with ambiguous lesions. It is seen that ambiguous lesions turn into SPs in a small group of patients with follow-up data.

P84. Table. The distribution of the lesions on lumbar spine.

Location	Osteophyte	Osteophyte ≥2	SP	Bridging SP	All SP	Erosion, Sclerosis, Squaring	Ambiguous
T12 L, n (%)	7 (3.8)	1 (0.5)	9 (4.9)	5 (2.7)	14 (7.7)	3 (1.6)	2 (1.1)
L1, U n (%)	6 (3.3)	0 (0)	10 (5.5)	5 (2.7)	15 (8.2)	2 (1.1)	2 (1.1)
L1, L, n (%)	10 (5.5)	6 (3.3)	8 (4.4)	6 (3.3)	14 (7.7)	4 (2.2)	0 (0)
L2, U, n (%)	15 (8.2)	8 (4.4)	8 (4.4)	7 (3.8)	15 (8.2)	4 (2.2)	4 (2.2)
L2, L n (%)	16 (8.8)	6 (3.3)	5 (2.7)	6 (3.3)	11 (6.0)	4 (2.2)	0 (0)
L3,U n (%)	31 (17.0)	13 (7.1)	4 (2.2)	6 (3.3)	10 (5.5)	10 (5.5)	2 (1.1)
L3 ,L n (%)	17 (9.3)	8 (4.4)	3 (1.6)	5 (2.7)	8 (4.4)	5 (2.7)	2 (1.1)
L4,U, n (%)	37 (20.3)	14 (7.7)	8 (4.4)	5 (2.1)	13 (7.1)	11 (6.0)	4 (2.2)
L4, L n (%)	10 (5.5)	1 (0.5)	3 (1.6)	1 (0.5)	4 (2.2)	6 (3.3)	4 (2.2)
L5, U n (%)	24 (13.2)	8 (4.4)	1 (0.5)	1 (0.5)	2 (1.1)	1 (0.5)	1 (0.5)
L5,L n (%)	8 (4.4)	3 (1.6)	1 (0.5)	1 (0.5)	2 (1.1)	0 (0)	0 (0)
S1, U, n (%)	3 (1.6)	3 (1.6)	0 (0)	1 (0.5)	1 (0.5)	0 (0)	0 (0)
All vertebral corners (n=2184)	184 (8.4)	75 (3.4)	60 (2.7)	49 (2.2)	109 (4.9)	50 (2.2)	21 (1.0)
All patients	77 (42.3)	33 (18.1)	36 (19.8)	17 (9.3)	44 (24.2)	22 (12.1)	13 (4.7)

SP:SyndeSmophyte, L:Lower, U:Upper

P85

ELECTRICAL TREATMENT ON SLEEP DISTURBANCE WITHIN AUTOIMMUNE DISEASES PATIENTS AND ITS EFFECTIVENESS ON IMMUNOLOGIC FACTORS

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Objectives. Sleep disturbance can accelerate disease process and affect the quality of life in AID. This study aim to evaluate the efficacy and acceptability of the ET-21 Electrical treatment on sleep disturbance within autoimmune diseases patients and its effect on immunologic factors.
Methods. 48 AID patients with sleep disturbance were enrolled in this study. The ET-21 Electrical Treatment consisted of daily session of 3-6 times and 15-30 minute a time. The Pitchburg Sleep Index (PSQI), Anxiety Self-Assessment Scale (SAS) were assessed and Immunologic function and serum level of 12 cytokines were detected at baseline and after 3 months treatment.
Results. Both PSQI and SAS scores significantly decreased after treatment. 29 participants have finished baseline and post-treatment detection of serum level of cytokines and immunologic function. Serum level of IL-8 (151.02±78.33 pg/ml) was significant decreased (6.54±7.60 pg/ml) after treatment. There were significant difference in the amount of $CD4^+CD8^+$T cell, naive $CD8^+$T cell, effector memory $CD8^+$Tcel, NFT cell, Tc cell, plasma cell, Tfh cell and Tfh2 cell (p<0.05) between two groups. The global score of PSQI was positively correlated with the serum level of IL-12p70, IL-2, IL-4 and IFN-α. There were also correlations between component scores of PSQI and serum level of cytokines. While sleep latency and use of sleep medications had no significant correlation with serum level of cytokines. However, neither global score not component scores had significant correlation with the amount of immune cells except Tfh cell.
Conclusions. ET-21 electrical treatment can effectively improve sleep disturbance and anxiety in patients with AID. It can also improve the level of IL-8 and regulate the immune function. However, the effectiveness in sleep disturbance has nothing to do with immunologic factors.

P86

ADIPSIN AND RESISTIN LEVELS ARE INCREASED IN SERUM OF SPONDYLOARTHRITIS PATIENTS

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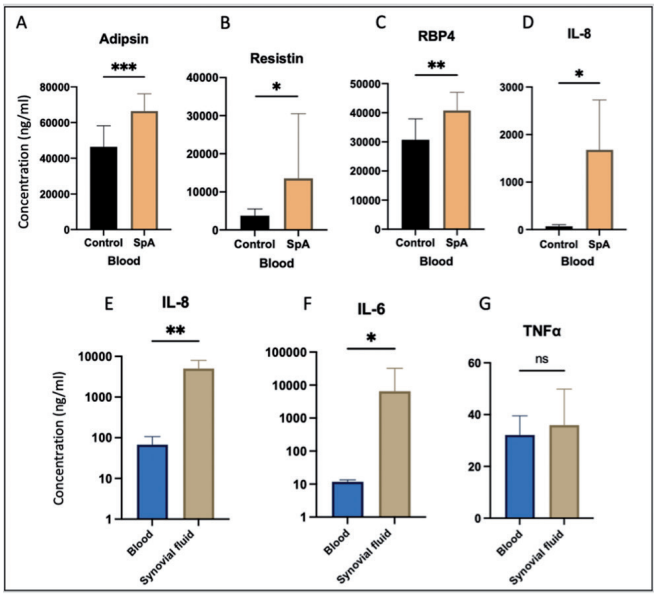
Introduction. Adipokines are inflammatory mediators secreted by the adipose tissue. Evidence supports that these mediators are increased in rheumatic diseases, especially in obese patients. Adipokines are suggested to be involved in the pathophysiology and treatment responses of Spondyloarthritis (SpA). Adipsin is an adipokine secreted by adipocytes in response to high serum glucose levels and increases insulin secretion. Resistin is an adipokine that mediates insulin resistance in mice. in inflammatory conditions, Resistin upregulates IL-6 and TNF-α via the NF-κB pathways. Moreover, when injected into mice joints, resistin induces an arthritis-like condition.
Materials and methods. After signed informed consent, a questionnaire was filled with the patient's data and clinical manifestations. Each patient was classified by the clinical activity of the disease with "inactive disease", "low disease activity", "high disease activity" or "very high disease activity", measured by the Ankylosing Spondylitis Disease Activity Score (ASDAS)-CRP. 10 ml of blood was withdrawn from each patient and centrifuged for plasma separation for analysis by a cytokines bead array to measure adipokine concentration of adipsin, resisitin, retinol-binding protein 4 (RBP4) and cytokines IL-6, IL-8, and TNF-α by flow cytometry.
Results. Our group has found high levels of adipsin in the serum of SpA patients compared to healthy controls (p=0.0007) (Fig. 1A). We have found elevated levels of resistin in serum of SpA patients compared with healthy controls (p=0.0150) (Fig. 1B). We categorized patients depending on their ASDAS-CRP activity in moderate, high and very high activity indexes, and measure levels of IL-6 (Fig. 2A) and TNF-α (Fig. 2B) in blood serum showing a positive tendency whereas higher activity shows higher cytokine levels.



P86. Fig. 1.

Conclusions. Patients with SpA have higher serum levels of adipsin and resistin. There is a trend of patients to present higher cytokine responses of IL-6 and TNF-α with higher disease activity.

P87

ELECTROCARDIOGRAPHIC DISTURBANCES IN PSORIATIC ARTHRITIS - A CASE-CONTROLLED STUDY

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Introduction/objectives. Cardiac involvement is well recognized in Spondylarthritis (SpA). Rhythm or conduction disturbances are possible cardiac manifestations, mainly described in axial SpA. Electrocardiographic disturbances in Psoriatic Arthritis (PsA) are less well studied.
The purpose of our study is to compare electrocardiographic findings between PsA patients and a matched healthy control group.
Materials and methods. Single-center, cross-sectional case-control study comparing the ECG findings of PsA patients fulfilling the CASPAR criteria with a matched healthy control group.
Each patient in the study group was matched by sex and age to an individual in the control group.
All the patients and controls have had a cardiac check-up with a 12-lead electrocardiogram (ECG), posteriorly evaluated by a blinded Cardiologist.
Sociodemographic and clinical characteristics, as well as current medication, were collected.
Descriptive analysis was performed using means and standard deviation (SD), medians and Interquartile range (IQR) for continuous data, and frequencies and percentages for qualitative variables.
ECG findings were compared between groups using parametric and non-parametric tests, and multivariable analysis was performed to evaluate factors associated with rhythm disturbances, with a p-value ≤0.05, with SPSS® software.
Results. We selected a total of 88 patients (44 PsA patients and 44 matched controls). 45.45% were women, and the mean age of patients was 54.84 years. Sociodemographic data are presented in Table I. We found no statistically significant differences regarding cardiovascular risk factors between groups. Electrocardiographic alterations (atrioventricular block, left anterior fascicular block, left axis deviation, or atrial fibrillation) were statistically more prevalent in PsA patients when compared to the control group [11.00 (25.00%) vs. 2.00 (4.55%); *p*=0.01] (Table II) When stratified for disturbance subtype, we found only statistically significance for left axis deviation (*p*=0.04)

P87. Table 1. Sociodemographic and clinical characteristics.

Sociodemographic and clinical characteristics	Psoriatic arthritis N=44	Controls N=44	*p*-value
Age, years (mean, SD)	54.84 (± 11.54)	54.84 (±11.54)	1.00
sex, female (number, %)	20.00 (45.45)	20.00 (45.45)	1.00
SpA characteristics			
Disease duration, years (median, IQR)	9.00 [5.25-11.75]	NA	
Enthesitis (number, %)	14.00 (31.80)	NA	
Dactilitis (number, %)	16.00 (36.60)	NA	
Uveitis (number, %)	0.00 (0.00)	NA	
HLA-27 (number, %)	4.00 (9.10)	NA	
Cutaneous Psoriasis (number, %)	44.00 (100.00)	NA	
Ungueal Psoriasis (number, %)	18.00 (40.90)	NA	
IBD (number, %)	1.00 (2.3)	NA	
Peripheric articular pattern (number, %)			
Oligoarticular (number, %)	9.00 (20.50)	NA	
Poliarticular RA-like (number, %)	32.00 (72.70)	NA	
Distal Interphalangic isolated (number, %)	3.00 (6.80)	NA	
CRP (median, IQR)	0.49 [0.16-1.32]	NA	
ESR (median, IQR)	12.00 [7.00-28.00]	NA	
BASDAI (median, IQR)	3.82 [1.45-6.40]	NA	
BASFI (median, IQR)	3.90 [1.20-6.45]	NA	
Cardiovascular risk factors			
Hypertension (number, %)	18.00 (40.90)	NA	
Diabetes (number, %)	7.00 (15.91)	NA	
Dyslipidemia (number, %)	19.00 (43.18)	NA	
Obesity (number, %)	4.00 (9.09)	NA	
Smoking history (number, %)	1.00 (2.27)	NA	
Spa related drugs			
DMARDs (number, %)	38.00 (86.36)	NA	
>Methotrexate (number, %)	24.00 (54.60)	NA	
>Sulfasalazine (number, %)	5.00 (11.40)	NA	
>Leflunamide (number, %)	6.00 (13.60)	NA	
>TNF-α inhibitors (number, %)	14.00 (31.82)	NA	
>Ustekinumab (number, %)	1.00 (2.30)	NA	
>Secukinumab (number, %)	1.00 (2.30)	NA	
Corticosteroids (number, %)	18.00 (40.90)	NA	
NSAIDs (number, %)	11.00 (25.00)	NA	

N: number of patients; Spa: spondylarthritis; IBD: intestinal bowel disease; CRP-:C-reactive protein; ESR: erythrocyte sedimentation rate; RA: rheumatoid arthritis; DMARDs: disease-modifying anti-rheumatic drugs; NSAID: non-steroidal anti-inflammatory drugs; SD: standard deviation; IQR: Interquartile range; NA: not applicable.

P87. Table 2. Electrocardiographic alterations and other characteristics.

Electrocardiographic Findings	Psoriatic arthritis (N=44)	Controls (N=44)	*p*-value
Electrocardiographic disturbances (number, %)	11.00 (25.00)	2.00 (4.55)	.01
>AV Block*	4.00 (9.30)	2.00 (4.55)	.40
>LAFB	3.00 (6.82)	0.00 (0.00)	.08
>Left Axis Deviation	4.00 (9.09)	0.00 (0.00)	.04
>Atrial Fibrillation	1.00 (2.27)	0.00 (0.00)	.32
>NICD	1.00 (2.27)	0.00 (0.00)	.32
Other electrocardiographic characteristics			
QRS interval (median, IQR)	93.50 [88.21-101.50]	94.50 [87.00-101.00]	.91
QTc interval (median, IQR)	417.50 [389.75-438.00]	403.50 [391.25-420.00]	.07
Heart Rate (mean, SD)	73.59 (±15.02)	68.20 (±11.39)	.06
PQ interval (median, IQR)	155.50 [146.25-173.75]	175.50 [140.50-172.00]	.22

N: number of patients; AV: atrioventricular; LAFB: left anterior fascicular block; SD: standard deviation; IQR: interquartile range; NICD: nonspecific intraventricular conduction delay; *1st degree AV block.

Discussion/Conclusions. Our study suggests an increased prevalence of subtle conduction disturbance in PsA. More studies with larger sample sizes are paramount to better estimating this association.

P88

MACHINE LEARNING CLASSIFICATION OF VITAMIN D LEVELS IN SPONDYLOARTHRITIS PATIENTS

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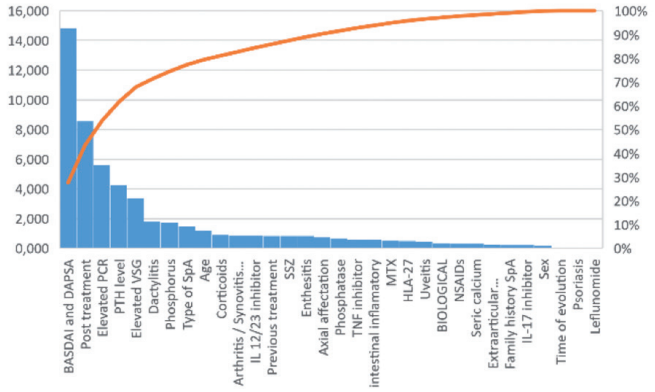
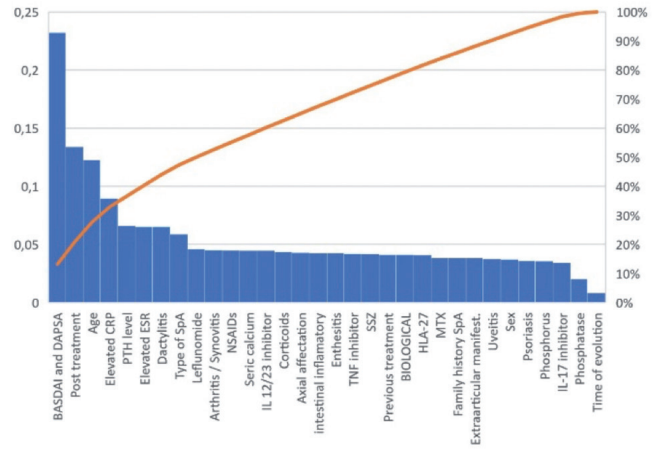
Background. In recent years, much attention has been paid to machine learning applications in Rheumatology. These models are used to predict or classify the value of dependent variables, or targets, from the value of other explanatory, or independent, variables. Using these methods, we offer a new perspective to address an issue on which there is still controversy: the relation between serum levels of 25-hydroxyvitamin D and inflammatory activity in spondyloarthritis patients. Spondyloarthritis (SpA) are a heterogeneous group of inflammatory chronic diseases primarily affecting both the axial skeleton and peripheral joints, sharing similar characteristics that differ from other inflammatory diseases.

