comparisons across outcomes, these were standardised (difference between the individual score and the mean of all scores divided by the standard deviation, per reader, wave and time-point) before running the models. The higher the standardised coefficient the more change in inflammation/damage is captured.

Results: In total, 345 patients were included (mean (SD) symptom duration: 1.6 (0.9) years; 53% males; 89% HLA-B27 positive). Inflammation on MRI-SIJ (according to both the ASAS definition of sacroiliitis and the continuous SPARCC score) was more sensitive to change as compared to inflammation on the spine that remained essentially unchanged regardless of the outcome (table 1). Structural damage on the SIJ was found to increase over time, but with a higher standardised yearly rate of change on MRI-SIJ (range: 0.015–0.274) as compared to X-SIJ (range: 0.043–0.126). Notably, ≥ 3 Fatty lesions on MRI-SIJ was the structural outcome in the SIJ with highest sensitive to change (0.274), while ≥ 3 erosions was the least sensitive (0.015). Spine structural damage slowly progressed over time but, in contrast to SIJ, radiographic outcomes (i.e. ≥ 1 syndesmophytes and mSASSS) were more sensitive to change than MRI structural outcomes.

Conclusions: Our data adds to the body of evidence showing that structural damage assessed in pelvic radiographs only has low sensitivity to change. MRI-SIJ is a promising alternative (especially fatty lesions) capturing more structural changes. In contrast, in detecting structural change in early axSpA radiographic outcomes outperform MRI outcomes.

Disclosure of Interest: None declared

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FRI0166 CHARACTERISATION OF PHOSPHODIESTERASE 4 (PDE4) BLOCKADE IN THE SYNOVIUM OF PSORIATIC ARTHRITIS PATIENTS: A FOCUS ON SYNOVIAL INVASIVENESS AND T-CELL POLYFUNCTIONALITY

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Background: Owing to the multi-faceted nature of the pathogenesis of psoriatic arthritis (PsA), the development of multi-targeted agents has been an area of intensive research. Such agents include the phosphodiesterase 4 (PDE4) inhibitors, Rolipram and Apremilast, which elevate intracellular cAMP levels to modulate a number of anti-inflammatory mechanisms. However, the effect of PDE4 blockade within the complex inflammatory environment of the inflamed synovium remains to be elucidated.

Objectives: To characterise the effect of PDE4 blockade in PsA using *ex vivo* synovial whole tissue explants and synovial single cell suspensions reflective of the complex synovial micro-environment.

Methods: *Ex-vivo* PsA whole tissue synovial explants were cultured in the presence of PDE4 inhibitor, Rolipram, for 24 hour. The expression of pro-inflammatory mediators were quantified by ELISA and MSD multiplex. A 21 day synovial explant matrigel model was utilised to examine synovial fibroblast (SFC) invasiveness to allow for a long-term assessment. For the characterisation of synovial T-cells, synovial explants were digested and cultured in the presence of Rolipram for 8 hours, stimulated and stained for surface and intracellular T-cell markers. Cell surface expression of CD161 was used to identify Th17 lineage (CD161+Th17 and exTh17 cells) or non-Th17 lineage (CD161-) Th1 cells. SPICE analysis was utilised to determine the proportions of mono- and polyfunctional T-cells, which were correlated with disease activity scores.

Results: Rolipram treatment inhibited the spontaneous secretion of inflammatory mediators IL-6, IL-8, MCP-1 and MMP-1 (all $p < 0.05$), with a parallel increase in IL-10 expression. Under DMSO control conditions, a significant increase in SFC outgrowths from PsA explants (indicative of SFC invasiveness) was observed from day 8–21 (all $p < 0.05$), effects of which were significantly decreased in the presence of Rolipram (all $p < 0.05$). A comparative analysis of T cells in PsA PBMC and synovial tissue revealed an enrichment of Th1 ($p < 0.05$), Th17 ($p = 0.06$) and exTh17 ($p < 0.05$) cells in PsA synovial tissue, which displayed distinct polyfunctional cytokine profiles, in particular Th17 cells, as compared to matched PBMC. The frequency of polyfunctional triple positive GM-CSF/TNF/IL-17 and or IFN γ producing Th1 ($r = 0.8$, $p < 0.05$), Th17 ($r = 0.6$, $p < 0.16$) and exTh17 ($r = 0.9$, $p < 0.05$) cells positively correlated with PsA disease activity, suggesting an important role of T-cell polyfunctionality in PsA synovial pathogenesis. Analysis of synovial tissue cell suspensions and matched PBMC cultured in the presence of Rolipram showed a significant decrease in the proportion of these triple positivesynovial T cells compared to DMSO ($p < 0.05$), suggesting that PDE4 blockade can effectively targets the polyfunctional hyper-pathogenic synovial T cells in PsA, particularly polyfunctional CD8 +T cells and Th17 lineage, Th17 and exTh17 cells.

