Abstract THU0348 – Table 1. Univariate Cox proportional hazard modelling investigating the association of various parameters and mortality showing that only one modifiable risk factor associated with prognosis (time on dialysis, the longer on dialysis the worse the prognosis) and one non-modifiable (rTp taking place after 2000 associated with better survival). SLE- Systemic Lupus Erythematosus, LN- Lupus Nephritis, ESRF- End Stage Renal Failure, rTp- renal transplantation, PD- Peritoneal Dialysis, HD- Haemodialysis, APLS- Antiphospholipid syndrome, MI- Myocardial Infarction, TIA- Transient Ischaemic Attack.

Factor	P value	HR	95% CI
Time on Dialysis/per month	0.031	1.013	1.001–1.026
Gender/male	0.442	0.038	0.001–161.3
Ethnicity	0.987	0.995	0.537–1.844
Age at SLE diagnosis	0.552	1.021	0.953–1.094
Age of LN	0.941	1.003	0.920–1.092
Age at rTp	0.431	1.026	0.963–1.092
Dialysis PD (vs HD)	0.764	0.706	0.073–6.862
Time between LN and Dialysis	0.540	0.999	0.994–1.003
LN Duration before Dialysis	0.152	1.066	0.977–1.164
Type IV LN	0.398	2.533	0.294–21.82
Dialysis Decade	0.712	0.872	0.420–1.807
Diabetes Mellitus	0.561	0.038	0.001–2319
Hypertension	0.323	0.329	0.360–2.987
Dyslipidaemia	0.905	0.872	0.092–8.234
APLS	0.508	0.036	0.000–672.6
Cardiac disease (MI, stroke, TIA)	0.873	1.071	0.463–2.476
Donor source living	0.353	0.459	0.089–2.372
Graft Failure post rTp	0.314	2.073	0.501–8.567

exposed to glucocorticoids. 40% had active renal disease at least once during the study period, and active renal disease was observed in 22% of visits (n=1238 visits). 41% of patients had organ damage at baseline and 14% accrued organ damage (272 damage accrual episodes in 250 patients). Active renal disease was significantly associated with damage accrual; after adjusting for confounders, patients with active renal disease were 66% more likely to accrue organ damage compared to those without active renal disease (adjusted hazard ratio=1.66 (95% CI: 1.26, 2.19), p-value<0.01 (table 1). High cumulative GC and age were also significantly associated with damage accrual.

	Univariable Cox regression analysis			Multivariable Cox regression analysis		
	HR	(95% CI)	p-value	HR	(95% CI)	p-value
Age at baseline (years)	1.02	(1.01,1.03)	<0.01	1.02	(1.01,1.03)	<0.01
Asian ethnicity	0.74	(0.52,1.05)	0.09	0.72	(0.50,1.04)	0.08
Cumulative glucocorticoid (GC) categories						
No GC	1.00	(1.00,1.00)		1.00	(1.00,1.00)	
Low GC (≤median PNL)	1.42	(0.94,2.14)	0.1	1.47	(0.97,2.23)	0.07
High GC (>median PNL)	1.51	(1.04,2.18)	0.03	1.46	(0.99,2.16)	0.05
Baseline organ damage present	1.56	(1.22,2.00)	<0.01	1.27	(0.97,2.23)	0.09
Active lupus nephritis	1.66	(1.29,2.14)	<0.01	1.66	(1.26,2.19)	<0.01

Conclusions: Active LN is an independent risk factor for damage accrual in SLE. The concomitant independent association of GC exposure with damage accrual suggests non-GC treatments to reduce active LN are needed to reduce damage burden in SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4328

THU0351

SUSCEPTIBILITY TO CEREBRAL ISCHEMIA IN EARLY LUPUS PATIENTS: A PILOT STUDY OF CO-REGISTRATION WITH CONVENTIONAL BRAIN MRI, DIFFUSION- AND PERFUSION-WEIGHTED IMAGING

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Background: Conventional brain Magnetic Resonance Imaging (cMRI) has a limited usefulness in patients with early diagnosis of Systemic Lupus Erythematosus (SLE), showing not specific abnormalities in up to half of the patients. No data are available about cMRI combined with advanced MRI techniques in early SLE patients.