Objectives. We aim to provide the best machine learning model to minimize the estimation of the generalization error, in terms of its accuracy, in a classification problem of the vitamin D levels in SpA patients. On the other hand, since this method, from a causal point of view, is a black-box, we aim to obtain a decision tree, that although having less predictive power, it is interpretable and classifies explicitly the levels of vitamin D.

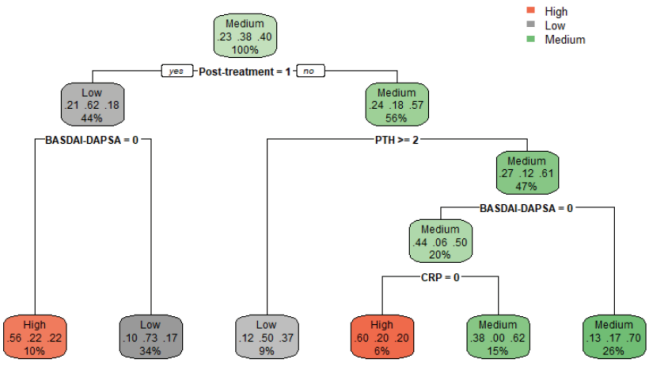
Methods. Observational, descriptive and cross-sectional study. We have collected information from 116 spondyloarthritis patients (according to ASAS 2009 criteria) treated during outpatient visits at the Rheumatology Department of Hospital General Universitario de Ciudad Real between June 2018 and June 2019. We have done a feature selection of the variables most related to Vitamin D. To do so, we computed mutual information and chi-square test, using the scikit-learn (python) library and Matlab, respectively.



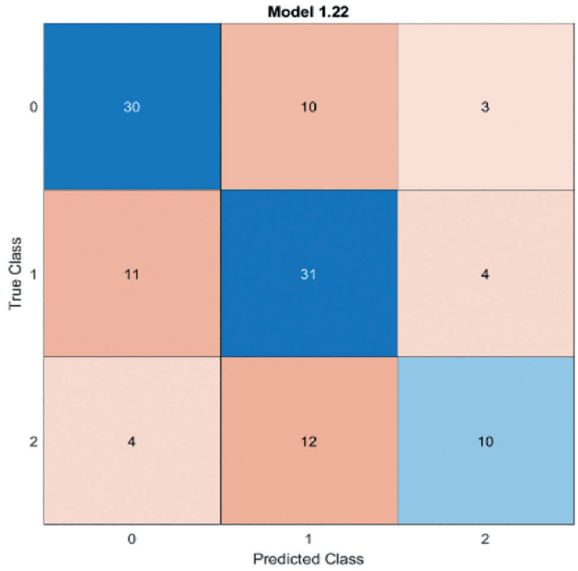
P88. Fig. 1. Pareto chart of chi-square of the variables with respect to vitamin D levels.



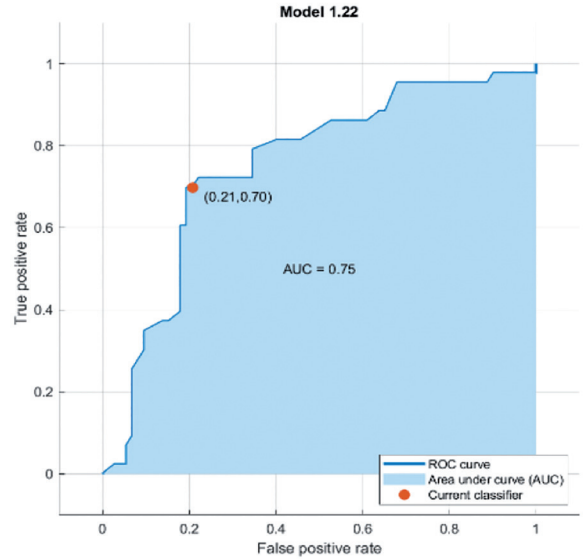
P88. Fig. 2. Pareto chart of mutual information of the variables with respect to vitamin D levels.



P88. Fig. 3. Decision tree computed by a random search that minimizes the generalization error estimated via repeated 10 fold cross validation.



P88. Fig. 4. Confusion matrix of the Ensemble method with 10-fold cross validation.



P88. Fig. 5. Roc curve of the Ensemble method with 10-fold cross validation.

Using Matlab Classification Learner package, we obtain the best Machine Learning classification model with the best acuracy of its confusion matrix for 10 fold cross-validation, which turned out to be an ensemble method. On the other hand, the decision tree has been computed using R.

Results. After doing feature selection using mutual information and chi-square test (see Fig 1 and Fig 2), we obtained that the most important variables to obtain ML models were: PTH levels, BASDAI-DAPSA activity; CRP levels and vitamin D post-treatment. We compute a decision tree with this variables (Fig. 3), and finally, we obtain the best ML classification model whose technical features can be consulted in Fig 6. For this model, we compute its confusion matrix (Fig. 4) and its Roc curve (Fig. 5).

P88. Fig. 6. Technical features of our Ensemble model.

Training Results

Accuracy (Validation)	61.7%
Total cost (Validation)	44
Prediction speed	~390 obs/sec
Training time	3.1678 sec

Model Type
Preset: Subspace Discriminant
Ensemble method: Subspace
Learner type: Discriminant
Number of learners: 30
Subspace dimension: 2

Conclusions. If we take into account the most relevant variables that we have obtained for the classification of vitamin D in patients with SpA, we observe that our research coincides with previous studies. The same occurs with respect to the inverse relationship between inflammatory levels measured by BASDAI-DAPSA and vitamin D levels. This relationship, observed in previous studies, is extended and explained in a deeper way thanks to our decision tree. Our Ensemble model, although not explanatory, offers the best classification of vitamin D levels in patients with SpA.

P89

MACHINE LEARNING MODEL OF THE ULTRASOUND INDEX OF MASEI ENTHESIS AND OTHER VARIABLES OF DISEASE ACTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS

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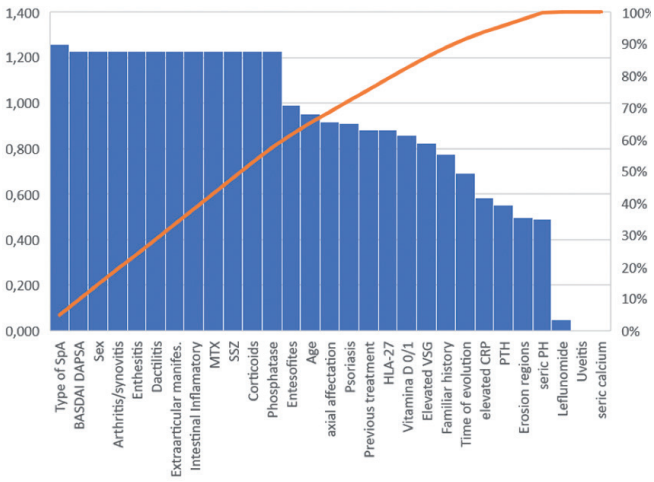
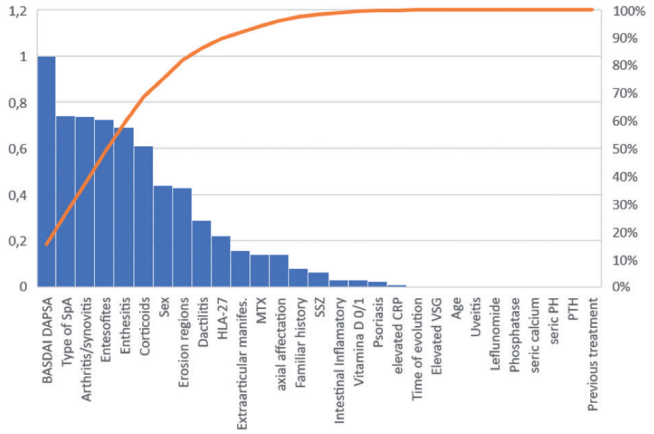
Introduction. Spondyloarthritis (SpA) are a group of chronic inflammatory diseases with affectation, mainly of the axial skeleton, and also of peripheral joints. The enthesis is one of the target organs, and its inflammation known as enthesitis could be unnoticed. Machine Learning is a branch of artificial intelligence that studies the construction of a function y=f(x), from a finite set of observations D={x,y}, where y is an endogenous variable and x are explanatory variables. The objective of this method is to obtain a model that best fit to the data without overfitting, that could be useful to make predictions.
Objectives. We try to find Machine Learning models that relate the MASEI index (Madrid Sonographic Enthesitis Index) in entheses depending on the activity of the disease (ASDAS, BASDAI and DAPSA) and other variables in patients with spondyloarthritis.
Material and methods. Observational, descriptive and cross-sectional study. We have analyzed 24 patients with SpA who underwent musculoskeletal ultrasound using the MASEI index and who were treated in our clinics from May 2021 to September 2021 and under the approval of the CEICm of our center. First, we have done a feature selection of the variables most related to MASEI. To do so, we compute mutual information and chi-square test, using the scikit-learn (python) library and Matlab, respectively. Using Matlab Regression Learner package, we obtain the best Machine Learning model with the lowest RMSE for 5-fold cross-validation, which turned out to be a linear regression.
Results. To obtain regressive models that explain TOTAL MASEI, the following variables have been chosen: Type of SpA, BASDAI-DAPSA-ASDAS activity, Arthritis, Enthesophytes, Corticosteroids and CRP because they present a high degree of mutual information with MASEI and a high chi-square index. (See Figures 1 and 2). With these variables we have obtained the model that presents a lower RSME error for validated data, which



P89. Fig. 1. Pareto chart of the Chi-square correspondence of the variables with MASEI.



P89. Fig. 2. Pareto chart of mutual information of MASEI with the rest of the variables.

P89. Fig. 3. Technical characteristics of our linear regression model.

Model 1.1: Trained

Training Results

RMSE (Validation)	8.6866
R-Squared (Validation)	0.66
MSE (Validation)	75.457
MAE (Validation)	7.177
Prediction speed	~960 obs/sec
Training time	11.357 sec

Model Type
Preset: Linear
Terms: Linear
Robust option: Off

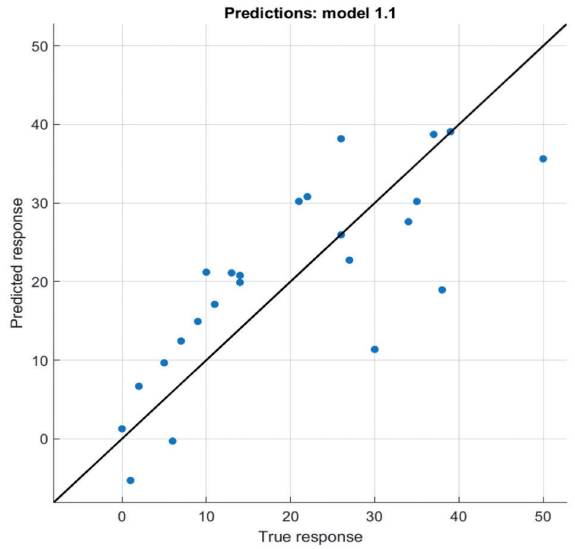
Optimizer Options
Hyperparameter options disabled

Feature Selection
All features used in the model, before PCA

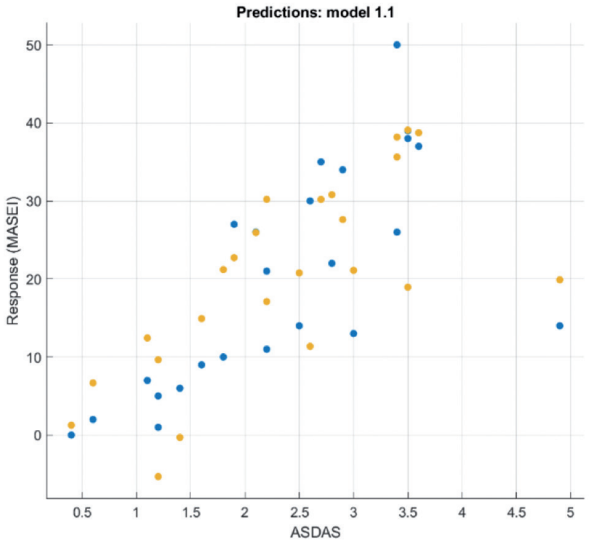
PCA
PCA disabled

has turned out to be a linear regression, given by the formula:
MASEI = -9.29-2,29* **type of SpA** + 10,42***ASDAS**+4,08***Corticoids** +8,2***Arthritis/sinov**.+4,46***Enthesithis**-8,6***CRP**
The basic statistical characteristics of the coefficients of this equation can be consulted in Figure 3. The characteristics of the model are specified in Figure 3. In Figure 4, we observe how the data fit the diagonal and in Figures 5 and 6, we have computed a prediction and confidence intervals of our model using ASDAS and MASEI as coordinate axes.
Discussion and Conclusions. We have obtained a linear model, which explains the MASEI variable as an explicit linear combination of the variables:

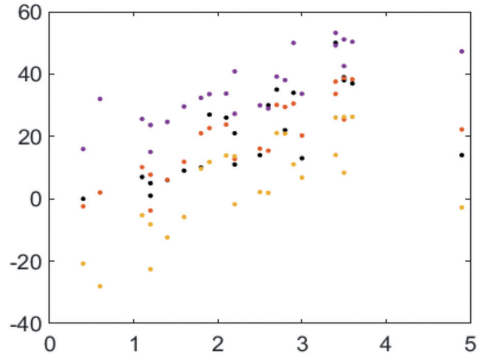
type of SpA, ASDAS, Corticoids, Arthritis/sinov, Enthesithis and CRP. Our model, not only is simple, but it is also optimal, in the sense that for 5-fold cross validation, it obtains the lowest RSME error, compared to other Machine Learning methods, such as: neural networks, SVM, Gaussian regression processes, etc. Our model is useful to build confidence intervals, make predictions and to understand the relation between the variables mentioned above.



P89. Fig. 4. Linear model fit.



P89. Fig. 5. Relationship between ASDAS and MASEI. Actual data (blue) and predictions from our model (yellow).



P89. Fig. 6. Confidence intervals at 90% for the ASDAS-MASEI relationship. True data in black, predictions in red, and confidence intervals in yellow and purple.