Abstract FRI0171 – Table 1. Standardised rate of change of imaging outcomes over 5 years of follow-up in early axSpA patients from the DESIR-cohort who fulfil the ASAS axSpA classification criteria.

Imaging outcomes	Baseline score* (N=313-344)	Standardized rate of change/year $\pm$
SACROILIAC JOINTS		
Inflammatory lesions (MRI-SIJ)		
Sacroiliitis (ASAS criteria)	134 (39.2%)	-0.278
SPARCC SIJ score (0-72)	4.7 (7.9)	-0.441
Structural lesions (MRI-SIJ)		
≥ 5 fatty lesion and / or erosions	66 (19.5%)	0.238 ^{††}
≥ 3 erosions	60 (17.7%)	0.015
≥ 3 fatty lesions	56 (16.5%)	0.274
Number of fatty lesions and/or erosions (0-80)	2.9 (4.9)	0.111
Number of erosions (0-40)	1.3 (2.2)	0.030
Number of fatty lesions (0-40)	1.5 (3.5)	0.140
Total structural lesions $\forall$ (0-144)	3.4 (5.9)	0.115
Total structural lesions without sclerosis (0-104)	3.2 (5.8)	0.124
Structural lesions (X-SIJ)		
mNY dichotomous	73 (21.2%)	0.044
mNY 1-grade change	NA	0.126
mNY 1-grade change and value ≥ 2	NA	0.119
mNY continuous grade (0-8)	1.7 (1.8)	0.043
SPINE		
Inflammatory lesions (MRI-Spine)		
BME: ≥ 3 lesions	32 (9.4%)	-0.032
BME: ≥ 5 lesions	19 (5.6%)	-0.030
SPARCC Spine score (0-414)	2.6 (7.7)	-0.050
Berlin Spine score (0-69)	0.9 (2.7)	-0.055
Structural lesions (MRI-Spine)		
≥ 5 fatty lesions	5 (1.6%)	-0.013
Total structural lesions [†] (0-322)	0.4 (1.0)	0.016
Number of fatty lesions (0-92)	0.3 (0.8)	0.008
Number of corner erosions (0-92)	0.1 (0.2)	0.012
Number of corner bone spurs (0-92)	0.1 (0.3)	0.027
Structural lesions (X-Spine)		
≥ 1 syndesmophyte	19 (5.5%)	0.037
mSASSS score (0-72)	0.3 (1.3)	0.043

* Agreement of ≥ 2 out of 3 readers for binary variables and mean (SD) of 3 readers for continuous variables from wave 3; $\forall$ fatty lesions, erosions, sclerosis, partial ankylosis, total ankylosis; [†]fatty lesions, erosions, bone spurs, ankylosis; NA, not applicable.

Conclusions: PDE4 blockade mediates broad anti-inflammatory mechanisms in PsA synovial tissue through the reduced expression of pro-inflammatory mediators, decreased invasiveness and reduced T cell polyfunctionality. We also demonstrate the feasibility of using *ex vivo* models to determine “*in situ* like” assessments of therapeutic agents and further our understanding of disease pathogenesis.

Disclosure of Interest: None declared

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FRI0167 EXPRESSION LEVELS OF IL-17, IL-22 AND IL-23 RECEPTORS IN FOUR OSTEOBLAST MODELS AND THE EFFECTS OF IL-17, IL-22 AND IL-23 ON OSTEOBLASTS

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory joint disease that chiefly affects the sacroiliac joints and the spine. Radiographs reveal erosive changes at the corners of the vertebral bodies in the early stages of disease, and outgrowth of bony spurs known as syndesmophytes in the later stages. Some data imply a pivotal role of IL-23/IL-17 axis in the regulation of bone homeostasis. However, it remains unknown whether IL-17, IL-22 or IL-23 has any direct effects on osteoblasts or new bone formation in AS.

Objectives: To examine the expressions of IL-17, IL-22, and IL-23 receptors in four osteoblast models and the effects of IL-17, IL-22, and IL-23 on osteoblasts.

Methods: Gene expression levels of receptors, alkaline phosphatase (ALP), osteocalcin (OCN), and Runt-related transcription factor 2 (Runx-2), were