Objectives: To evaluate differences between early SLE patients, even without overt neuropsychiatric (NP) manifestations, and healthy controls (HCs) in a mono-centric cohort, using data derived from cMRI, diffusion-weighted imaging (DWI) and perfusion-imaging (PWI).

Methods: Patients referred to a single tertiary rheumatologic centre with early diagnosis of SLE (less than 24 months), aged less than 55, were consecutively enrolled (01/05/2013–31/12/2017) and imaged with cMRI, DWI and PWI (1.5 Tesla Philips "Signa Achieva" scanner). Data were analysed with a semi-automated measuring system (Diffusion/Perfusion Project Suite, developed in Multiple Sclerosis patients) to co-registrate apparent diffusion coefficient (ADC), cerebral blood flow (CBF) and volume (CBV), mean transit time (MTT) in normal appearing grey (NAGM) and white matter (NAWM), deep GM (putamen, pallidus, caudate, thalamus) and lesions. Demographic, clinical, serological and treatment information were collected as well as NP events at baseline attributed to SLE according to a validated algorithm. Statistical analysis were performed by comparing median (interquartile range, IQR) values for skewed variables between SLE and HCs and with quantile regression adjusted for cardiovascular comorbidities (hypertension, diabetes, previous coronary heart disease, hyperlipidaemia, obesity).

Results: 30 patients with early SLE (mean age 37.0 years, standard deviation SD 10.7, 27 females) and 8 HCs (mean age 40.6, SD 11.2, 6 females) were enrolled. MRI was performed after a mean period of 259 days from diagnosis; mean (SD) Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2k) was 8.87 (3.85) while mean (SD) Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) was 0.40 (0.72); 3 patients were classified as NPSLE at diagnosis. Median (IQR) values of ADC in NAGM and NAWM were 1.15 × 10⁻³ mm²/s (1.12–1.16) and 0.86 (0.85–0.88) in SLE, 1.28 (1.16–1.33) and 0.97 (0.87–0.98) in HCs respectively (table 1). After adjusting for comorbidities, median differences between ADC values remained significant (p<0.001). SLE patients had lower median ADC values at bilateral putamen and pallidus. No differences were found in perfusion parameters in all the regions of interest (ROI) and lesions. A trend towards lower CBV and CBF and higher MTT values for NAGM-NAWM in NPSLE compared to non-NPSLE was found.

Abstract THU0351 – Table 1. Differences in diffusion and perfusion parameters at normal appearing GM and WM level in SLE patients and HCs.

ROI	NAGM ADC	NAWM ADC	NAGM CBF	NAWM CBF	NAGM CBV	NAWM CBV	NAGM MTT	NAWM MTT
SLE (30), median (IQR)	1.15 (1.12-1.16)	0.86 (0.85-0.88)	37.09 (30.97-47.21)	29.42 (26.00-37.48)	2.43 (2.20-2.58)	1.95 (1.80-2.26)	4.31 (3.80-5.23)	4.87 (4.12-5.85)
HCs (8), median (IQR)	1.28 (1.16-1.33)	0.97 (0.87-0.98)	33.89 (25.38-47.79)	26.54 (20.16-39.79)	2.57 (2.19-3.07)	2.11 (1.77-2.54)	5.11 (4.11-6.18)	5.78 (4.58-6.72)
p	0.004	0.009	0.591	0.519	0.283	0.452	0.123	0.124

Unit of measurement: ADC (x10⁻³mm²/s); CBF (ml/100g/min); CBV (ml/100g); MTT (s).

Conclusions: Lower ADC values in normal appearing GM and WM in early SLE patients could reflect susceptibility to cerebral ischemia, partially confirmed analysing perfusional data in NPSLE patients. Further prospective studies with higher sample size are necessary to confirm these findings.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5702

THU0352

ASSOCIATION BETWEEN MEMORY B-CELLS AND PHENOTYPIC FEATURES OF SJÖGREN'S SYNDROME

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Background: B-cell disturbances are a hallmark of pSS and play a pivotal role in the disease pathogenesis and clinical evolution, and may as well have a potential role in diagnosis. In pSS, an increase of the naïve subset and a decrease of memory B-cells have been reported. A decreased frequency of memory cells has also been identified in patients with Sicca syndrome without criteria for pSS.