P90

DO LATERAL AND AP RADIOGRAPHS TELL DIFFERENT STORY IN PATIENTS WITH PSORIATIC ARTHRITIS?

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Introduction. The aim of this study is to determine whether lumbar AP radiographs have an additional contribution to the evaluation of syndesmophytes in PsA patients.
Methods. Lumbar lateral radiographs and AP radiographs of 274 PsA patients receiving bDMARD therapy were evaluated. A total of 182 lateral lumbar radiographs and 144 AP radiographs were evaluated. On lateral lumbar radiographs each lumbar vertebral unit was evaluated between T12 -S and on AP radiographs between L1-L5 were evaluated.
Results. 182 patients had lumbar radiographs with the mean (SD) age of 44.9 (12.7) years and the mean (SD) PsA duration of 4. 8 (6.1) years at the time of the radiographs were taken. The rate of females was 70.3%. When the lateral lumbar radiographs were evaluated, 42/182 (23.1%) patients had at least one syndesmophyte. These 42 patients had a total of 80 syndesmophytes, 41 of which were bridging and 39 were corner syndesmophytes. The distribution of syndesmophytes is shown in the table. The mean number of syndesmophytes in patients with at least one syndesmophyte on the lumbar lateral radiograph is 80/42 (1.9). In patients with at least one syndesmophyte, 14/42 (33.3%) patients had additional syndesmophytes not seen on lateral radiographs but on AP. When lumbar and AP radiographs are evaluated together, 44/182 (24.2%) patients have at least one syndesmophyte. When the lumbar lateral and AP radiographs are evaluated together, there are 96 syndesmophytes in 44 patients with syndesmophytes, 46 of which are bridging and 50 are corner syndesmophytes.

P90. Table. The distribution of syndesmophytes.

Lateral Lumbar X-ray	Patients with syndesmophytes n (%)	Total syndesmophyte count n (%)	Number of bridging syndesmophyte n (%)	Number of corner syndesmophyte n (%)
L1 lower-L2 upper border	14	29	16	13
L2 lower-L3 upper border	14	21	12	9
L3 lower-L4 upper border	15	21	10	11
L4 lower-L5 upper border	4	6	2	4
L5 lower-S1 upper border	2	3	1	2

Conclusions. When AP radiographs are evaluated, new syndesmophytes that are not seen on lateral radiographs are seen in one-third of patients with at least one syndesmophyte. Although it does not cause a significant change in the number of patients with syndesmophytes, it should be kept in mind that the use of AP radiographs in PsA patients.

P91

DEVELOPMENT AND VALIDATION OF A SCREENING TOOL FOR SPONDYLOARTHRITIS IN SUB-SAHARAN AFRICA: SPASSS QUESTIONNAIRE

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Objective. To develop and validate a screening tool to identify patients with a high likelihood for Spondyloarthritis (SpA) in the Democratic Republic of the Congo (DR Congo).
Methods. The development of the SpASSS questionnaire followed 3 steps: The item generation was carried out by a review of the literature on the clinical manifestations of SpA, interviewing clinical experts and the classification criteria for Spondyloarthritis. The candidate questions were tested in a population of 50 consecutive patients with confirmed diagnosis of spon-

dyloarthritis, in a control population of rheumatic disease excluding SpA and in a group of 200 non-rheumatic participants, randomly chosen in the general population for question reduction and validation. Descriptive statistical analyses were performed to assess socio-demographic characteristics and response distribution for each item. Their diagnostic performance was investigated using ROC curves. For validation, principal component analysis was performed using factor analysis. Referral strategy score for SpA was determined by adjusted Cronbach's alpha coefficient.

Results. Mean±SD age of SpA cases was 41.8±14.4 years, 56% were men compared to diseased controls 60.0±12.5 years, 28.7% men (p<0.001). 14/20 items showed a statistically significant difference (p<0.05) between SpA cases and control groups. Six components were identified. Only the two first components (C1 with 8 items, C2 with 3 items) showed a significant threshold for reliability in detection of suspected SpA with a Cronbach's alpha of 0.830 and 0.708. All validated items of these two components showed the global reliability threshold with α-adjusted Cronbach calculated at 66.9%. The performance for screening SpA was demonstrated with an area under the curve of 0.938 (0.884-0.991) and 0.794 (0.728-0.861) for C1 and C2 respectively.

Conclusions. This validation and item reduction of the screening tool for SpA might identify patients to refer for case ascertainment and will help conducting future epidemiological and clinical studies in the DR Congo.

P92

SELF-REPORTED PHYSICAL ACTIVITY IN PATIENTS WITH AXSPA: ADHERENCE TO PUBLIC HEALTH RECOMMENDATIONS AND ASSOCIATION WITH HEALTH STATUS IN TWO DUTCH COHORTS

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Introduction. Regular physical activity (PA) has shown beneficial effects on function, spinal mobility and pain in patients with axial spondyloarthritis (axSpA). The World Health Organization (WHO) developed public health recommendations for the frequency, intensity and duration of PA in adults required to offer significant health benefits and mitigate health risks. Our aim was to assess the proportion of axSpA patients fulfilling the WHO PA recommendations and to investigate the association of the amount of PA with health status and quality of life.

Methods. Patients from two Dutch axSpA cohorts were included: GLAS cohort (n=148) and LUMC cohort (n=193). The (m)SQUASH was used to assess the type, intensity and time spent on PA during a normal week in the past month. Fulfillment of the WHO PA recommendations was defined as aerobic PA of least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity (or an equivalent combination), and muscle-strengthening activities twice a week. Univariate linear regression analysis was used to explore the association of (m)SQUASH total score with health status (ASAS-HI) and quality of life (ASQoL). Multivariate regression analysis was used to correct these associations for age, gender, BMI and ASDAS as potential confounders.

P92. Table I. Association between total (m)SQUASH score and health status or quality of life in axSpA patients.

	ASAS-HI			ASQoL		
	R^2	B (95% CI)	p-value	R^2	B (95% CI)	p-value
GLAS cohort						
mSQUASH total score	0.16	-2.9 (-4.3;-1.6)	<0.001	0.18	-2.4 (-3.5;-1.4)	<0.001
mSQUASH corrected for age, gender	0.19	-2.8 (-4.1;-1.5)	<0.001	0.21	-2.4 (-3.4;-1.3)	<0.001
mSQUASH corrected for age, gender, BMI, ASDAS	0.30	-4.5 (-6.4;.2.6)	<0.001	0.31	-3.5 (-5.1;-1.9)	<0.001
LUMC cohort						
SQUASH total score	0.13	-3.2 (-4.4;-2.0)	<0.001			
SQUASH corrected for age, gender	0.24	-2.8 (-3.9;-1.6)	<0.001			

Results. In the GLAS and LUMC cohort, 57 (40%) and 62 (35%) patients fulfilled the WHO PA recommendations, respectively. Total (m)SQUASH score was significantly associated with ASAS-HI and ASQoL. These associations remained significant after correcting for age, gender, BMI and ASDAS (Table I).

Conclusions. In both Dutch cohorts, only 35-40% of axSpA patients fulfilled the WHO PA recommendations, which seems less compared to the average 48% in the Dutch adult population (1). AxSpA patient reporting a higher level of PA had better health status and QoL. Therefore, in daily clinical practice, greater awareness and focus on moderate-to-high intensity and muscle strengthening activity is desirable for axSpA patients.

Reference

1. DUIJVESTIJN *et al.*: *Int J Environ Res Public Health* 2020.

P93

APPLICABILITY OF THE MASEI INDEX IN ENTHESIS AND ITS ASSOCIATION WITH OTHER INDICES/SEROLOGICAL MARKERS OF ACTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS

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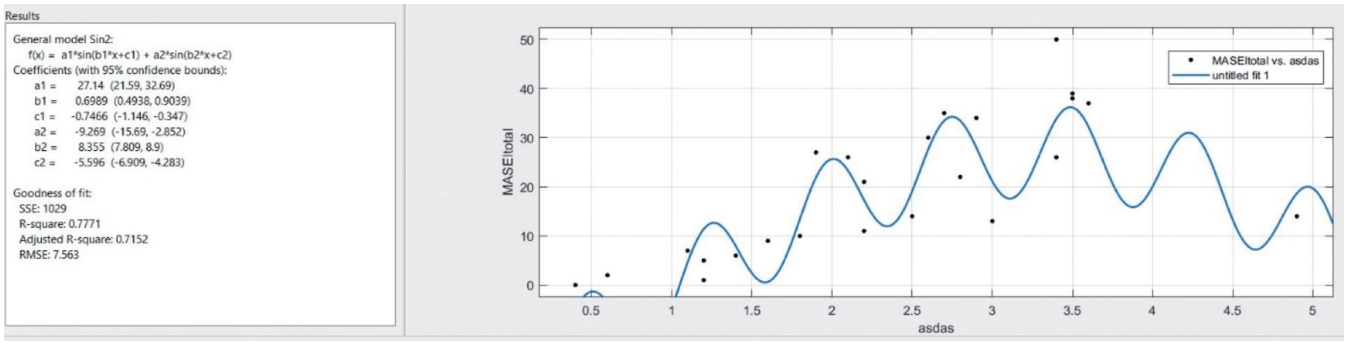
Introduction. Spondyloarthritis (SpA) are a group of chronic inflammatory diseases with affectation, mainly of the axial skeleton and, also, of peripheral joints. The enthesis is one of the target organs, since an inflammation of it, known as enthesitis, can be observed, which in many patients with spondyloarthritis could be unnoticed.

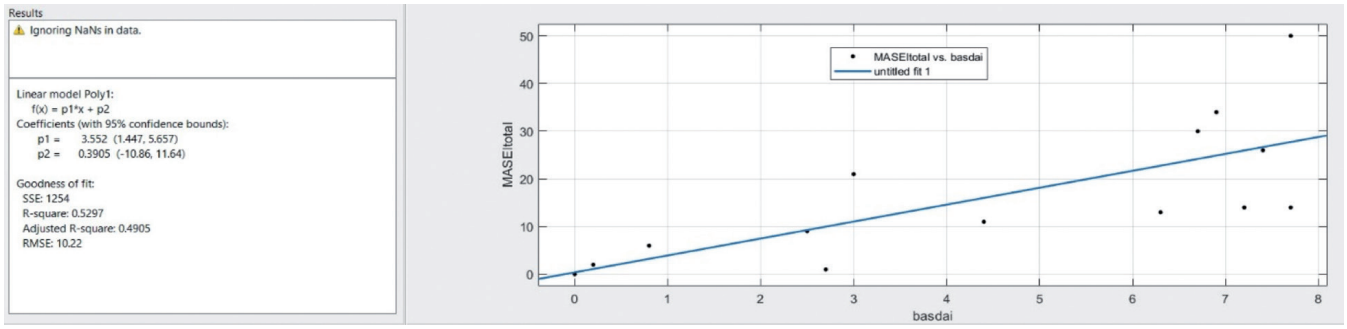
Objective. Find the relation between the MASEI index (Madrid Sonographic Enthesitis Index) in entheses and other indices/serological activity markers (such as BASDAI, DAPSA or ASDAS and ESR, CRP) in spondyloarthritis patients.

Material and methods. Observational, descriptive and cross-sectional study. Data were collected from patients with SpA who underwent musculoskeletal ultrasound using the Madrid Sonographic Enthesitis Index (MASEI) and who were treated in our clinics from May 2021 to September 2021 and under the approval of the CEICm of our center. The variables evaluated were described using measures of frequency and measures of central tendency/dispersion, as appropriate. First, we tested the normality of all the variables, using a Shapiro-Wilk test. We studied the correlation of parametric numerical variables (such as MASEI-Vitamin D, MASEI-ASDAS), using the Pearson coefficient. On the other hand, for non-parametric numerical variables (such as MASEI-BASDAI) we use Spearman's coefficient. For parametric numeric and categorical variables (such as MASEI-VITAMINA D, ASDAS-VITAMINA D) we contrast the mean of differences using the T-Student test, while for non-parametric numerical and categorical variables, we contrast the difference of means with the Mann-Whitney U test (MASEI-PCR, MASEI_VSG). Finally, to find out the correlation between categorical variables (such as VITAMIN D-PCR), we used a chi-square test. Finally, we have done a curve-fitting study with Matlab, obtaining the functions that better adjust the data avoiding overfitting. We have done this parametric optimization with the following pairings: MASEI-ASDAS, MASEI-BASDAI and MASEI DAPSA.

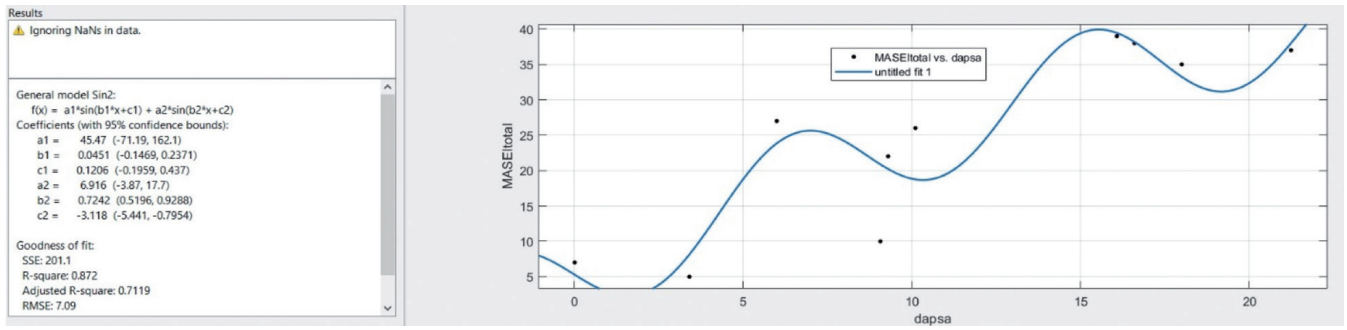
Results. We analyze twenty-four patients with SpA (with mean age 50.50 ± 10.63 years) 8 women and 16 men. They present: radiographic axial spondyloarthritis (5 patients), non-radiographic axial spondyloarthritis (4 patients), psoriatic arthritis (10 patients), spondyloarthritis associated with inflammatory bowel disease (2 patients), reactive arthritis (2 patients), and, finally, one patient has undifferentiated peripheral spondyloarthritis. The variables have the following average levels: ASDAS, 2.35 (±1.09); BASDAI (for those with axial involvement) 4.54 (±2.93); DAPSA (for psoriatic arthritis) 10.98 (± 6.85) and total MASEI 19.88 (± 14.77). We have found a correlation between the total MASEI and the following variables: ASDAS (Pearson coefficient=0.696), BASDAI (Spearman coefficient=0.823) and DAPSA (Pearson coefficient=0.823). The mean vitamin D levels were 25.98 (±12.05), and it has a negative correlation with the MASEI equal to -0.317. As far as curve fitting is concern, a couple of sinusoidal functions were obtained for the MASEI-ASDAS and MASEI DAPSA pairings (see Figure 1 and Figure 3) and a linear regression for MASEI-BASDAI (see



P93. Fig. 1. MASEI-ASDAS curve fitting.



P93. Fig. 2. MASEI-BASDAI curve fitting.



P93. Fig. 3. MASEI-DAPSA curve fitting.

Figure 2). These three curves have an R-squared fit of 0.77, 0.87 and 0.52, respectively.

