Here, we report enthesitis response to secukinumab over 24-weeks using two novel ultrasound composite enthesitis scores.
Methods. Study design was previously reported. Inclusion criteria required ≥1 clinical enthesitis as per SPARCC enthesitis index, but not ultrasound-assessed enthesitis. Throughout the study, enthesitis was assessed with SPARCC and ultrasound across six sites. Two exploratory global OMERACT-ultrasound enthesitis scores were tested: Definition-1 combining Power Doppler (PD; 0–3) and Grey Scale (0–1) inflammation and Definition-2 rating PD only (0–3) across six sites.
Results. Of 166 patients enrolled, 93% completed 24 weeks of treatment. Mean clinical enthesitis count at baseline was 4. Higher proportion of patients met Global OMERACT-ultrasound enthesitis score with Definition-1 vs. Definition-2 (81% vs. 33%) at baseline. Mean reduction from baseline to Week 24 in enthesitis (SPARCC) was 3 each for secukinumab and placebo-secukinumab groups. Resolution of enthesitis (SPARCC) was 46% for secukinumab and 54% for placebo-secukinumab groups at Week 24. Comparable decrease in OMERACT-ultrasound enthesitis (Definition-1, 2) score was observed from baseline to Week 24 for secukinumab and placebo-secukinumab groups (Fig. 1).
Conclusions. Consistent clinical and ultrasound responses on enthesitis were shown through 24-weeks across secukinumab and placebo-secukinumab groups.

O11

INTERLEUKIN-23 INHIBITORS AND THEIR APPARENT INEFFECTIVENESS IN TREATING AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW WITH META-ANALYSIS

Vanhoutte L.[1], Lories R.[1,2]
[1]Division of Rheumatology, University Hospitals Leuven; [2]Skeletal Biology and Engineering Research Center, Dept. of Development and Regeneration, KU Leuven, Leuven, Belgium

Introduction and Aim. The interleukin-23 – interleukin-17 axis is proposed as a critical immune-activator in the pathophysiology of axial spondyloarthritis. Emerging clinical trial data from interleukin-23 inhibitors fail to meet key efficacy endpoints. We set up a systematic review with meta-analysis contrasting interleukin-23 to interleukin-17A therapies in axial spondyloarthritis and related spondyloarthritis-phenotypes.
Methods. We searched databases Clinicaltrials.gov, Pubmed and Embase. Randomized controlled trials addressing interventions with interleukin-23 or interleu kin-17A inhibitors in axial spondyloarthritis or psoriatic arthritis were eligible. ASAS40 was chosen as primary outcome measure. ASAS20 and ASDAS-CRP, BASDAI, hS-CRP, SPARCC change from baseline (spine and SI joints) were chosen as secondary outcome measures. Effect estimates were reported as odds ratios or mean differences, with corresponding confidence intervals.
Results. 1693 records were identified, 18 randomized controlled trials were incorporated for meta-analysis. For axial spondyloarthritis, no interleukin-23 inhibitor met ASAS 40 endpoints (OR 1.51 [CI 0.98, 2.31]). All interleukin-17A inhibitors, however, did (OR 2.89 [CI 2.02, 4.13]). For risankizumab, ASDAS-CRP (MD -0.30 [CI -0.41, -0.19]), hS-CRP (MD -2.10 [CI -2.56, -1.64]), and SPARCC spine (MD -3.1 [CI -4.50, -1.70]) reductions were statistically significant. Axial outcomes were inconsistently reported for other spondyloarthritis-phenotypes, hence no comparisons could be drawn.
Conclusion. This systematic review summarizes IL-23 and IL-17A inhibitor interventions targeting axial spondyloarthritis. Regarding the observed ineffectiveness for interleukin-23 inhibitors on ASAS40 and ASAS20 key composite outcome measures, this systematic review confirms superior efficacy for treatment with interleukin-17A inhibitors. Interestingly, we observed a pooled statistically significant reduction in disease activity, inflammatory markers, and structural damage (as reported by ASDAS-CRP, hS-CRP and SPARCC) after treatment initiation with risankizumab. These data could suggest disease-modifying properties for interleukin-23p19 targeting, despite the observed ineffectiveness on composite efficacy outcomes.

