adipocytokines were significantly higher in PsA compared to HD. The body mass index values were significantly correlated with the clinical inflammatory parameters (CRP and ESR) and activity of the disease (swollen joints count and DAS28). Increased levels of HOMA-IR also correlated with DAS28, clinical and serological inflammatory markers, and diverse adipokines. Elevated levels of cytokines correlated with the activity of the disease and lipid alterations.

Significant improvements in efficacy outcomes, including DAS-28 using erythrocyte sedimentation rate (ESR), tender and swollen joint count, Visual Analogue Scale (VAS), enthesitis and morning stiffness severity, were observed with apremilast at week 4. No changes on BMI were noticed. A significant reduction of intra-arterial blood pressure was evidenced since the first 4 weeks. Serum levels of Apolipoprotein A and B, insulin and HOMA-IR values were also significantly reduced after 24 weeks of treatment. Endothelial dysfunction was significantly restored shown by an increase of the peak flow and hyperaemia area and decreased adhesion molecules in serum. Levels of interleukins and adipokines were also modulated after apremilast treatment.

Conclusions:

- PsA is associated with an increase in inflammatory cytokines and adipokines, alongside with an endothelial dysfunction. These alterations are related to the disease activity and the presence of metabolic comorbidities such as insulin resistance or obesity, contributing to the burden of cardiovascular disease risk.
- Apremilast might reduce IR, inflammation, hypertension, lipids and endothelial dysfunction, parameters strongly involved in cardiovascular disease.

Acknowledgements: Supported by the Minister of Health (ISCIII, PI17/01316, RIER RD16/0012/0015) cofinanced with FEDER funds.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6259

SAT0332

A HIGH-DIMENSIONAL APPROACH TO DISSECTING THE ROLE OF THE TISSUE MICROENVIRONMENT IN SHAPING THE IMMUNE RESPONSE IN PSORIATIC ARTHRITIS

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Background: Psoriasis (Ps) currently inflicts 2%–3% of the population globally and one-third of patients have psoriatic arthritis (PsA). Up to 30% of PsA patients with active psoriasis (Ps) do not respond adequately to any treatment. Understanding the immune mechanisms contributing to the initiation and disease progression of PsA and Ps is crucial for devising novel therapeutic strategies.

Objectives: To address the current unmet clinical need and bridge the knowledge gap in the pathogenesis underlying PsA/Ps, we perform transcriptomic analyses of the skin microenvironment and deep immunophenotyping of immune cells from PsA patients with active disease. We hypothesise that the interaction between the tissue microenvironment and the peripheral immune system dictates the immune response that impacts upon the development and progression of PsA/Ps. This multi-dimensional strategy will also enable the distillation of immune cell subsets in the periphery that can potentiate pathogenic responses in the microenvironment.

Methods: Total RNA was extracted from skin punch biopsies of lesional and morphologically normal sites from 7 patients with active disease. RNASeq was performed to decipher the transcriptomes of the skin punch biopsies. Peripheral Blood Mononuclear Cells (PBMCs) from 17 PsA patients and 12 healthy donors were stimulated with PMA-Ionomycin, stained with 37 phenotypic T cells markers and interrogated with the CyTOF platform. Dimensional reduction and unsupervised clustering analyses were performed with Multi-dimensional Automated Reduction and Visualisation (MARVis).

Results: Transcriptomic analysis of skin punch biopsies of psoriatic and morphologically normal sites revealed a gene signature in lesional skin that promotes the infiltration of multiple immune cell subsets into the microenvironment. The expression of chemokine genes such as CXCL8, CCL4, and CCL20 suggests a role for the accumulation of neutrophils, monocytes, natural killer (NK) cells and lymphocytes in the establishment of a pro-inflammatory microenvironment that is perpetuated by the presence of TNF and IFN γ .