Conclusions. Patients with spondyloarthritis who present greater activity of the disease measured by ASDAS, BASDAI/DAPSA and by the serological markers of inflammation CRP and ESR, present a higher total MASEI than patients who are controlled. In addition, it has been observed that patients with low levels of vitamin D have higher disease activity and a higher total MASEI.

P94

HOW IS EARLY SPONDYLOARTHRITIS DEFINED IN THE LITERATURE? RESULTS FROM A SYSTEMATIC REVIEW

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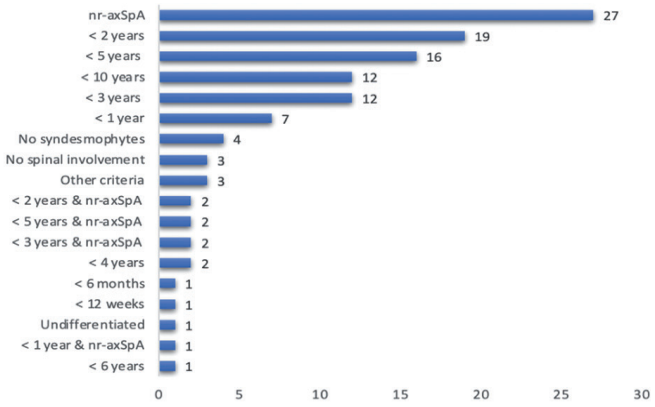
Introduction. The term "early spondyloarthritis (SpA)" has been frequently used to refer to the first phase of the disease, however, no standardized definition on "early" has been established. The objective of this study was to identify all possible definitions of "early SpA" used in the literature, including "early axial SpA (axSpA)" and "early peripheral SpA (pSpA)".

Methods. A systematic literature review was conducted in Medline, EMBASE and the Cochrane Library for studies that included any mention of "early SpA" or its subtypes. The proportion of studies including a definition was calculated, and the different definitions were assessed.

Results. Out of 9651 titles identified, 336 publications reporting data from 183 studies were included. Over time, an increasing number of publications was identified. In total, 114 (62%) studies reported a specific definition: 33% of them based it on symptom duration, 31% on radiographic damage, 28% on disease duration, 5% on both symptom/disease duration and radiographic damage, and 3% on other aspects. Figure 1 shows the 18 distinct definitions that were identified (after combining some similar categories). Overall, 61 (33%) studies included the term "early axSpA", whereas 60 (33%) included "early ankylosing spondylitis (AS)". Regarding the studies that referred to "early axSpA", the most used definition was symptom/disease duration <5 years, whereas for "early AS" was symptom/disease duration <10 years (Table I). After 2010, the definition of "early axSpA" based on the absence of radiographic sacroiliitis was less used compared to before 2010 (17% vs 38%).



P94. Fig. 1. Number of studies stratified by the core of the definition.

P94. Table I. Top 3 candidate definitions for "early SpA" and subtypes.

	Core of the definition	Number of studies, n (%)
SpA (n= 35)	nr-axSpA	10 (29%)
	< 2 years duration	10 (29%)
	< 1 year duration	6 (17%)
AxSpA (n=38)	< 5 years duration	12 (34%)
	< 3 years duration	9 (24%)
	nr-axSpA duration	8 (21%)
AS/r-axSpA (n=38)	<10 years duration	9 (24%)
	nr-axSpA	7 (18%)
	< 2 years duration	6 (16%)
nr-axSpA (n=4)	nr-axSpA	2 (50%)
	< 1 year & nr-axSpA	1 (25%)
	< 5 years & nr-axSpA	1 (25%)
pSpA (n=1)	< 12 weeks duration	1 (100%)

"Duration" refers to symptom duration or disease duration.

Conclusions. Over time, the term "early SpA" and its subtypes is increasingly used. More than one third of the studies did not include a definition of the term and the studies reporting one showed a large heterogeneity. These results emphasize the need for a standardised definition of early SpA.

Acknowledgements. This work was supported by the Assessment of Spondyloarthritis international Society (ASAS) in the context of the ASAS-SPEAR project.

P95

PELVIS RADIOGRAPHY FINDINGS AND PROGESSION RATES IN PATIENTS WITH PSORIATIC ARTHRITIS UNDER BIOLOGIC TREATMENT

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Introduction. This study aimed to understand the involvement of all pelvic structures on radiography, and progression rates during follow-up in patients with Psoriatic arthritis (PsA) under biologic treatment.
Methods. PsA patients from the Hacettepe University biological database (HUR-BIO), were retrospectively analyzed for their pelvis radiographs. Modified New York (mNY) criteria and BASRI-hip score was used to assess sacroiliitis and hip involvement respectively and ischium/ iliac wing/ greater-lesser trochanteric enthesopathy and symphysis pubis osteitis assessments were done using a grade 0, no changes, 1, minimal changes and grade 2 and more counted as significant changes. All of the assessments were done by an experienced rheumatologist (UK) another experienced rheumatologist reviewed the cases (LK) when there is suspicion, and a consensus was reached.

Results. Overall 273 patients (69.6% of females) with the mean (SD) age at the time of first radiography 43.3 (12) years were included. At their initial radiographic assessment, the median (IQR) PsA duration was 2 (7) years. Baseline radiographs showed 10 (%3.7) of the patients had transitional vertebra and 137 (50.2%) patients had sacroiletis according to mNY criteria. From patients without sacroileitis (n=136), 67 patients had following radiographs. After a mean (SD) 47.1 (37) months, 16 (23.8%) of them progressed to sacroiletitis according to mNY criteria. Enthesopathies and BASRI scores were given in the Table. There was no correlation between meeting mNY criteria and having iliac, ischium, and pubis involvement ≥ 2.

P95. Table. Distribution of major entheseal involvement and BASRI-hip socres and progression rates.

Location	Grades	First assessment N (%)	Progression rate*
Ischium (n=164)	Grade 4	0	9/65 (13.8)
	Grade 3	11 (6.7)	
	Grade 2	33 (20.1)	
	Grade 1	74 (45.1)	
	Grade 0	46 (28)	
Symphysis Pubis (n=191)	Grade 4	0	8/78 (10.2)
	Grade 3	5 (2.6)	
	Grade 2	32 (16.8)	
	Grade 1	60 (31.4)	
	Grade 0	94 (49.2)	
Iliac wing (n=174)	Grade 4	0	3/72 (4.1)
	Grade 3	9 (5.2)	
	Grade 2	14 (8.0)	
	Grade 1	28 (16.1)	
	Grade 0	124 (71.3)	
BASRI score (right) (n=220)	Grade 4	3 (1.4)0	
	Grade 3	2 (0.9)	
	Grade 2	1 (0.5)	
	Grade 1	0	
	Grade 0	214 (97.3)	
BASRI score (left) (n=219)	Grade 4	0	0
	Grade 3	4 (1.8)	
	Grade 2	2 (0.9)	
	Grade 1	0	
	Grade 0	213 (97.3)	
Trochantor major enthesitis (right) (n=204)	Grade 4	0	NA
	Grade 3	1 (2.5)	
	Grade 2	4 (2)	
	Grade 1	5 (2.5)	
	Grade 0	194 (95.1)	
Trochantor major enthesitis (left)(n=203)	Grade 4	0	NA
	Grade 3	2 (1)	
	Grade 2	1 (0.5)	
	Grade 1	5 (2.5)	
	Grade 0	195 (96.1)	
Trochantor minor enthesitis (right) (n=203)	Grade 4	0	NA
	Grade 3	0	
	Grade 2	0	
	Grade 1	0	
	Grade 0	203	
Trochantor minor enthesitis (left) (n=203)	Grade 4	0	NA
	Grade 3	0	
	Grade 2	0	
	Grade 1	1 (0.5)	
	Grade 0	202	

*Defined as one unit increase in the grade.

Conclusions. Half of the patients with PsA requiring advanced treatment modalities, had sacroileitis in a median 2 years of disease duration and the rest may progress to sacroileitis during the follow- up period. Major enthesopathy involvement was also seen in more than half of the patients. Further assessment is needed to correlate those radiographic changes to clinical symptoms.

P96

CLINICAL CHARACTERISTICS OF LATE-ONSET ANKYLOSING SPONDYLITIS IN KOREA

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Introduction. Ankylosing spondylitis (AS) is a chronic inflammatory condition that mainly involves axial joints. AS tends to first emerge in young adults but considerable number of aged patients are also diagnosed. We aimed to investigate the clinical profiles of patients with late-onset ankylosing spondylitis (LOAS) by comparing with early-onset ankylosing spondylitis (EOAS).
Methods. This study included 180 patients diagnosed with AS followed up in a single rheumatology clinic regularly for more than 1 year. The patients who were diagnosed after 50 years of age were defined as LOAS group. We compared clinical features of 90 patients of LOAS with 90 EOAS patients.
Results. The mean (SD) age at diagnosis for both groups were 33.9 (9.5) and 62.8 (7.7) years respectively. Male sex was less dominant in LOAS, which was 66.7% and 85.6% in EOAS. The patients with LOAS demonstrated higher frequency of peripheral feature while axial symptom and uveitis were lower than EOAS group with $p<0.05$. Inflammatory marker at diagnosis was significant higher in LOAS group. Higher HLA-B27 positivity and more severe radiographic findings were found in EOAS. Regarding medication use, more use of corticosteroid was detected in LOAS group and other medications use such as sulfasalazine and anti-tumor necrosis factor(TNF) alpha had shown no significant different between the two groups. Considerable number LOAS patients were initially misdiagnosed as other disease such as polymyalgia rheumatic or rheumatoid arthritis due to substantially high inflammatory marker and absence of axial symptoms. The effect of biologics, however was dramatic with significant decrease in inflammatory marker and disease activity.

Table I. Clinical, laboratory and radiological characteristics of patients with EOAS and LOAS.

Variables	Early AS (N=90)	Late AS (N=90)	*p*-value
Demographics			
Age at onset, years, mean (SD)	28.7 ± 10.8	49.9 ± 11.3	<0.001
Age at diagnosis, years, mean (SD)	33.9 ± 9.5	62.8 ± 7.7	<0.001
Male sex, n (%)	77 (85.6)	60 (66.7)	0.003
Disease duration, years, mean (SD)	22.9 ± 10.4	8.5 ± 6.5	<0.001
BMI, mean (SD)	23.9 ± 3.6	24.4 ± 3.5	0.497
Smoking status (%)	34/67 (50.7)	24/67 (35.8)	0.081
Family history of AS	12 (13.3)	11 (12.2)	0.823
Clinical features			
Inflammatory back pain	88 (97.8)	74 (82.2)	0.001
Enthesitis	15 (16.7)	33 (36.7)	0.007
Peripheral arthritis	13 (14.4)	27 (30.0)	0.012
Uveitis	35 (38.9)	22 (24.4)	0.037
Dactylitis	3 (3.3)	3 (3.3)	1.000
Inflammatory bowel disease	3 (3.3)	3 (3.3)	1.000
BASDAI	6.0 ± 1.8	6.5 ± 1.8	0.256
Laboratory findings			
HLA-B27 (+)	75/79 94.9)	67/87 (77.0)	0.001
ESR (mm/h)	32.0 ± 29.9	47.4 ± 32.8	0.001
CRP (mg/dl)	1.9 ± 3.7	2.7 ± 3.8	0.176
Radiological findings			
Low grade (I-II)	31 (34.4)	36 (40.0)	0.441
High grade (III-IV)	59 (65.6)	54 (60.0)	
Syndesmophytes	65 (72.2)	58 (64.4)	0.262
Treatment			
Steroid	12 (13.3)	25 (27.8)	0.016
Sulfasalazine	34 (37.8)	30 (33.3)	0.533
Methotrexate	18 (20.0)	12 (13.3)	0.230
NSAIDS	88 (97.8)	90 (100)	0.155
Anti-TNF-alpha	39 (43.3)	41 (45.6)	0.764
Adverse effect d/t anti-TNF	9/39 (23.1)	16/41 (39.0)	0.124

Conclusions. The diagnosis of LOAS is sometimes challenging due to higher inflammatory marker with more peripheral involvement and less associated with axial symptom and HLA-B27. The use of anti-TNF alpha in LOAS are effective showing the efficacy in lowering disease activity and inflammatory marker.

P97

TRANSLATION AND CROSS-CULTURAL ADAPTATION OF COPING WITH RHEUMATIC STRESSORS (CORS) INTO TURKISH LANGUAGE

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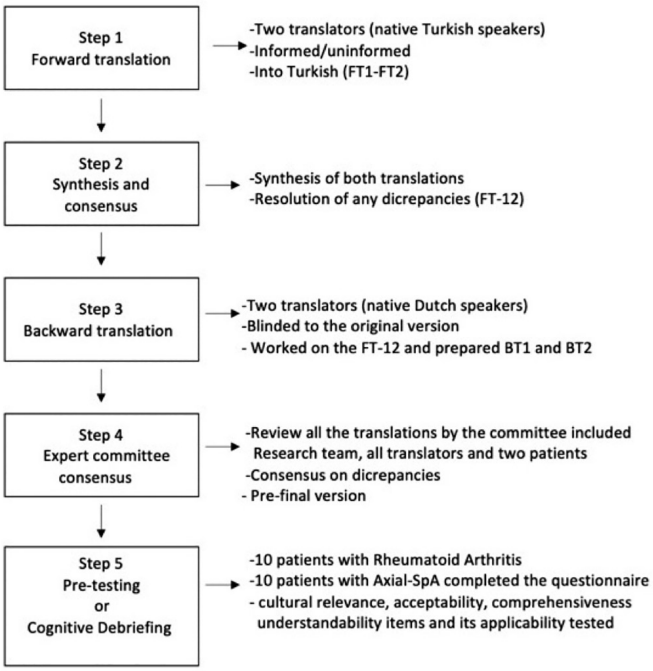
Introduction. To describe the translation and cross-cultural adaptation process of the CORS tool into Turkish among patients with Rheumatoid Arthritis (RA), axial Spondyloarthritis (axSpA).
Methods. The CORS was firstly translated following the Beaton's method (Figure) (1). A consensus was reached on the pre-final version by expert committee. The field test with the pre-final version and cognitive debriefing involved a sample of RA, axSpA patients with different gender, age, disease duration, and educational background. According to the feedback from patients the final version was obtained.



P97. Fig. 1. Flow-chart of the translation and cross-cultural adaptation process.

Results. Minor incompatibilities arose from the translation process of CORS have been easily resolved by the expert committee. For example, 'Ik concentreer me op iets anders' was translated as 'Başka seylere odaklanırım'. The discrepancy was raised whether to use a word equivalent 'to concentrate' or 'to focus' and decision was made to use 'to focus' while there was no exact Turkish word of 'to concentrate'. A total of 10 patients with RA [9 females, mean (SD) age of 49 (13)] and 10 patients with axSpA [7 females, mean (SD) age of 38 (10), r- AxSpA, n=7, nr-AxSpA, n= 3] participated in the field test. Mean (SD) time to complete the CORS was 8.3 (3.4) minutes. CORS was shown as clear, relevant, understandable, and easy to complete and wording of one item had to be changed to provide better understanding (Section B, item 22 the word 'stop' in Dutch and which was translated as 'durdurmak' in Turkish changed to 'sonlandırmak'.
Conclusions. The final Turkish version of the CORS showed acceptable linguistic validity and can be used in both clinical practice and for research purposes, in patients with RA and in patients with axSpA after further assessment is to test its psychometric properties (validity and reliability).