Objectives: Our study aims to evaluate the distribution of B-lymphocyte subpopulations in pSS and Sicca patients and to establish cut-off points for pSS classification in relation to healthy controls. Moreover, we aim to evaluate the relation between lymphocyte subpopulations and phenotypic features in pSS.

Methods: Fifty-seven pSS patients, 68 non-Sjögren Sicca patients and 24 healthy controls were included. Circulating B-cell frequencies were determined by flow cytometry, and the naïve and memory (switched and unswitched) subsets were characterised based on surface marker expression of the following monoclonal antibodies: CD19, CD24, CD27, Anti-IgD and Anti-IgM.

Kruskal-Wallis test was applied for groups' comparison. ROC curves were used to establish cut-off points in the B-cells subset levels and to estimate corresponding sensitivity and specificity. Data analysis was performed with R software.

Results: Absolute numbers of lymphocytes in pSS were lower compared to controls, with Sicca presenting intermediate levels.

Significant differences were found between pSS and controls in absolute counts of all memory populations: total memory (TMem) (CD19⁺CD27⁺), switched (SwM) (CD19⁺IgD⁺CD27⁺) and unswitched memory (UnSwM) (p<0.001 for all). Comparing pSS with controls, we found lower percentages of TMem in patients (p=0.078) and more significant differences in the UnSwM subset (p=0.043). Percentages of memory B-cells in Sicca were not significantly different from pSS and controls. Absolute memory B-cells numbers in Sicca were intermediate between those of pSS and controls.

Through ROC curves, the B-cell subsets that better discriminate between pSS and controls were TMem and SwM. A cut-off of equal to 58 TMem cells/μl yielded a specificity of 0.88 and a sensitivity of 0.60 for pSS, and was met by 59.6% of pSS, 12.5% of controls and 38.8% of Sicca, and a cut-off of equal to 23.5 SwM cells/μl yielded a specificity of 0.88 and a sensitivity of 0.54 and was met by 54.4% of pSS, 12.5% of controls and 37.3% of Sicca.

pSS patients with lower values than the established cut-off points had longer disease duration, higher disease activity (ESSDAI), and were more likely to present auto-antibodies and positive biopsy. Several Sicca patients also presented memory B-cell subsets counts lower than the pSS cut-off, but no consistent differences in clinical profile were identified.

Conclusions: Decreased numbers of memory B-cell subsets clearly discriminate pSS from healthy controls. Lower memory B-cells counts are associated with more active pSS disease profile. It remains to be clarified whether Sicca patients with decreased memory B-cells represent pSS and if B-cell profiling could help in the diagnosis of pSS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5717

THU0353

LUNG ULTRASOUND OF PLEURAL IRREGULARITIES (PI-US) IN PRIMARY SJÖGREN'S SYNDROME (PSS)-ASSOCIATED INTERSTITIAL LUNG DISEASE (ILD): CLINICAL, FUNCTIONAL, RADIOGRAPHIC AND ULTRASONOGRAPHIC SHORT-TERM FOLLOW-UP

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Background: Ultrasound of Pleural Irregularities (PI-US) has recently been suggested as a useful tool for the diagnosis and the assessment of interstitial lung disease (ILD) in primary Sjögren's Syndrome (pSS). However, no data are available regarding its role in the post-therapy evaluation of pSS-ILD.

Objectives: Aim of this study was to describe the post-therapeutic changes of the pleural profile in a monocentric cohort of pSS-ILD patients analysing clinical, functional, US and radiographic features.

Methods: Eighteen patients with pSS-ILD were included in the study. PI-US, HRCT and pulmonary function test (PFT) were performed in each patient at baseline. In 15/18 patients who had been treated according to international guidelines for ILD, clinical assessment, PFT and PI-US were repeated after 6 months. PI-US was performed by a single operator using a MyLab-25 (Esaote), 10 MHz, 5 cm linear probe. PI was defined as the loss of normal hyperechoic linear pleural contour

(score 0–2: normal, minimal and major changes at each intercostal space). PI-US total score represented the sum of partial scores assigned to 6 lung fields (2 for the anterior, 2 for postero-superior and 2 for postero-inferior chest surface). HRCT- abnormal findings, distinguishing C-NSIP, F-NSIP and UIP pattern, were quantified using the Warrick score system.