Examination of the immune landscapes of PsA patients highlights multiple perturbations in various immune cell subsets. Specifically, we observed declines in CD8⁺CD161⁺TCR α 7.2⁺Mucosal Associated Invariant T (MAIT), CD4⁺CD45RO⁺CXCR5⁺TFH as well as CD45RO⁺Tbet⁺IFN γ ⁺TNF α ⁺IL17A⁺ memory TH1 cells in PsA patients. This decline is potentially attributed to the trafficking of these immune cell subsets into the microenvironment in response to chemokine signals. Conversely, we observed enrichments of CD56⁺Tbet

+GranB⁺IFN γ ⁺NK and activated CD4⁺CD127⁺CCR7⁺CD69⁺effector T cells in PsA patients that can contribute to the pathogenic immune response.

Conclusions: Our multi-dimensional approach resolves the complex interactions between the tissue microenvironment and the peripheral immunome that shapes the immune response and dictates the cellular composition in lesional skin. These findings possess translational value and will facilitate the identification of novel immune therapeutic targets.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6115

SAT0333

DRUG SURVIVAL ON FIRST TNF INHIBITORS IN PATIENTS WITH PSORIATIC ARTHRITIS: COMPARISON ACROSS ETANERCEPT, ADALIMUMAB, GOLIMUMAB AND INFILIXIMAB

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Background: It is commonly accepted that additional methotrexate (MTX) does not increase efficacy for treatment with TNF in psoriatic arthritis (PsA) but concomitant MTX has been also associated with increased drug survival in register studies. However, the role of MTX comedication in PsA is still unclear.

Objectives: We aim was to evaluate TNF- α inhibitor (TNFi) persistence when used as first -line biologic therapy for the management of PsA naïve to biologic and determine features of patients as MTX comedication that are associated with TNFi persistence.

Methods: A ambispective longitudinal observational multi-centre cohort study was performed on all patients with PsA starting first TNFi therapy (etanercept, adalimumab, golimumab and infliximab) between 01/JUN/2003 and 01/12/2015. Demographic and clinical data, concomitant treatment with MTX, were compared with TNFi persistence, using Kaplan-Meier survival and Cox regression analysis.

Results: Were included 468 patients starting treatment with etanercept (242), adalimumab (120), golimumab³¹ and infliximab (75); 235 receiving TNFi as monotherapy (50.2%) and 233 receiving concomitant MTX (49.8%). Mean age was 53.3 $\pm$ 12.6 years (men 53.3 $\pm$ 12.9 and women 53.2 $\pm$ 12.3, p=0.928) and 55.2% were men. Obesity (BMI $\geq$ 30) was similar in patients with or without persistence on treatment: 30.39 (13.32) vs 29.20 (5.44), p=0.355). At 60 months of follow-up 50.6% of patients persisted with TNFi therapy (55.8% with etanercept, 50.0% with adalimumab, 29.3% with infliximab and 67.7% with golimumab). Infliximab had the lowest retention rate (p=0.006). Drug survival analyses had not differences between patients receiving co-medication or not (p=0.849). In the Cox regression analysis lack of concomitant MTX and gender female were predictors of discontinuation of TNFi (0.014).

Conclusions: At 60 months infliximab had the lowest percentage of treatment continuation compared with etanercept, adalimumab and golimumab. Patients with PsA who are female and have not concomitant treatment with MTX could have lower TNFi persistence.

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Acknowledgements: The authors are grateful for the support of the members of the Galician Society of Rheumatology (SOGARE)

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4951

SAT0334

CLINICAL AND SONOGRAPHIC ANALYSIS OF PSORIASIS PATIENTS WITHOUT MUSCULOSKELETAL COMPLAINTS. PRELIMINARY RESULTS OF A PROSPECTIVE STUDY: THE PRE-APS COHORT

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Background: Early diagnosis in psoriatic arthritis (PsA) is mandatory in order to initiate early therapy and prevent disability. Around 20% of patients with Psoriasis (PsO) routinely visited in Dermatology departments have PsA previously undiagnosed.

Objectives: The aim of this study is to evaluate the presence of inflammation by clinical examination and ultrasound in joints and entheses of patients with PsO without musculoskeletal symptoms.