Reference
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P98

WORK ABANDONMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS UNDER 45 YEARS OF AGE

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Introduction. We aimed to investigate the factors associated with work abandonment in young patients with Ankylosing Spondylitis (AS).
Methods. We conducted a prospective observational study including working-age patients with AS between January 2020-December 2021.
Results. During the study period, we included 200 professionally active patients with AS, of which 103 were under 45 years of age and constituted the final group. The mean age in the final study cohort was 38±5.82 years, while the mean disease duration was 11.73±5.22 years. Work abandonment was found in 47.6% of the group and did not differ significantly according to gender, disease activity (BASDAI and ASDAS), HLA-B27 positivity, disease duration, the presence of uveitis, interstitial lung disease, or cardiovascular comorbidities and complications. Nevertheless, functional impairment (p<0.001 for BASFI, and p<0.05 for each BASFI subsection), a restrictive respiratory pattern (p<0.001), comorbid depression or chronic anxiety (p=0.002), and the presence of gastritis or gastric ulcers (p=0.023) demonstrated notable connections with the subjects' retirement from the workforce. Rural dwellers were more likely to retire (p=0.01). Moreover, restrictive lung disease was associated with work abandonment within 5 years and 10 years from diagnosis (p=0.024, p<0.001).
Conclusions. Work disability was significantly associated with functional impairment, comorbid depression or chronic anxiety, and a restrictive respiratory pattern. Moreover, the early onset of restrictive lung disease was linked to work abandonment within 5 and 10 years from diagnosis.

P99

RE-INDUCTION WITH CERTOLIZUMAB PEGOL AFTER SECONDARY LOSS OF RESPONSE IS A VALID THERAPEUTIC STRATEGY IN AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS

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Introduction. Certolizumab pegol (CZP) is the only biological drug that inhibits tumor necrosis factor alpha (TNFi) (Fab' therapy) PEGylated without Fc region, indicated as treatment for axial Spondyloarthritis (SpA) and Psoriatic Arthritis (PsA). CZP has shown a rapid and sustained reduction in disease activity in the short and long term, inhibition of radiographic progression, improvement of PROs, as well as effective control in the approach of the extra-articular manifestations, maintaining an appropriate security profile, superimposable to the TNF-i. Although biological treatment with TNF-i has represented a great advance in the treatment of Spondyloarthritis, approximately, between 20 to 45% of patients discontinue the treatment within the two firsts years, mostly due to secondary loss of response, followed by intolerance or adverse events related to the administered drug. Nevertheless, there are few published data in the scientific literature related to the strategy of therapeutic intensification trying to solve therapeutic failure with TNF-i in patients with Spondyloarthritis. However, in other pathologies such as Crohn's disease or Psoriasis, the therapeutic strategy of intensification such as re-induction with different biological therapies (CPZ, Infliximab or Ustekinumab), have been shown to be capable of inducing and maintaining remission of the disease for a long time, without an increased risk of side effects.
Objectives. The objective is to determine the efficacy and safety of the re-induction strategy with certolizumab pegol (CPZ) in patients with Axial Spondyloarthritis (axSpA) and Psoriatic Arthritis (PsA) after a secondary loss of response during maintenance therapy.
Patients and methods. Descriptive retrospective observational study of patients (pts) from University General Hospital of Castellon (HGUCS). A total of 32 pts affected of axSpA and PsA were included with at least one re-induction with CPZ after a secondary loss of response during the study period (January 2016 to January 2022). Variables were collected: demographic, clinic, biological and disease activity scores (BASDAI and ASDAS) for axSpA, (DAPSA) for PsA. axSpA relapse was defined as an ASDAS≥2.1 and in PsA as a DAPSA>14. It was established the CPZ re-induction dose: CPZ 400 mg 0, 2 and 4 weeks followed by usual maintenance doses. Statistical analysis was done using SPSS for Windows (v23). The study was approved by CREC (HGUCS) and all participants signed an IC agreeing to participate in the study.
Results. 32 pts with SpA (16 pts PsA, 10 pts axSpA-r, 6 pts axSpA-nr) treated with CPZ that have presented at least one re-induction during the course of the disease, were included in the study. The mean age of the study population 44 ± 6.5 years, being the 72% of the pts women. The mean duration of disease 7.2±3.9 years. 70.3% of the pts were bDMARD *naive* and 29.7% TNF-IR (exposed to 1 or 2 TNF-i before CPZ treatment). The median duration of CPZ treatment between the beginning of the treatment and re-induction was 18.1 months (p25p75: 12.4-24.5). After the re-induction with CPZ, the 63% of the patients with SpA reached an ASDAS<2.1 at 12 weeks and the 37% an ASDAS remission maintained until week 52. 75% of patients affected of PsA presented improvement at 12 weeks, reaching a DAPSA/LDA (low activity) and the 25% a DAPSA remission, maintained until week 52. There are not serious adverse events reported nor higher infection risks. The loss of response ocurred in 3% of the pts. Only one patient discontinued the CPZ treatment who developed *paradoxical* psoriasiform skin lesions during re-induction period.
Conclusions. This work is characterized by being the first study where an intensification strategy such as re-induction with CPZ is implemented in patients with SpA and PsA after secondary loss of response, proving to be a valid, rapid and effective option in the short and long term to control of active disease without showing a higher risk of adverse events of CPZ compared to usual doses.

P100

ADAPTING TO LIVING WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

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Introduction. Axial spondyloarthritis (axSpA) is associated with a high disease burden which may require patients to make functional adaptations in response to the disease. The aim is to identify factors associated with implementing functional adaptations due to axSpA.
Methods. Data from 2,846 unselected patients participating in EMAS, an online survey (2017-2018) across 13 European countries, were analysed. Adaptations were assessed by: "Please indicate any steps you have taken since you have been affected by Spondylitis/ Spondyloarthritis?" with possible answers: purchasing customized or comfortable shoes, workplace or home or car adaptations. Univariable and multivariable logistic regression models were used to identify variables associated with life adaptations, including sociodemographic factors, PROs, employment status, health behaviours, and comorbidities (n=2,754).
Results. Mean age was 43.8 years and 61.5% were female. A total of 76.9% (n=2,118) patients had made at least one adaptation: 72.0% (n=1,525) purchased customised or comfortable shoes, 54.9% (n=1,163) adapted their workplace, 40.7% (n= 861) their home, and 29.0% (n= 614) their car.
Those requiring functional adaptations reported greater BASDAI (5.7 vs. 4.9), functional limitations (21.4 vs. 16.5), poorer mental health (5.2 vs. 4.3), and longer diagnostic delay (7.9 vs. 6.0), all p<0.001.
The variables associated with functional adaptations were being physically active (OR=1.98), patient organisation membership (OR=1.39), female gender (OR=1.31), being overweight or obese (OR=1.26), separated, divorced or widow status (OR=1.20), higher BASDAI (OR= 1.14) and functional limitation (OR=1.01; Table I).

P100. Table I. Regression analysis for variables associated with the presence of at least one functional adaptations (n=2,162).

	Univariable logistic analysis		Multivariable logistic analysis	
	OR	95%CI	OR	95%CI
Gender. Female[1]	1.34	**1.12, 1.60**	1.31	**1.06, 1.63**
Marital status. Separated/divorced or widow[2]	1.33	**1.14, 1.55**	1.20	**1.00, 1.44**
Employment status. Sick leave or early retirement[3]	1.83	**1.45, 2.32**	1.17	0.89, 1.53
Patient organization. Member[4]	1.55	**1.29, 1.88**	1.39	**1.12, 1.74**
Physical activity. Yes	1.88	**1.51, 2.35**	1.98	**1.52, 2.59**
Body Mass Index. Overweight/obesity[5]	1.22	**1.02, 1.46**	1.26	**1.02, 1.55**
BASDAI (0-10)	1.21	**1.16, 1.27**	1.14	**1.07, 1.22**
GHQ-12 (0-12)	1.06	**1.03, 1.08**	1.01	0.98, 1.04
Functional limitation (0-54)	1.02	**1.01, 1.03**	1.01	**1.00, 1.02**
Spinal stiffness (3-12)	1.10	**1.06, 1.14**	0.99	0.94, 1.03
Diagnostic delay	1.03	**1.02, 1.04**	1.01	0.99, 1.03
Anxiety	1.26	**1.03, 1.54**	0.87	0.65, 1.18
Depression	1.56	**1.25, 1.95**	1.31	0.95, 1.79
Sleep disorders	1.54	**1.27, 1.86**	1.17	0.91, 1.51

[1]Male *vs*. female; [2]Separated/divorced or widow vs. married and single; [3]Sick leave or early retirement *vs*. other employment status; [4]Member *vs*. non-member; [5]Overweight/obesity vs. underweight/normal weight.

Conclusions. Three out of four axSpA patients made at least one functional adaptation due to their axSpA, which were often implemented by those with higher body weight, disease activity, engaging in physical activity, and patient organization membership. This is most likely explained by need as those with high disease burden or weight may face limitations, which can be alleviated through functional adaptations, enabling them to engage in physical activity.

P101

ASSESSMENT OF THE IMPACT OF AXIAL SPONDYLOARTHRITIS ON PATIENT'S SOCIAL LIFE: RESULTS OF THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS)

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Introduction. Spinal impairment can make it difficult to perform simple physical routines, placing a huge burden on axial spondyloarthritis (axSpA). The aim is to evaluate the impact of axSpA on patients' social life.
Methods. 2,846 unselected patients participated in EMAS, an online survey (2017-2018) across 13 European countries. Impact of axSpA on social life was assessed by: axSpA relationship affect (Much worse to much better with spouse, family, friend, and neighbours), and axSpA frequency of activities affect [Much less frequent to much more frequent in restaurants, cultural outings, travel, and sports]. Patients who rated at least one relationship as "worse/much worse" and at least one of social activity as "less/much less" were considered to have a negatively impacted social life. Univariable and multivariable logistic regression were used to identify variables possibly explaining negative impact on social life.
Results. Mean age was 43.8 years and 61.5% were female. A total of 44.9% (n=1,205) patients had their social life negatively impacted since the onset of axSpA.Those whose social life was negatively impacted reported greater BASDAI (6.2 vs. 5.0), functional limitation (24.4 vs. 17.4), spinal stiffness (8.4 vs. 7.3), longer diagnostic delay (9.7 vs. 7.4) and poorer mental health (6.7 vs. 3.6), all $p<0.001$.
The variables associated with negative impact on social life were higher disease activity (OR=1.15), poor mental health (OR=1.14), being on a sick leave or unemployed (OR=1.49), divorced or separated (OR=1.46), anxiety (OR=1.41) and female gender (OR=1.30; Table I).

P101. Table I. Factors associated with a worsening social life (n= 2,120).

	Univariable logistic analysis		Multivariable logistic analysis	
	OR	CI 95%	OR	CI 95%
Age	0.99	**0.98, 0.99**	1.00	0.99, 1.01
Gender. Female[1]	1.63	**1.39, 1.91**	1.30	**1.06, 1.60**
Marital status. Divorced/separated[2]	1.93	**1.48, 2.50**	1.46	1.05, 2.04
Employment status. Sick Leave/ Unemployed[3]	2.66	**2.24, 3.17**	1.49	**1.20, 1.85**
BASDAI (0-10)	1.41	**1.35, 1.48**	1.15	**1.08, 1.22**
Functional Limitation (0-54)	1.03	**1.02, 1.03**	1.02	**1.09, 1.02**
Spinal Stiffness (3-12)	1.20	**1.16, 1.24**	1.06	**1.01, 1.11**
Diagnostic delay	1.02	**1.01, 1.03**	1.01	0.99, 1.02
GHQ-12 (0-12)	1.22	**1.19, 1.24**	1.14	**1.11, 1.17**
Anxiety	2.84	**2.39, 3.37**	1.41	**1.08, 1.83**
Depression	2.59	**2.17, 3.10**	1.14	0.87, 1.49
Sleep disorders	2.10	**1.79, 2.46**	1.02	0.81, 1.27

[1]Female *vs*. male; [2]Divorced/separated *vs*. single, married and widow; [3]Sick leave/unemployed *vs*. other employment status.

Conclusions. Almost half of axSpA patients reported it to have negatively impacted on their social life. Being female, divorced/separated, on sick leave/unemployed, higher disease activity, poor mental health, and anxiety increase the likelihood of worsening social life. More attention should be paid to enabling individuals to participate socially through controlling disease activity and addressing mental health comorbidity in the management of axSpA.

P102

ROLE OF PATIENT ORGANIZATIONS IN IMPLEMENTATION OF RECOMMENDED NON-PHARMACOLOGICAL TREATMENT MODALITIES IN SPONDYLOARTHRITIS: EVIDENCE FOR THE EFFECTIVENESS OF SELF-MANAGEMENT STRATEGIES

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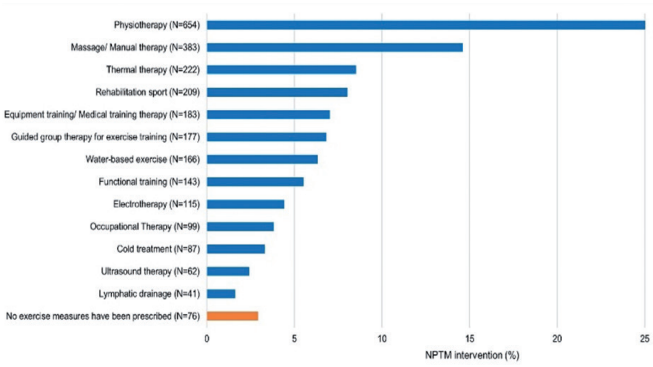
Introduction/objectives. EULAR recommends participation in patient (pt) organizations to improve pt self-management of axial spondyloarthritis (axSpA) (1). Non-pharmacological treatment modalities (NPTM) are recommended in axSpA treatment guidelines (2). The aim of this study was to characterize the impact of pt advocacy group membership and its association with NPTM frequency and clinical parameters in axSpA.
Methods. Pts with a confirmed axSpA diagnosis were enrolled in the multicenter, observational ATTENTUS-axSpA survey conducted across Germany (11/2019–07/2020). Demographics, clinical and pt-related data were collected electronically.
Results. Of the 787 enrolled axSpA pts, this analysis was conducted on the working population (n=695) (3). Overall, 12.2% (n=85) pts were members of a pt advocacy group and 87.8% (n=610) were not. Pt advocacy group members had higher Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores, increased functional impairment (BASFI, Bath Ankylosing Spondylitis Functional Index) and higher impact of axSpA on health (ASAS-HI, Assessment of SpondyloArthritis International Society-Health Index; Table I). Despite worse prognostic factors, there was no significant difference in Work Productivity and Activity Ipairment (WPAI) score [40.6 (27.0) for pt advocacy group members vs 36.8 (29.9) for non-members; $p=0.380$]. Membership in a pt advocacy group was associated with increased prescribed, supervised NPTM (57.6% [n=49] vs 34.4% [n=210]). Pts reported to have ever received 2.6 rehabilitation measures, and ≥3.0 different rehabilitation NPTM measures. Cumulatively, 25.0% (N=654) of rehabilitation measures were physiotherapy (Fig. 1).
Conclusions. Pt advocacy group membership was associated with increased prescribed NPTM in axSpA. Pt organizations may support the implementation of guidelines and improvement of self-management strategies in pts with axSpA, which may influence work participation.