O12

A FIRST IN DISEASE PHASE 2A TRIAL OF GRANULOCYTE MONOCYTE COLONY STIMULATING FACTOR NEUTRALISATION FOR AXIAL SPONDYLOARTHRITIS (NAMASTE STUDY)

Al-Mossawi M.H.*[1], Worth C.*[1], McDonald J.[1], Machado P.M.[2], Fisher B.[3], Chan A.[4], Gaffney K.[5], Gullick N.[6], Packham J.[7], Sengupta R.[8], Corn T.[9], Teh J.[1], Taylor P.C.[1]*, Bowness P.[1]*
[1]Nuffield Dept. of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford and Oxford University Hospitals; [2]UCL and Northwick Park Hospitals UK; [3]University Hospitals Birmingham; [4]Royal Berkshire Hospital, Reading; [5]Norfolk and Norwich University Hospital; [6]University Hospital Coventry and Warwick; [7]Haywood Hospital, Stoke-on-Trent; [8]Royal United Hospitals Bath; [9]Izana Bioscience, UK
*Equal contribution

Introduction. Granulocyte monocyte colony stimulating factor (GM-CSF) is a proinflammatory cytokine overproduced in a number of inflammatory and autoimmune diseases. In AxSpA we have demonstrated enhanced GM-CSF production by lymphoid cells including T cells, NK cells and Innate lymphocytes within inflamed joints. Therefore there is a rationale for the GM-CSF neutralisation as novel therapy for the treatment axSpA.
Methods. We report a phase 2a investigator initiated, proof-of-concept, Bayesian randomised, double-blind, placebo-controlled study to evaluate the safety/tolerability and efficacy of GM-CSF neutralisation with namilumab in 42 subjects with moderate-to-severely active axSpA (NAMASTE study, ClinicalTrials.gov NCT03622658). Namilumab is a human IgG1 monoclonal anti-GM-CSF antibody. Patients with previous inadequate response/intolerance to anti-TNF therapy were included. The primary endpoint was percentage of patients achieving ASAS20 response. Secondary and exploratory endpoints were also assessed including ASDAS score and ASAS40.
Results and Conclusions. Four sc injections of namilumab 150 mg given over 10 weeks were broadly safe and well tolerated. This study failed to meet its primary endpoint (ASAS20 at 12 weeks versus placebo). However, namilumab treatment improved ASDAS-CRP score at week 6 versus placebo (secondary endpoint), raising the question of a potential benefit in a subgroup of patients.

Acknowledgements. The study received funding from Izana Bioscience. The study received support from the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC) (PT and PB). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

O13

METABOLOMICS PROFILING OF SERUM FOR BIOMARKER DISCOVERY TO IDENTIFY PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS

Han W.[1], Wang X.[1], Li L.[1], Wichuk S.[2], Hutchings E.[3], Dadashova R.[3], Paschke J.[3], Maksymowych W.P.[2,3]
[1]Dept. of Chemistry, University of Alberta, Edmonton; [2]Dept. of Medicine, University of Alberta, Edmonton; [3]CARE Arthritis, Edmonton, Canada

Aim. We aimed to apply high-performance chemical isotope labeling (CIL) LC-MS platform to identify biomarker candidates of PsA and AS in human serum.
Methods. Serum samples were collected from 331 subjects, including 100 healthy controls, 48 PsA, 52 AS, and 131 RA patients. Each sample was incubated with ^{12}C-dansyl chloride, which labels the amine/phenol-containing metabolites. The reference sample for relative quantification was prepared by mixing individual samples and then labeled by ^{13}C-dansyl chloride. With this normalization, the individual samples and the reference sample were mixed in an equal amount. Finally, we used an LC-QTOF-MS platform to analyze the mixtures and measure the ^{12}C/^{13}C peak pairs.
Results. We first visualized the entire amine/phenol-submetabolome for all phenotypes using the partial least squares discriminant analysis (PLS-DA). PsA and AS samples were closely clustering, while the RA and control groups were well separated. We first differentiated PsA patients from controls/RA patients and then filtered out the AS patients wrongly classified as PsA. The same strategy was conducted for AS. Stipulating a fold change >1.5 with the false discovery rate <5%, we found 74 metabolites distinguishing the PsA group from the control or RA group. We selected significant metabolites to build a classification model based on the linear support vector machine (SVM) method, and the area-under-the-curve (AUC) value of the resulting receiver operating characteristic (ROC) curve was 0.929 (95% confidence interval: 0.899-0.956) (Fig. 1). Similarly, 37 metabolites could differentiate AS samples from RAs and controls (Fig. 2). A