Methods: Patients with PsO under topic or PUVA therapy without musculoskeletal symptoms were referred to our Arthritis Unit. Clinical and demographic data were collected. The patients were evaluated for Body Surface Area (BSA), Swollen Joint Count (SJC) (66 joints), Tender Joint Count (TJC) (68 joints) and enthesitis (MASES). Psoriatic Arthritis Impact of Disease tool questionnaire (PsAID) and Psoriasis Epidemiology Screening tool questionnaire (PEST) were used to assess the impact of the disease. A comprehensive ultrasound evaluation of 46 joints and 12 entheses was made (ESAOTE MylabTwice, 12–18 Mhz probe). Enthesitis score was calculated using the Madrid Sonographic Enthesitis Index (MASEI) and a total score for synovitis (synovial hypertrophy and Power Doppler) was also calculated.

Results: 42 patients were included. 20 patients were female (48%), mean age (SD) was 48.3 y (14.6) and disease duration was 17.9 y (15.9). Mean BMI was 24.6 (5.2) and BSA 5 (8.7). 13 out of 42 (31%) had severe PsO (systemic treatment or BSA >10% at any time of evolution). 4 patients (9.5%) had Power Doppler signal and 2 (4.8%) fulfilled criteria for ultrasound-defined active synovitis ($SH \geq 2$ + PD) despite no signs or symptoms of musculoskeletal disease. However, although structural alterations such as calcifications and enthesophytes were frequent, no PD was found at any enthesitis.

In the univariate analysis, higher BMI ($p=0.013$), weight ($p=0.010$), waist ($p=0.033$) and hip ($p=0.014$) circumferences were significantly associated with severe PsO. In the same way, CRP serum levels were also significantly higher in patients with severe PsO ($p=0.027$). A strong trend was found between higher MASEI scores and onychopathy ($p=0.09$).

pan>

Conclusions: Patients with PsO under topic or PUVA therapy without musculoskeletal symptoms have a low prevalence of findings in the joints and enthesitis ultrasound evaluation. Of note, 9.5% of PsO patients had subclinical synovitis defined as PD. No changes in those finding were found in a short follow-up (6 months) in these patients. A higher number of patients would be necessary to have strong results. These patients will be followed in order to confirm if they develop Psoriatic Arthritis.

Acknowledgements: This work was partially financed by Pfizer-Spain

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6311

SAT0335

SECUKINUMAB PROVIDES RAPID AND SUSTAINED RESOLUTION OF ENTHESITIS IN PSORIATIC ARTHRITIS PATIENTS: POOLED ANALYSIS OF TWO PHASE 3 STUDIES, FUTURE 2 AND FUTURE 3

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Background: Enthesitis, one of the key features of psoriatic arthritis (PsA), shows chronicity in 50–70% of affected patients (pts).¹ Secukinumab (SEC), a fully human monoclonal antibody that selectively neutralises IL-17A, provided significant and sustained improvement in the signs and symptoms of active PsA, with sustained resolution of enthesitis in Phase 3 studies.^{2,3}

Objectives: Comprehensive *post-hoc* analysis to evaluate the effect of SEC on resolution of enthesitis count (EC; defined by Leeds Enthesitis Index) in PsA pts using pooled data from two Phase 3 studies, FUTURE 2 (NCT01752634) and FUTURE 3 (NCT01989468).

Methods: SEC and placebo (PBO) were administered weekly during the first 4 weeks (wks) followed by subcutaneous maintenance dosing every 4 weeks thereafter (PBO until Wk 16/24). The results are reported only for SEC 300 and 150 mg (approved doses). Pts with baseline (BL) enthesitis (BLE) or without BLE (No BLE) were included. Evaluation through Wk 104 included: time to first resolution of enthesitis (i.e. EC=0); shift analysis of BL EC (1, 2 or 3–6) to full resolution (FR) and partial resolution (PR; reduction of EC) at Wks 24 and 104; and number of new enthesitis sites developed in No BLE pts. Individual status over time with respect to resolution of EC was also determined by heat map analysis using last observation carried forward. Data are as observed in the overall population; time to first resolution of enthesitis was analysed in the overall population and by prior use of tumour necrosis factor inhibitor (TNFi-naïve and -inadequate responders [IR]).