P102. Table I. Descriptive characteristics and ompact of membership in pt advocacy group.

Characteristic	Patient advocacy group member (n=85)	Not patient advocacy group member (n=610)	Total (n=695)	p-value
Age (yrs), mean (SD)	50.2 (7.7)	44.6 (11.1)	45.3 (10.9)	**<0.001**
BMI (kg/m2) mean (SD)	27.5 (5.0)	28.0 (12.7)	28.0 (12.0)	0.713
Male, n (%)	45 (52.9)	378 (62.0)	423 (60.9)	0.128
Disease duration (yrs) mean (SD)	13.7 (10.3)	12.5 (11.1)	12.6 (11.0)	0.303
ASAS-HI, 0-17	7.3 (3.4)	6.4 (3.9)	6.5 (3.8)	**0.045**
BASDAI, 0-10	4.3 (1.9)	3.8 (2.2)	3.9 (2.2)	**0.044**
BASDAI ≥4, n (%)	49 (57.6)	275 (45.1)	324 (46.6)	**0.025**
BASFI, 0-10	3.9 (2.3)	3.2 (2.5)	3.3 (2.5)	**0.015**
Biologic treatment, n (%)	52 (61.2)	312 (51.1)	364 (52.4)	0.072
Full time employment, n (%)	48 (56.5)	410 (67.2)	458 (65.9)	0.06
Absenteeism*, mean (SD)	8.4 (21.2)	10.9 (26.8)	10.6 (26.2)	-
Presenteeism*, mean (SD)	38.4 (24.6)	31.8 (25.7)	32.6 (25.7)	-
Overall work impairment score*, mean (SD)	40.6 (27.0)	36.8 (29.9)	37.2 (29.6)	0.380
Activity impairment, mean (SD)	46.7 (21.7)	40.5 (26.8)	41.3 (26.3)	0.058
Pts having ever received medicinal rehabilitation measures, mean (SD)	67 (78.8)	328 (53.8)	395 (56.8)	**<0.001**
Prescribed supervised group NPTM#, mean (SD)	49 (57.6)	210 (34.4)	259 (37.3)	**<0.001**
Regular physical training†, mean (SD)	76 (89.4)	515 (84.4)	591 (85.0)	0.231

*Work-related questions of WPAI-score have been calculated for pts in employment (N=340); †regular physical training in the context of axSpA; arehabilitation sport and/or functional training. ASAS-HI: Assessment of SpondyloArthritis International Society-Health Index; BASDAI: Bath Ankilosing Spondylitis Disease Activity Index; BASFI: Bath Ankilosing Spondylitis Functional Index, BMI: Body Mass Index; n: number of pts, patients; SD: Standard Deviation; WPAI: Work Productivity and Activity Impairment; yrs: years.



P102. Fig. 1. NPTM measures ever received in patients with axSpA (2617 answers from 770 pts).
Multiple answers were permitted. A total of 2617 answers were submitted from 770 patients. N: total number of pts; NPTM: non-pharmacological treatment modalities; pt: patient.

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P103

DIFFERENCES IN EARLY-ONSET VS. LATE-ONSET PSORIATIC ARTHRITIS: DATA FROM THE RESPONDIA AND REGISPONSER STUDIES

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Objectives. The objective was to evaluate the association of the age at onset of symptoms with the characteristics and burden of the disease in patients with Psoriatic Arthritis (PsA).
Methods. Observational study including 231 patients with PsA with <10 years of disease duration from the REGISPONSER and RESPONDIA studies. Patients were divided into two groups according to the age of PsA onset (early-onset: ≤40 years and late-onset: ≥60 years). The characteristics and burden of the disease were compared using the Student's t-test/Mann-Whitney U test or using the chi-square/Fisher test.
Results. 231 patients were included [early-onset 179 (77.5%); late-onset 52 (22.5%)] (Table 1). There was a significant higher percentage of men in the late-onset group [94 (62.3%) vs. 38 (86.4%)]. A lower presence of sacroiliitis was found in patients with late-onset PsA [6 (12.2%) vs 58 (32.6%)] as well as enthesitis [5 (9.8%) vs 44 (24.6%)]. Regarding the comorbidities, there was a higher frequency of heart disease among patients with late-onset PsA [4 (7.8%) vs. 0 (0%)]. In respect of the outcome measures, the late-onset group showed higher scores in BASFI [3.3 (2.5) vs. 2.2 (2.2)] and lower scores in FSF12 component [34.6 (8.7) vs. 38.7 (10.5)]. The radiographic indices measured by BASRI showed worse results in those patients with late-onset disease both in the spine [2.9 (3) vs 1.6 (2)] and in the total BASRI [3.4 (3 .4) vs 1.9 (2.4)].

P103. Table 1. Description of different characteristics in two groups: early and late onset.

	Early-onset N=179 n (%)=77.5	Late-onset N=52 n (%)=22.5	*p*-value
Sex (male)	94 (62.3)	38 (86.4)	0.003
Age (SD)	38.7 (9.3)	71.3 (7.5)	0.000
Enthesitis	44 (24.6)	5 (9.8)	0.023
Dactilytis	36 (20.1)	9 (17.6)	0.695
Sacroiliitis	58 (32.6)	6 (12.2)	0.005
Diagnostic delay, mean (SD)	4 (7.7)	1.5 (2.7)	0.036
Disease duration, mean (SD)	4.2 (2.7)	2.9 (2.4)	0.012
Arthritis (lower limbs)	118 (65.9)	33 (64.7)	0.872
Arthritis (upper limbs)	82 (45.8)	31 (60.8)	0.059
BASDAI, mean (SD)	3.9 (2.5)	3.8 (2.4)	0.932
BASFI, mean (SD)	2.2 (2.2)	3.3 (2.5)	0.002
ASDAS, mean (SD)	2.3 (1.1)	2.3 (0.9)	0.894
FSF12, mean (SD)	38.7 (10.5)	34.6 (8.7)	0.001
MSF12, mean (SD)	47.7 (10.6)	49.3 (9.2)	0.341
BASRI spine	1.6 (2)	2.9 (3)	0.020
BASRI total	1.9 (2.4)	3.4 (3.4)	0.012
ESR mm/h, mean (SD)	17.2 (14.2)	23.9 (19.1)	0.005
csDMARDs (ever)	111 (62.7)	31 (63.3)	0.943
bDMARDs (ever)	21 (11.9)	3 (6)	0.234

Conclusions. Our study suggests that the age of onset of PsA was associated with different characteristics of the disease. Patients with late-onset PsA were more frequently males, showed worse functionality and more structural damage. Sacroiliitis and enthesitis were found less frequently in the late-onset group. Quality of life, disease activity and treatments taken were not associated significantly with age of onset.

P104

EXPERIENCE OF CLINICS SPECIALIZED IN MULTIDISCIPLINARY CARE (MCC) IN PSORIATIC ARTHRITIS (APs) IN DIFFERENT HEALTH SYSTEMS IN MÉXICO

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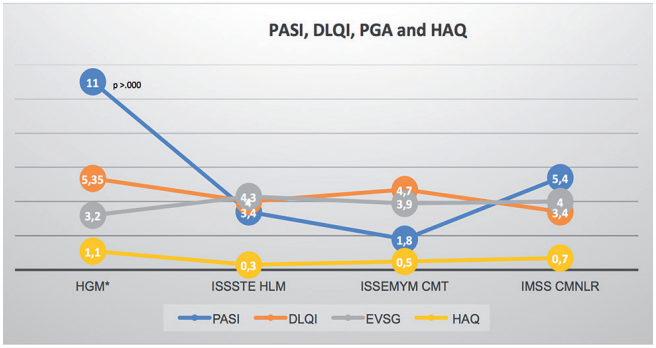
Introduction. Multidisciplinary care in APs recommended to improve the results of medical care. In Mexico there are different health systems in the population, some without cost to the patients and others with direct costs for them.
Objective. To describe and compare the clinical characteristics of a cohort of patients with Psoriatic Arthritis in four MCC in México.
Material and methods. Patients with Psoriasis from four MCC in the country was analyzed, three centers with social security (Sos) and one without Sos. MCC: A rheumatologist and a dermatologist attending the same patient jointly or independently, but with direct communication for joint decision-making. Demographic and clinimetric data were collected for skin and joint affection, the type of treatment, and questionnaires were applied to evaluate the quality of life, functionality, and the care satisfaction.
Results. 527 patients with psoriasis were evaluated, of which 80 (15%) had PsA, average age 53.6 (ds14), women: 48%, 72% with polyarticular pattern, 30% had metabolic syndrome, the average PASI was 5.9, HAQ: 1.32, DLQI: 4.9, swollen joints: 3.1, Treatment: 92% used DMAR´S, 59% used biological therapy. Treatment modification was reported in 40% in first visit. In two centers, the quality of care was evaluated, the patients rated the care with a 9.5 (0 Poor-10 excellent), 95% considered that the multidisciplinary care is better, in addition, the 70% affirm that the information provided to patients is clearer and more complete.
Patients without Sos had higher PASI scores, more painful and swollen joints, higher HAQ, lower use of biological therapy. There was no difference in quality of life assessed by the DLQi. (Fig 1, 2)



P104. Fig. 1. Some clinical differences between the different centers.
*Without social security.

Treatment	HALM ISSSTE, n=14	HGM* n=23	CM ISSEMYM Toluca n=20	CMN La Raza, IMSS n=23
MTX, n (%)	4 (35)	19 (84)	15 (77)	13 (60)
Leflunomide (%)	0	4 (16)	9 (44)	3 (15)
All DMAR´s	10 (71)	23 (100)	20 (100)	23 (100)
Biologic, (%)	12 (85)	02 (8)	16 (80)	10 (45)
Anti TNF, (%)	10 (83)	1 (4)	14 (87)	10 (100)
No Anti- TNF, (%)	2 (17)	1 (4)	2 (13)	0
Topic therapy	10 (73)	20 (90)	12 (60)	19 (85)

P104. Fig. 2. Treatment in patients with APs in clinics multidisciplinary care.
* Without social security.

Conclusions. The differences between patients with and without Sos, was more active skin and joint disease and less frequent use of biologicals, the prevalence of the disease is like that reported in the literature.

P105

HEALTH-RELATED QUALITY OF LIFE MEASURES IN AXIAL SPONDYLOARTHROPATHY OF RECENT DIAGNOSIS

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Objectives. To analyze the association between patient reported outcomes (quality of life (QoL), functional disability and fatigue) and disease activity in patients with recent axial spondyloarthritis (axSpA) diagnosis.
Materials and methods. We performed an observational, descriptive, cross-sectional and single-center study of patients with diagnosis of axSpA from June 2019 to June 2021 and stable therapy for at least 3 months. Demographic, clinical and analytical data were collected. ASQoL, FACIT, and ASAS-HI questionnaires as patient reported outcome, HAQ and BASFI index as functional disability parameters and BASDAI index as clinical activity evaluation were fulfilled by patients. Statistical analyses were achieved using R software, through multivariate linear regression models.
Results. We included 75 patients (56% male) diagnosed with axSpA. Mean age was 39.79 (12.74) years and mean age at diagnosis was 38.16 (12.58) years old. Demographic and clinical variables are described in Table I.

P105. Table I.

Variables	Mean (SD) / n(%)	Variables	Mean (SD) / n(%)
Months from diagnosis	19.39 (8.68)	ASQoL	6.03 (5.22)
Delay from onset of symptoms to diagnosis (months)	34.2 (44.07)	ASAS-HI	6.01 (4.29)
Radiographic			
Non-radiographic	33 (44%) 42 (56%)	FACIT	36.2 (12.72)
Peripheral arthritis	28 (37.33%)	BASFI	2.89 (2.72)
HLA.B27 +	38 (57.58%)	HAQ	0.57 (0.61)
Biological treatment		BASDAI	3.68 (2.31)
No treatment	36 (48%)		
Anti-TNF	24 (32%)		
Anti-IL17	11 (14.67%)		
Others	4 (5.34%)		
		ASDAS-CRP	1.85 (0.68)
		BASDAI < 4	48 (64%)
		ASDAS-CRP <1.3	44 (64.71%)

We observed a high correlation among ASQoL, FACIT and ASAS-HI values and functional disability (HAQ, BASFI). The statistical analyses showed a significant association of BASDAI and ASDAS-CRP with HAQ (p<0.001), FACIT (p<0.001), ASAS-HI (p<0.001), ASQoL (p<0.001), BASFI (p<0.001). No effect of the age, years of disease evolution, peripheral arthritis, radiographic alterations and the biological treatment in the patient reported outcomes (PROs) values was observed. In addition, CPR levels showed a significant association with FACIT (p=0.034), ASQoL (p=0.034), ASAS (p=0.034), BASFI (p=0.015).
Conclusions. The ASQoL, ASAS-HI, FACIT, BASFI and HAQ questionnaire results are associated with disease activity in patients with recent diagnosis of axSpA. The introduction of PROs in the clinical practice could be extremely useful in a better management and control of the disease.

P106

AXIAL SPONDYLOARTHRITIS, AGE AND MALE GENDER IMPACT COVID VACCINATION ADVERSE EVENTS MORE THAN RHEUMATOID ARTHRITIS

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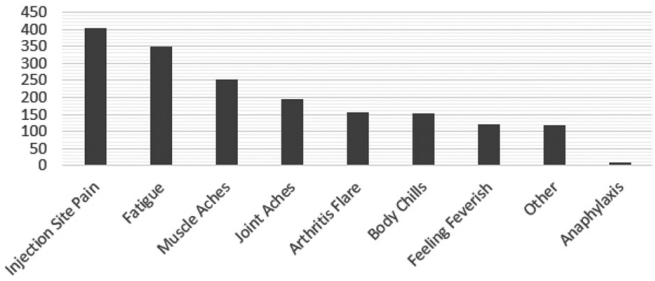
Introduction. We aimed to compare the uptake of COVID vaccination in RA and axSpA, the frequency of AEs and disease flares, and identify risk factors associated with vaccine AEs in these patients.
Methods. We surveyed two prospective cohorts of established RA and axSpA patients in northern Alberta, Canada from November 2020-2021 who answered at least one or more surveys through de-identified email link surveying demographics, disease characteristics, COVID symptoms, treatment of RA and axSpA, health care utilization, vaccination status, vaccine AEs and use of cannabis. Univariate analyses evaluated independent variables associated with the dependent variables of (1) any AE, (2) any severe AE, (3) any arthritis flare, and (4) any severe arthritis flare, followed by multivariate analyses of these four dependent variables using all clinically relevant variables from the univariate analysis.
Results. 773/2167 patients (RA 574, axSpA 197) responded to at least one survey. 32/663 (5%) were single vaccinated, 631 (95%) double vaccinated and 230 (54%) triple vaccinated with 80% receiving Pfizer, 24% Moderna, 28% AstraZeneca and 30% "other". 456 (69%) reported at least one AE (Figure) with 21 (3%) patients seeing a physician for their AE. Increased age was associated with all AEs. RA patients had lower reported AEs versus axSpA patients for all AE definitions except for severe arthritis flares. Generally, males reported worse AEs (Table). "Any arthritis flare" was lower in patients reporting cannabis use.
Conclusion. RA and axSpA patients showed high uptake of COVID vaccination with largely minor AEs. Older age and male gender were associated with more general and arthritis specific AEs. The association of any AE and/or arthritis-specific AEs in axSpA versus RA patients is a novel finding which may correlate with the male predominance of axSpA. The association of cannabis with fewer arthritis AEs may reflect the nociceptive properties of cannabis.



