normal (within 10% of normal GFR if previously abnormal) GFR. Partial Response (PR) was defined as $\geq 50\%$ reduction in proteinuria to subnephrotic levels and normal or near-normal GFR. Renal outcomes were assessed at one year post biopsy. **Results:** The mean age of the patients was 38.9 ± 15.2 years (range, 13–69 years). The study included 85 females (87.6%) and 12 males (12.4%). The clinical presentations were nephrotic syndrome, nephritic syndrome, and asymptomatic urinary abnormalities in 38 (39.2%), 20 (20.6%), 39 (40.2%) patients, respectively. Nine patients were classified Class III (9.3%, including 2 as Class III +V), 82 as Class IV (84.5%, 10 as Class IV-segmental (IV-S) (10.3%) and 72 as Class IV-global (IV-G) (74.2%), including 4 as Class IV-G+V and 6 as Class V (6.2%). Forty-two (43%) patients presented with acute and 55 (57%) with features of chronic TMA. All patients had received treatment with standard immunosuppressants (55% mycophenolate, 39% cyclophosphamide, 6% other regimen) and steroids.

Abstract OP0201 – Table 1

Acute TMA features	Chronic TMA features
• Endothelial swelling with partial or complete occlusion of lumina;	• Capillary wall thickening with double contours;
• Microthrombi, focal or global;	• Organizing capillary thrombi;
fragmented RBC on glomerular subendothelial space and/or mesangial areas;	• Glomerular ischemic collapse with afferent arteriolar occlusion;
• Mesangiolysis, focal, segmental/global;	• Segmental/global glomerulosclerosis
• Glomerular congestion with efferent arteriolar occlusion	

At 12 months, CR was observed in 37 patients (38.1%), PR in 22 (22.6%) and no response in 38 (39.1%). Sixty-one patients (62.9%) were antiphospholipid positive (aPL) and 37 (38.1%) received anticoagulation with vitamin-K antagonist (VKA) and/or heparins. Presence of aPLs (OR, 2.4; 95% confidence interval CI-, 1.2–7.3; $p=0.03$), anti-DNA positivity (OR, 12.8; 95% CI: 3.0 to 71.3; $p=0.002$), and chronic features of TMA (OR, 3.0; 95% CI: 1.2 to 17.5; $p=0.04$) were all found to be associated with no response. When limiting the analysis to aPL positive patients, after adjusting for type of immunosuppressant therapy and LN class on biopsy, variables that were significantly associated with CR +PR were features of acute TMA rather than chronic (OR, 8.62; 95% CI: 1.4 to 97.1; $p=0.03$) and the use of VKA/heparins (OR, 2.1; 95% CI, 1.02–16.2; $p=0.046$).

Conclusions: In patients with concomitant LN and TMA, the presence of aPL and chronic features of TMA were associated with poorer renal outcomes. In patients with aPL, the use of anticoagulation appeared protective and warrants further investigation as a therapeutic tool, especially in the setting of acute TMA.

Disclosure of Interest: None declared

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OP0202

GENE EXPRESSION PROFILES IN PRIMARY SJÖGREN'S SYNDROME WITH AND WITHOUT SYSTEMIC MANIFESTATIONS

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Background: Different phenotypes characterise the clinical spectrum of primary Sjögren's syndrome (SjS). Patients with a clinical expression limited to glandular features (GFs) are classically distinguished from patients with extra-glandular manifestations (EGMs). The former patients often complain higher level of fatigue and widespread pain (WP). (Segal et al. 2013) This suggests that gene expression pattern may be different in the two subgroups.

Objectives: To investigate the differences of gene expression in SjS patients with GFs and in those with EGMs.

Methods: Nineteen patients with SjS were selected for the study. Gene expression in peripheral blood mononuclear cells (PBMCs) was analysed in 4 patients with EGMs and 4 patients with GFs alone using Clariom D human Affymetrix gene chip (Affymetrix, Santa Clara, CA, USA), and compared to that found in healthy controls. Differences in gene expression were evaluated by analysis of variance (ANOVA) and Step-Up FDR-controlling procedure, being FDR corrected p value ≤ 0.01 and fold change > 2 considered as statistically significant.