Results: A total of 466 pts had BLE with a mean EC of 3.1 ± 1.6 , and 246 pts had no BLE. Median days to resolution of EC in BLE pts for SEC 300, 150 mg and PBO groups were 57, 85 and 167 in overall population; 57, 85 and 120 in TNFi-naïve pts; and 92, 82 and 169 in TNFi-IR pts, respectively. In pts with BL EC=1/2,

72%/61% (SEC 300 mg), 71%/66% (SEC 150 mg) and 45%/44% (PBO), respectively, achieved FR at Wk 24, with FR in SEC groups sustained or increased to 77%/81% (SEC 300 mg) and 75%/88% (SEC 150 mg) at Wk 104. In BL EC=3–6, 81% (SEC 300 mg), 73% (SEC 150 mg) and 71% (PBO) of pts achieved FR and PR at Wk 24, with an increase of FR and PR to 88% (in both SEC 300 and 150 mg) at Wk 104 (figure 1). A total of 89% of pts with No BLE did not develop enthesitis by Wk 104. Heat map analysis showed that SEC-treated pts at individual level had more resolution of EC than PBO pts at Wk 24.

Data presented for SEC 300 mg, 150 mg and PBO. EC 3–6 group includes patients with baseline EC 3, 4, 5 or 6. Shift Analysis on resolution of EC from baseline to Wk 24 or 104 is categorized based on the four criteria of resolution: FR (EC = 0); PR (EC 1 and < baseline EC); Stable (EC = baseline EC); and Worse (> baseline EC). EC, enthesitis count; FR, full resolution; N = number of patients who completed Wk 24 or 104 and had EC available at both baseline and Wk 24 or 104; PBO placebo; PR, partial resolution; SEC, secukinumab

Abstract SAT0335 – Figure 1. Shift Analysis of EC from Baseline to Wk 24 or 104

Conclusions: Time to resolution of enthesitis was earlier with SEC than PBO in the overall population, with faster resolution observed in TNFi-naïve than TNFi-IR pts. Majority of SEC-treated pts with BL EC=1/2 had FR by Wk 24, with further an improvement by Wk 104. In pts with BL EC=3–6, greater improvement was observed with SEC 300 mg vs PBO in the proportion of pts with FR and PR of enthesitis at Wk 24; further improvements were observed in both SEC groups at Wk 104.

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Disclosure of Interest: L. Coates Grant/research support from: AbbVie, Janssen, Novartis, Pfizer, Consultant for: AbbVie, Amgen, BMS, Celgene, Pfizer, UCB, MSD, Boehringer Ingelheim, Novartis, Lilly, Janssen, Sun Pharma, Prothena, D. McGonagle Grant/research support from: Novartis, Janssen, Pfizer, AbbVie, Speakers bureau: Novartis, Janssen, Pfizer, AbbVie, G. Schett Grant/research support from: BMS, Celgene, GSK, Lilly, Novartis, Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, UCB, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, P. Mease Grant/research support from: AbbVie, Amgen, Biogen Idec, BMS, Celgene, Crescendo, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Consultant for: AbbVie, Amgen, Biogen Idec, BMS, Celgene, Covagen, Crescendo, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, Biogen Idec, BMS, Crescendo, Janssen, Lilly, Pfizer, UCB, E. Quebe-Fehling Shareholder of: Novartis, Employee of: Novartis, D. Asquith Shareholder of: Novartis, Employee of: Novartis, L. Rasouliyan Consultant for: Novartis, Employee of: RTI Health Solutions, S. Mpofu Shareholder of: Novartis, Employee of: Novartis, C. Gaillez Shareholder of: Novartis, Employee of: Novartis

DOI: 10.1136/annrheumdis-2018-eular.4436