P106. Fig. 1. #of patients with COVID vaccine side effcts.

P107

LESS THAN EXPECTED IMPACT OF RHEUMATOID ARTHRITIS AND AXIAL SPONDYLOARTHRITIS DISEASE ON COVID SEVERITY

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Introduction. There has been ongoing concern that people with autoimmune diseases such as rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA) will have more severe COVID-19 disease due to immune dysfunction and treatment. We aimed to compare the severity of COVID-19 in patients with RA versus axSpA and characterize the predictors of COVID-19 severity during the pre-Omicron pandemic phases.
Methods. The IMPact of inflammatory Arthritis on COVID Outcomes Study (IMPACT) is a prospective cohort of RA and axSpA patients surveyed monthly from November 2020-2021. We assessed patient demographics, disease characteristics, COVID-19 symptoms, treatment of RA and axSpA, health care utilization, vaccination status and vaccine adverse events. Descriptive and regression analyses were performed to identify vari-

P106. Table. Summary of multivariate level mixed-effect logistic regression models evaluating the IMPACT of RA and SpA disease characteristics on vaccine adverse events including any, severe, and arthritis specific flares.

Variable		Any adverse event Odds ratio (95% confidence interval) *p*-value	Severe adverse event* Odds ratio (95% confidence interval) *p*-value	Any arthritis flare or joint ache adverse event Odds ratio (95% confidence interval) *p*-value	Any severe arthritis flare or joint ache* Odds ratio (95% confidence interval) *p*-value
Gender	Male Female	1.47 (0.89–2.43) p=0.1314	**2.10 (1.30–3.41)** **p=0.0026**	**2.05 (1.20–3.50)** **p=0.0088**	**3.97 (1.84–8.57)** **p=0.0004**
Age		**1.06 (1.04–1.08)** **p<0.0001**	**1.05 (1.03–1.06)** **p<0.0001**	**1.03 (1.01–1.04)** **p=0.0031**	**1.03 (1.01–1.06)** **p=0.0035**
Rheumatic disease type	RA SpA	**0.42 (0.23–0.76)** **p=0.0046**	**0.55 (0.31–0.98)** **p=0.0415**	**0.52 (0.28–0.98)** **p=0.0442**	0.78 (0.34–1.78) p=0.553
Steroids	Yes No	0.85 (0.40–1.83) p=0.6844	0.66 (0.32–1.35) p=0.2500	0.84 (0.36–1.95) p=0.6856	**0.38 (0.15–0.97)** **p=0.0419**
NSAIDS	Yes No	1.11 (0.81–1.52, p=0.510	1.03 (0.75–1.41) p=0.8557	1.05 (0.74–1.48) p=0.7997	1.17 (0.73–1.89) p=0.5218
Current disease activity		0.95 (0.88–1.03) p=0.2318	0.90 (0.83–0.97) p=0.1883	0.92 (0.85–1.00), p=0.0598	**0.82 (0.74–0.92)** **p=0.0005**
HAQ		1.08 (0.73–1.61) p=0.7014	**0.77 (0.52–1.14)** **p=0.0071**	0.74 (0.48–1.13) p=0.165	0.65 (0.38–1.11) p=0.1151
Nicotine products	Yes No	1.33 (0.75–2.37) p=0.3350	1.42 (0.80–2.52) p=0.2350	1.15 (0.60–2.01) p=0.7591	0.97 (0.43–2.17) p=0.9385
Cannabis products	Yes No	0.78 (0.49–1.25) p=0.3046	0.87 (0.55–1.38) p=0.5516	**0.51 (0.31–0.83)** **p=0.0068**	0.66 (0.35–1.26) p=0.2070
DMARDs	Yes No	1.98 (1.28–3.06) p=0.0022	**1.52 (1.01–2.28)** **p=0.0466**	1.43 (0.91–2.23) p=0.1184	**1.86 (1.0 –3.36)** **p=0.0411**
Biologic DMARD	Yes No	0.72 (0.42–1.25) o=0.2412	0.79 (0.45–1.41) p=0.4293	1.20 (0.66–2.18) p=0.5414	1.39 (0.63–3.08) p=0.4150

*Severe = Any of the following: ranked moderate to severe and/or lasting more than 7 days and/or saw physician.

ables associated with severe Covid. Infection severity was defined as any patient with COVID-19 symptoms who visited a doctor, Emergency Department (ER), or required hospital admission.

Results. 773 of 2167 (36%) patients (RA n=574, axSpA n=197) registered in both cohorts answered at least one baseline survey, 28 (4%) reporting positive COVID-19 tests (24 positive once). Of 442 reporting COVID-19 symptoms during the survey, 11 (3%) were admitted for a mean of 4 days, 2 requiring ICU or blood clot treatment and 1 requiring advanced therapy. 116 (26%) visited a physician for Covid symptoms. Univariate analysis showed that the use of steroids, NSAIDs and increased disease activity were associated with having less severe infection, but these associations were not significant in the multivariate analysis (Table). There were no significant impacts of RA vs axSpA, age, gender, treatment, disease activity, or smoking.

P107. Table. Multivariate level mixed-effect logistic regression model: IMPACT of RA and SpA disease characteristics on COVID infection severity defined as patients with COVID symptoms requiring visit to doctor, emergency room or hospital admission.

Variable		Coefficient (S.E)	Odds ratio (95% confidence interval)	*p*-value
Gender	Male Female	0.17 (0.34) Reference	1.18 (0.61 – 2.31)	0.6193
Age		-0.01 (0.01)	0.99 (0.97 – 1.01)	0.2543
Rheumatic Disease Type	RA SpA	0.18 (0.40) Reference	1.20 (0.58 – 2.48)	0.6213
Steroids	Yes No	-0.40 (0.56) Reference	0.67 (0.23 – 2.01)	0.4757
NSAIDS	Yes No	-0.20 (0.26) Reference	0.82 (0.49 – 1.37)	0.4508
Current Disease Activity		-0.04 (0.06)	0.96 (0.85 – 1.09)	0.5275
HAQ		-0.03 (0.29)	0.97 (0.55 – 1.70)	0.9041
Nicotine products	Yes No	-0.67 (0.37) Reference	0.51 (0.25 – 1.06)	0.0714
Cannabis products	Yes No	-0.45 (0.31) Reference	0.64 (0.35 – 1.18)	0.1510
DMARDs	Yes No	0.26 (0.30) Reference	1.30 (0.72 – 2.35)	0.3860
Biologic DMARD	Yes No	-0.46 (0.43) Reference	0.63 (0.27 – 1.46)	0.2813

Conclusions. Possible disease related risk factors for increased COVID-19 severity in RA and axSpA patients, including use of steroids or DMARDs, were not associated with severe infection. These findings are consistent with other international studies whereby other non-rheumatic disease comorbidities played a greater role in infection severity.

P108

PREVALENCE OF OBESITY AND ITS RELATIONSHIP WITH THE LEVEL OF JOINT ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS

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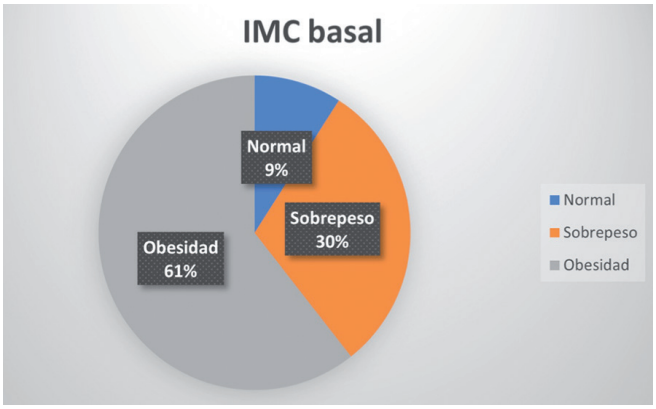
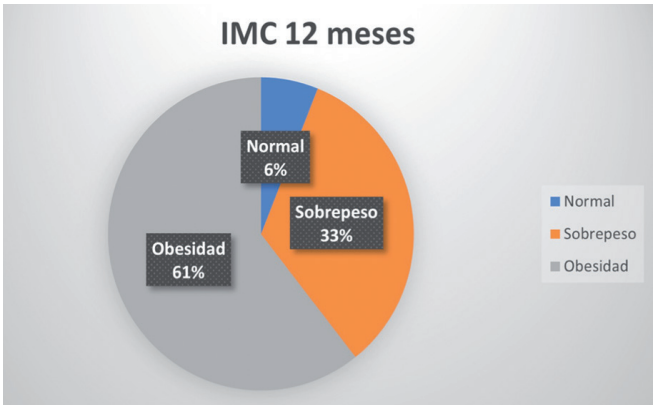
Objectives. To evaluate the prevalence of obesity, as well as its relationship with joint inflammatory activity in patients with psoriatic arthritis who start treatment with biological drugs or DMARDs (Targeted Synthetic Disease-Modifying Drugs). Assess response to non-pharmacological treatment (dietary advice aimed at achieving weight loss).

Material and methods. Retrospective longitudinal observational study on a database of patients with a practice diagnosis of psoriatic arthritis who start treatment with biological drugs or DMARDs according to usual clinical practice. The degree of joint activity of the disease is determined, as well as the weight of the patients at baseline, at 6 and 12 months.

Results. At the start of treatment (Fig. 1), 91% of the patients were above normal weight (61% obese). At 6 and 12 months (Fig. 2), this percentage remained stable. At 12 months, 58% of patients achieved or maintained remission or low disease activity. The correlation coefficient was for BMI (Body Mass Index) and DAPSA 12 months Kendal b 0.348 (p-value 0.039) for women at 12 months.



P108. Fig. 1



P108. Fig. 2

Conclusions. In our series of patients, obesity/overweight is higher compared to the general population and against series of patients affected by psoriatic arthritis. No linear connections were found, but we found a low non-linear association between DAPSA and BMI in women. Non-pharmacological treatment measures did not obtain results in weight reduction.

P109

THE PRACTICAL UTILITY OF SUPERB MICROVASCULAR IMAGING TECHNIQUE IN EVALUATION OF ENTHESITIS: PICTORIAL CASE SERIES

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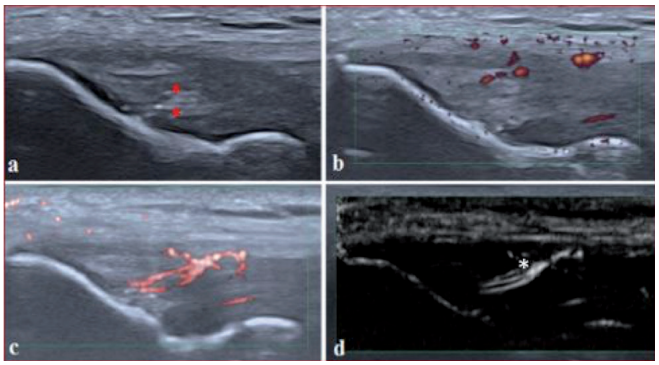
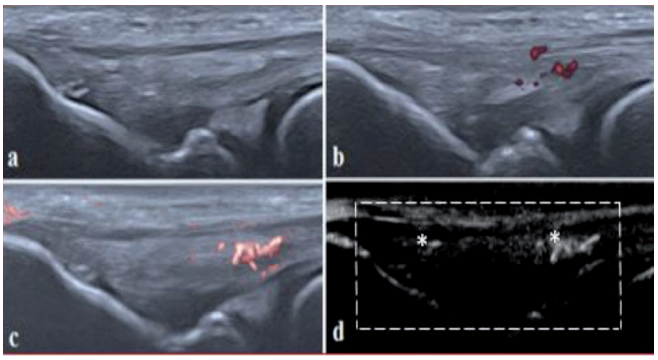
Background. The evaluation of enthesitis in spondyloarthropathies is challenging. The currently available scoring methods for enthesitis are mostly measures of pain but not for inflammation at entheseal sites. In rheumatology, the superb microvascular imaging technique (SMI) is known to be more sensitive than conventional power Doppler (PD) in identifying the slow flow of synovitis without motion artefacts. There is only one known original study of using the SMI technique for assessment of lateral epicondylitis (1).
Objectives. To demonstrate the diagnostic performance of PD and SMI techniques for evaluating vascularity of enthesitis in spondyloarthropathies.
Methods. Three patients with active spondyloarthropathy accompanied with enthesitis are presented. The attention is focused on the interpretation of ultrasound images from the SMI aspect. Diagnostic ultrasound system (CANON TUS-AI800) equipped with linear transducers: 14 MHz and 24 MHz ultrahigh frequencies were used.
Results. 1. 49-year-old man with psoriatic arthritis of 3 years. The activity of the disease was high (DAS28(ESR)-3,24), the palpation of both lateral epicondyles was unpainful. Ultrasound confirmed active subclinical enthesitis (Fig. 1).

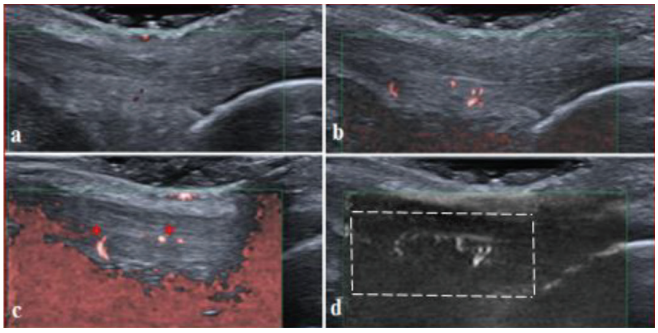


P109. Fig. 1. Subclinical enthesitis: a) B mode image shows an inhomogenous flexor tendon with focal compactions (*red asterisks*); (b) Pd reveals slow flow vascularity by several active dots (gain 50); colour SMI (c) more sensitive violation of enthesis and monochrome SMI (d) confirms true flow (*white asterisks*).



P109. Fig. 2. Painful enthesitis: a) B mode image shows an inhomogenous flexor tendon with focal compactions distally from the insertion; b) PD reveals slow vascularity by several active dots with an optimal gain; colour SMI (c) more sensitive violation of enthesis insertion and monochrome SMI (d, *white asterisks*) confirms inflammation at the entheseal area (*white dotted lines*).

2. 45-year-old man suffering from ankylosing spondylitis for 15 years, with high disease activity (BASDAI-6,4). Palpation of both lateral epicondyles was painful. Ultrasound confirmed active enthesitis (Fig. 2).
3. 51-year-old woman with psoriatic arthritis of 4 years. Disease activity remained moderate (DAS28(ESR)-3,6) despite biological therapy. Most entheses were painful, especially sites of Achilles insertions. Ultrasound confirmed active Achilles tendinitis (Fig. 3). In addition, the ACHILLES trial involves tendinitis with/without bursitis in assessment criteria of MRI positive heel enthesitis (2).



P109. Fig. 3. Enthesitis of Achilles insertion a) PD of Achilles tendon shows an inhomogenous tendon hyperechogenicity/loss of fibrillary structure with focal compaction close to the retrocalcaneal bursa and several small dots of PD signal; Colour SMI (b) detects slow flow vascularity by active dots in the tendon; colour SMI (c) with higher gain highlights active vascular dots (*red asterisks*) and monochrome SMI (d) confirms neoangiogenesis by exclusively true white flow dot (*white dotted lines*).