Results: Eighteen pSS-ILD patients (14 F:4 M, mean age=68.8±9.9 years) were included in the study. The median PI-US score was 45 (range 25.5–73.5). Both PI-US total score and partial postero-inferior PI-US score strongly correlated with the Warrick HRCT score (r=0.813, p=0.000 and r=0.914, p=0.000) and inversely correlated with FVC (r=-0.849, p=0.000 and r=-0.836, p=0.000), TLC (r=-0.895, p=0.000 and r=-0.829, p=0.000), and DLCO (r=-0.953, p=0.000 and r=-0.883, p=0.001). Both PI-US score and PI-US of the poster-inferior field directly correlated with FEV1/SVC (r=0.701, p=0.004 and r=0.619, p=0.01) and with FEV1/FVC (r=0.600, p=0.02 and r=0.501, p=0.05). After 6 months of therapy, 15 patients (12F:3M, mean age 65.3 years) presenting at HRCT different ILD pattern distributions (4 C-NSIP, 7 F-NSIP, 4 UIP), were re-evaluated after appropriate medical treatment. Out of these 15 patients, 5 had been treated with glucocorticoids (GC) alone, 2 with azathioprine, 4 with hydroxychloroquine, 2 with Mycophenolate Mofetil, 1 with Rituximab and 1 with abatacept. Clinical, radiographic and functional evaluation showed stability of all parameters in the majority of the patients (13/15), maintaining unchanged the correlations with PI-US scores. Moreover, 2/15 patients with active C-NSIP pattern, showed a significant improvement in clinical, radiographic and functional parameters. In these patients a significant reduction of the PI-US scores was also observed (PI-US score from 22 to 10 and from 57 to 30).

Conclusions: This study confirms the usefulness of PI-US evaluation for the diagnosis and assessment of pSS-ILD, demonstrating a strong correlation between PI-US and both HRCT findings and PFT. Furthermore, the significant reduction of PI-US score in patients with clinical, radiographic and functional improvement suggests that this tool may play a role in the follow-up of treated patients with active pSS-ILD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5955

THU0354

IMPACT OF BIOLOGIC THERAPY IN SJÖGREN'S SYNDROME PATIENTS WITH OVERLAPPING AUTOIMMUNE DISEASES OR EXTRAGLANDULAR MANIFESTATIONS. A SYSTEMATIC REVIEW OF LITERATURE

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Background: Treatment of Sjögren's syndrome (SS) has traditionally focused on conventional synthetic DMARDs (csDMARDs), with encouraging evidence on the benefit of biologic therapies emerging, mainly for treatment of SS extraglandular manifestations. Overlapping autoimmune diseases in SS are poorly studied; yet evidence primarily from case reports suggest a beneficial effect with biologics.

Objectives: To systematically review the literature on the treatment of SS with biologics, taking a focus on case reports and overlapping autoimmune conditions or extraglandular manifestations (defined here as those described in the EULAR SS disease activity index - ESSDAI).

Methods: A literature review was performed independently by two reviewers, using Pubmed and the following search terms: "Sjögren" or "Sjögren's" AND any of the following: "biologics", "Etanercept", "Adalimumab", "Infliximab", "Golimumab", "Certolizumab", "Tocilizumab", "Abatacept", "Rituximab", "Belimumab", "Secukinumab", "Ustekinumab" and "Anakinra". Inclusion criteria were: articles in English; published until January 2018; case reports of patients with primary or secondary SS. Initial screening was based on title/abstract, followed by full-text review for articles fulfilling inclusion criteria. For articles written in a different language, information was obtained from abstract if available, otherwise excluded. Concordance in article screening was 95% across the two reviewers. Data extraction focused on reporting overlapping autoimmune diseases and extraglandular manifestations, treatment and response data.

Results: Out of 679 papers screened, 39 articles were included. 22 overlapping autoimmune conditions were reported in 22 SS patients (table 1). Most of the patients were treated with Rituximab (63.6%), while TNF-inhibitors (22.7%), Tocilizumab (9.1%) and Ustekinumab (4.5%) were also used. Concurrent treatment with csDMARDs and steroids was used in 28.6% and 42.9% of the cases, respectively. 61.9% and 13.6% of the patients were csDMARDs- and biologic- experienced, respectively. Good response of overlapping condition was seen in 86.4% of them, while in 13.6%, control or partial response was reported. Although, most of the studies do not mention the effect of biologic treatment on SS, general