Validation of the gene overexpression was performed by quantitative Real Time (qRT)-PCR in PBMCs from all the selected SjS patients, using the $\Delta\Delta C_t$ method for comparing relative fold expression differences.

Results: All the enrolled SjS patients (18 females and 1 male) had a positive lip biopsy, while anti-SSA/Ro antibodies were detected in 10/11 and 6/8 of the patients with EGMs and with GFs alone, respectively. ESSDAI value ranged from 7 to 55 in patients with EGMs (median 17), and from 0 to 2 in patients with GFs alone (median 1).

In both types of patients, the functional analysis of the two transcriptomes showed a large number (> 1000) of modulated genes that are involved in the well-known pathological processes of SjS, i.e., apoptosis, inflammatory response, immune response, type I and type II interferons, and Toll-like receptors signalling.

Genes modulated only in patient with EGMs showed a significant enrichment of the biological processes associated with immune response (79% of all enriched processes) and, namely, of the molecular pathways related to B cell activation. The analysis of the transcripts expressed only in patients with GFs alone showed instead a preponderant enrichment in different metabolic processes (43%) and in processes associated with the central perception of the stimuli. Indeed, genes involved in sensory perception and in nociceptive signals (i.e., ANPEP, TNFRF1, P2RY1, IFNG) were modulated exclusively in patients with GFs alone. The significant differential expression of selected genes in the two SjS subgroups was confirmed by the qRT-PCR analysis.

Conclusions: These data indicate that in SjS patients with GFs alone a dysregulation of pain pathways (namely beta-adrenergic receptor and Notch signalling) may play a role in the development of WP that is common in this subset of patients. The biological mechanisms triggering the activation of these genes remain to be completely clarified.

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THURSDAY, 14 JUNE 2018

How monogenetic autoinflammatory diseases help to understand and treat rheumatic diseases

OP0203

SAFETY AND EFFICACY OF INTRAVENOUS ADMINISTRATION OF BONE-MARROW DERIVED MESENCHYMAL STROMAL CELLS IN THERAPY REFRACTORY JUVENILE IDIOPATHIC ARTHRITIS PATIENTS, A PHASE IB/IIA PILOT-STUDY

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Objectives: To compare the total number of adverse events (AE's) before and after mesenchymal stromal cell (MSC) infusion in refractory JIA and to evaluate its effectiveness.

Methods: Single-centre Phase Ib/IIa, open label intervention study in JIA patients previously failing all biologicals registered for their diagnosis. Six patients will receive 2 million/kg intravenous infusions of allogeneic bone-marrow derived MSC. In case of ACR-Ped30-response but subsequent loss of response one and maximal two repeated infusions are allowed.

Results: Six JIA patients with 9.2 years median disease duration, still active arthritis and damage were included. All had failed methotrexate, corticosteroids and median 5 different biologicals. MSC were administered twice in 3 patients. No acute infusion reactions were observed and a lower post-treatment than pre-treatment incidence in AE's was found. The one sJIA patient had again an evolving macrophage activation syndrome, 9 weeks after tocilizumab discontinuation and 7 weeks post- MSC infusion.

Eight weeks after one MSC infusion, 4 patients showed less active joints, 5 patients improved in many clinical parameters and inflammatory parameters decreased in 3/4. After 1 year, we found significantly lower active joint counts,

improved well-being scores, normalised median ESR- and CRP-levels. Inactive disease was reached by 3 patients at 1 year.

Conclusions: MSC infusions in refractory JIA patients are safe, although in sJIA stopping the 'failing' biologic treatment carries a risk of a MAS flare since the drug might still suppress the systemic features. Furthermore, intravenous administration of MSC might be efficacious even in multiple biological-failing JIA patients with damage.