Conclusions. SMI provides unprecedented and detailed visualization of very-low-velocity microvascular flow (neovascularization) at the entheseal sites compared to conventional PD imaging.

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P110

TUMOR NECROSIS FACTOR RECEPTOR ASSOCIATED FACTOR 1 (TRAF1) IS A GREAT THERAPEUTIC TARGET FOR RA PATIENTS AS SEEN BY ITS OPPOSING EFFECTS ON MONOCYTES AND T LYMPHOCYTES

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Introduction. Chronic inflammation leads to Rheumatoid Arthritis (RA) and activation of the NF-kB is critical. TRAF1 is involved in the regulation of inflammation and a SNP in TRAF1 leads to higher risk of RA. The exact role of TRAF1 in the regulation of NF-kB in different cell types are unknown. Here we dissected the role of TRAF1 in monocytes versus T cells *in vitro* and *in vivo* to determine its overall effect on RA and arthritis in general.
Methods. Using CRISPR-Cas9, I created TRAF1$^{-/-}$ - THP-1 cells. Following LPS stimulation, the inflammatory cytokine profiles of WT and TRAF1$^{-/-}$-THP-1 cells was determined. We used mixed BM chimeras to determine the effects of TRAF1 loss in monocytes in the presence or absence of T cells in vivo: Group I (WT recipient) – mixed TRAF1 & TCR$\alpha^{-/-}$ BM donors; Group II (WT recipient) – mixed WT & TCR$\alpha^{-/-}$ BM donors. We injected ankles and knees of arthritic BPSM1 mice with macrophages grown in vitro from WT-BM or TRAF1$^{-/-}$- BM. To find out the role of TRAF1 expression in monocytes vs. T lymphocytes, I also created TRAF1 floxed mice and bred them to LyzM-cre and Lck-cre mice.
Results. TRAF1$^{-/-}$-THP-1 cells had higher inflammatory cytokines compared to WT-THP-1 cells following LPS stimulation. Similarly, group I mice had higher inflammatory cytokine profiles compared to group II mice following LPS injection. Arthritic BPSM1 mice injected with WT-BM

grown macrophages had lower inflammatory profile and delayed arthritis onset compared to TRAF1$^{-/-}$- BM grown macrophages.
Discussion. We show for the first time that TRAF1 inhibits the NF-kB pathway in monocytes while promoting its activation in lymphocytes. Our data confirm this bi-directional role of TRAF1 and shows that in the absence of TRAF1 there is an increase in inflammatory cytokines production, cellular infiltration, and enhanced bone damage. This increase is absent when TRAF1 is present.
Conclusions. TRAF1 can be used as a therapeutic target for RA.

P111

REAL-LIFE EFFICACY OF UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS: PRELIMINARY RESULTS OF A MULTICENTRIC ITALIAN STUDY

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Objectives. Safety and efficacy of Upadacitinib (UPA) in PsA patients has been recently reported in randomized clinical trials. This study aims to verify the real-life UPA efficacy/safety in an Italian multicentric study.
Methods. PsA patients (n.54) were enrolled in n.6 rheumatologic centres, according to the following inclusion criteria: 1) active disease, defined with the treat to target strategy and by the absence of MDA (Minimal Disease Activity), and 2) failure or intolerance towards at least one csDMARD (bio-naive patients) or one bDMARD (bio-failure patients). All patients will be evaluated at week 12, 24 and 52, recording DAPSA, ASDAS-CRP, PASI and assessing MDA, VLDA and ACR response. Any type of adverse event will also be monitored.
Results. Preliminary results in nineteen patients (15 females, 78.9%; age 57.5 yrs, BMI 25.2) evaluated at baseline are reported. Patient profiling, according to 2021 GRAPPA Guideline, is: active peripheral domain in all patients (100%); n.10 patients (52.6%) presented an axial domain, n.13 (68.4%) enthesitis, n.5 (26.3%) dactylitis, n.11 (57.9%) skin and n.9 (47.4%) nails domain. A complete patient profiling with comorbidities will be presented at the conference.
Bio-naive patients (n.5, 26.3%) presented at baseline a mean DAPSA 31.9; PASI 0.4 and LEI 1.1; one of them (20%) had axial involvement, with mean ASDAS-CRP of 2.9.
Bio-failure patients (n.14, 73.7%) presented a mean DAPSA 32.9; PASI 0.4 and LEI 1; n.9 (64.3%) had axial involvement, with mean ASDAS-CRP of 3.2.
Currently n.3 (15.8%) patients have achieved week 12 evaluation (mean DAPSA 8, PASI 0.35, LEI 0), n.2 (10.5%) completed the study (mean DAPSA 2.5, PASI 2.3, LEI 1) and n.1 (5.3%) discontinued Upadacitinib due to inefficacy.
Conclusions. These preliminary data suggest a possible profiling for UPA therapy in PsA patients and confirm its real-life efficacy on peripheral and enthesis domains.

P112

TURKISH TRANSLATION AND CROSS-CULTURAL ADAPTATION OF THE MODIFIED SHORT QUESTIONNAIRE TO ASSESS HEALTH-ENHANCING PHYSICAL ACTIVITY (MSQUASH)

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Introduction. To translate and cross-cultural adapt the mSQUASH tool into Turkish among patients with axial Spondyloarthritis (ax-SpA) (1).
Methods. The mSQUASH was translated into Turkish according to the Beaton method (Figure) (2). Pre-final version was used in a field-test with cognitive debriefing and involved a sample of axSpA patients with variation in, gender, age, disease duration, and educational background. The final Turkish mSQUASH version was reached after the patients were interviewed to check understandability, interpretation, and cultural relevance of the translation.
Results. Small incompatibilities were resolved during the expert committee meeting. For example: 'Ander transport (heen en terug)' was translated as 'Diğer hedeflere (gidip gelmek)'. The discrepancy raised whether to use 'transportation' or the 'target' as the title. Consensus was reached to use a word equivalent to 'the target' which is semantically equal to the Dutch version. A total of 10 patients with axSpA [7 females, mean (SD) age of 38 (10)] participated in the field test. Mean (SD) time to complete the mSQUASH was 6.1 (2.4) minutes. mSQUASH was shown as clear, relevant, understandable, and easy to complete. None of the patients indicate any important aspect of physical activity that is missing from the questionnaire items. During the cognitive debriefing, 2 patients suggested a change in the wording of an item of the sample sport activities, ice-skating, tennis, handball. They suggested they are not culturally suitable. According to their comments these items were replaced by other examples such as football.
Conclusions. The final Turkish version of the mSQUASH showed acceptable linguistic validity and can be used in both clinical practice and for research purposes. However, further assessment of its psychometric properties (validity and reliability) is needed.

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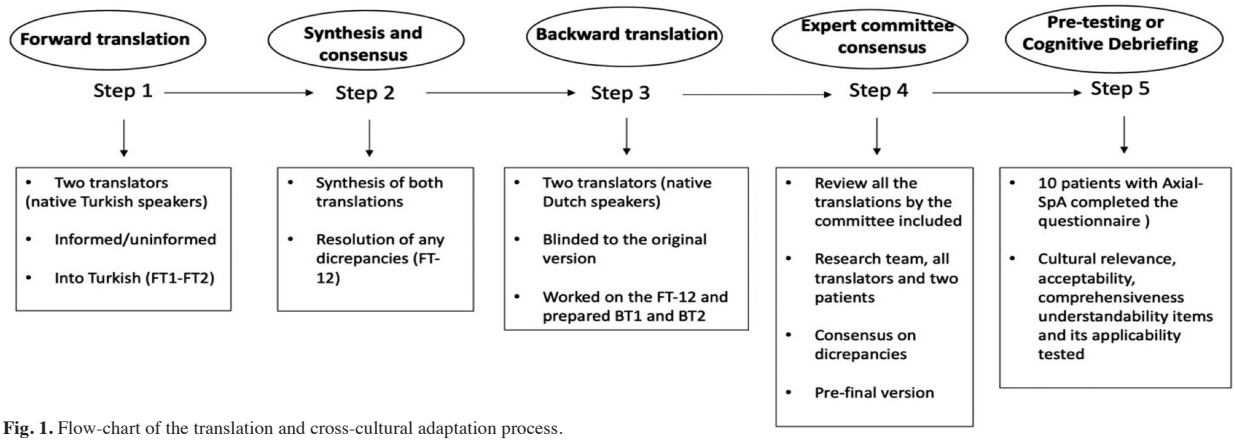

P112. Fig. 1. Flow-chart of the translation and cross-cultural adaptation process.

P113

ELECTROCARDIOGRAPHIC FINDINGS IN AXIAL SPONDYLARTHRITIS COMPARED TO PSORIATIC ARTHRITIS - A CROSS-SECTIONAL STUDY

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Introduction/objectives Cardiac involvement is a well-established complication of Spondylarthritis, namely in Axial Spondylarthritis (aSpA). The spectrum of cardiac manifestations in aSpA is extensive, ranging from valvular pathology to cardiac rhythm disturbances. Despite that, scant information regarding electrocardiographic alterations in psoriatic arthritis (PsA) is available. The purpose of our study is to compare electrocardiographic findings between aSpA and PsA patients.

Materials and methods. Single-center, retrospective cross-sectional study including aSpA and PsA patients from January 2018 to January 2022. All aSpA and PsA fulfilled the 2009 ASAS and the CASPAR criteria, respectively. Patients suffering structural cardiac disease and PsA patients with axial involvement were excluded. All patients had a cardiac check-up with a 12-lead electrocardiogram (ECG), posteriorly evaluated by a blinded cardiologist. Sociodemographic and clinical characteristics, and current medication, were collected. Descriptive analysis was performed. ECG findings were compared between groups and multivariable analysis was performed using-SPSS® software. The level of significance was a p-value ≤0.05.

Results. We selected 89 patients (45 and 44 patients in aSpA and PsA groups, respectively).

Sociodemographic and clinical characteristics of the population are presented in Table I.

P113. Table I. Sociodemographic and clinical characteristics.

Sociodemographic and clinical characteristics	Axial spondylarthritis N=45	Psoriatic arthritis N=44	*p*-value
Age, years (mean, SD)	50.00 (± 12.75)	54.84 (± 11.54)	.64
Sex, female (number, %)	25.00 (55.56)	20.00 (45.45)	.34
SpA characteristics			
Disease duration, years (median, IQR)	8.00 [4.00-13.50]	9.00 [5.25-11.75]	.63
Enthesitis (number, %)	8.00 (17.80)	14.00 (31.80)	
Dactilitis (number, %)	6.00 (13.30)	16.00 (36.60)	
Uveitis (number, %)	3.00 (6.70)	0.00 (0.00)	
HLA-27 (number, %)	21 (46.70)	4.00 (9.10)	
Cutaneous Psoriasis (number, %)	0.00 (0.00)	44.00 (100.00)	
Ungueal Psoriasis (number, %)	0.00 (0.00)	18.00 (40.90)	
IBD (number, %)	0.00 (0.00)	1.00 (2.3)	
Radiographic Sacroiliitis (number, %)	25 (55.60)	NA	
Peripheric articular pattern (number, %)			
>Oligoarticular (number, %)	NA	9.00 (20.50)	
>Poliarticular RA-like (number, %)	NA	32.00 (72.70)	
>Distal Interphalangic isolated (number, %)	NA	3.00 (6.80)	
CRP (median, IQR)	0.46 [0.16-1.03]	0.49 [0.16-1.32]	.42
ESR (median, IQR)	12.00 [7.00-20.00]	12.00 [7.00-28.00]	.49
BASDAI (median, IQR)	3.80 [1.40-6.42]	3.82 [1.45-6.40]	
BASFI (median, IQR)	3.97 [1.30-6.44]	3.90 [1.20-6.45]	
Cardiovascular risk factors			
Hypertension (number, %)	19.00 (42.22)	18.00 (40.90)	.90
Diabetes (number, %)	4.00 (8.89)	7.00 (15.91)	.31
Dyslipidemia (number, %)	4.00 (8.89)	19.00 (43.18)	<.01
Obesity (number, %)	0.00 (0.00)	4.00 (9.09)	.04
Smoking history (number, %)	5.00 (11.11)	1.00 (2.27)	.10
SpA related medication			
DMARDs (number, %)	19.00 (43.18)	38.00 (86.36)	<.01
>Methotrexate (number, %)	1.00 (2.20)	24.00 (54.60)	
>Sulfasalazine (number, %)	1.00 (2.20)	5.00 (11.40)	
>Leflunamide (number, %)	1.00 (2.20)	6.00 (13.60)	
>TNF-α inhibitors (number, %)	16.00 (35.56)	14.00 (31.82)	
>Ustekinumab (number, %)	0.00 (0.00)	1.00 (2.30)	
>Secukinumab (number, %)	1.00 (2.20)	1.00 (2.30)	
Corticosteroids (number, %)	4.00 (8.89)	18.00 (40.90)	<.01
NSAIDs (number, %)	26.00 (59.09)	11.00 (25.00)	.01

N: number of patients; Spa: spondylarthritis; IBD: intestinal bowel disease; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; DMARDs: disease-modifying anti-rheumatic drugs; NSAID: non-steroidal anti-inflammatory drugs; N: not applicable.

No statiscally significant differences were found between groups regarding age, sex, or disease duration. More patients in the PsA group were under corticotherapy or disease modifying anti-rheumatic drugs (DMARD) (p 0.01 and p=0.01, respectively) and more were obese and dyslipidemic (p=0.04 and p<0.01, respectively).

We found a higher frequency of electrocardiographic alterations in PsA group [3.00(6.82%) vs. 11.00(25.00%), p=0.02]. (Table II)

P113. Table II. Electrocardiographic findings and characteristics.

	Axial Spondylarthritis (N=45)	Psoriatic arthritis (N=44)	*p*-value
ECG findings (number, %)	3.00 (6.67)	11.00 (25.00)	.02
> AV Block*	0.00 0.00	4.00 9.09	.12
> LAFB	0.00 0.00	3.00 6.82	.08
> LPFB	1.00 2.22	0.00 0.00	.32
> LBBB	1.00 2.22	0.00 0.00	.32
> NICD	0.00 0.00	1.00 2.27	.31
> Left axis deviation	0.00 0.00	4.00 9.09	.04
>Atrial fibrillation (number, %)	1.00 (2.22)	1.00 (2.21)	.99
Other ECG characteristics			
QRS interval (mean, SD)	95.78 (±11.21)	94.34 (±20.84)	.69
QTc interval (mean, SD)	414.40 (±26.05)	417.25 (±28.59)	.62

N: number of patients; Spa: spondylarthritis; IBD: intestinal bowel disease; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; DMARDs: disease-modifying anti-rheumatic drugs; NSAID: non-steroidal anti-inflammatory drugs; AV: atrioventricular; LAFB: left anterior fascicular block; LPFB: left posterior fascicular block; LBBB: left bundle branch block; NICD: nonspecific intraventricular conduction delay; ECG: electrocardiogram; SD: standard deviation; * 1st degree AV.

No association between disease duration, laboratory findings, disease-related medication, or extra-articular manifestations and the presence of electrocardiographic changes were found, except for ungueal psoriasis, that seems to be a protector factor.

Discussion/conclusions. Our findings suggest that electrocardiographic changes are more frequent among PsA patients when compared to aSpA patients, despite more robust evidence in the literature of their presence in aSpA.

Author index