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THURSDAY, 14 JUNE 2018

Joint EULAR – EFIS session: I've got a B in my bonnet

OP0204

DOMINANT B CELL RECEPTOR CLONES IN PERIPHERAL BLOOD PREDICT ONSET OF ARTHRITIS IN INDIVIDUALS AT RISK FOR RHEUMATOID ARTHRITIS – A VALIDATION COHORT

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Background: A phase characterised by the presence of specific autoantibodies and arthralgia's in the absence of clinically evident synovial inflammation often precedes the onset of rheumatoid arthritis (RA). However, only a subset of these *RA-risk* individuals will develop active disease in the short term¹. Recent findings show that dominant B-cell receptor (BCR) clones in peripheral blood can accurately predict imminent onset of arthritis in these *RA-risk* individuals.²

Objectives: To validate the predictive role of BCR clones in peripheral blood in *RA-risk* individuals in a larger cohort.

Methods: The BCR repertoire in peripheral blood was analysed using next-generation BCR sequencing in a prospective cohort study of 129 *RA-risk* individuals from Reade. Like earlier, BCR clones expanded beyond 0.5% of the total repertoire were labelled highly expanded clones (HECs), shortly referred to as dominant BCR clones, and individuals were labelled BCR-positive if peripheral blood at study baseline showed ≥ 5 dominant BCR clones.

Results: We observed that the number of dominant BCR clones was increased in *RA-risk* individuals who developed arthritis within 3 years, compared to *RA-risk* individuals who did not 10.6 ± 5.3 vs 2.2 ± 2.8 (mean $\pm$ SD; $p < 0.0001$). When creating a ROC curve we could replicate that the most optimal cut-off for this test is at ≥ 5 dominant BCR clones in the peripheral blood (figure 1A), dividing the cohort

in 45 BCR-positive individuals and 84 BCR-negative individuals. None of the BCR-clone negative individuals developed arthritis within 36 months. Within the total follow-up of 104 months only 8% of the BCR-clone negative individuals developed arthritis compared to 76% of the BCR-clone positive individuals, resulting in a relative risk of 9.1 (95% CI: 4.4 to 18.8, $p < 0.0001$).

To test whether a higher number of dominant BCR clones correlates with higher risk of arthritis BCR-clone positive individuals were subdivided into three groups: 5–9 HECs ($n=27$), 10–14 HECs ($n=13$) and ≥ 15 HECs ($n=5$). The Kaplan-Meier curve for all groups is shown in figure 1B (logrank test between BCR-clone negative group and positive subgroups: $p < 0.0001$). Having 10 or more HECs corresponded with a positive predictive value of 83% and a negative predictive value of 87% within 3 years. The BCR clonality test clearly added to existing indices of RA risk in *RA-risk* individuals (data not shown).

Abstract OP0204 – Figure 1 Predictive value of dominant BCR clones (A) receiver operating characteristic (ROC) curves for the number of dominant clones, in at-risk individuals (dotted line at 36 months)

Conclusions: In this external validation cohort we could replicate the fact that dominant BCR clones in peripheral blood predict imminent onset of clinical symptoms of RA in seropositive arthralgia patients with high accuracy. Furthermore, a highly significant association correlating a higher number of dominant BCR clones with higher risk was shown. We hope these results will support evaluation of early interventions that prevent onset of arthritis.

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OP0205

APRIL INDUCES A NOVEL SUBSET OF IGA+ REGULATORY B CELLS THAT SUPPRESS INFLAMMATION THROUGH THE EXPRESSION OF IL-10 AND PD-L1

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Background: Regulatory B cells (Bregs) are immunosuppressive cells that modulate immune responses through multiple mechanisms, such as the production of IL-10 and the skewing of T cell differentiation in favour of a regulatory phenotype. However, the signals required for the differentiation and activation of these cells remain still poorly understood. We have already shown that overexpression of the TNF family member A Proliferation-Inducing Ligand (APRIL) reduces the incidence and severity of collagen-induced arthritis (CIA) in mice.