Table 1. “Classical” and “Extra-criteria” APS clinical manifestations of each group (considering solely patients with a confirmed diagnosis of APS).

	Group 1: isolated aPS/PT+ IgG/IgM (16)	Group 2: isolated aβ2GPI+ IgG/IgM (20)	Group 3: aPS/PT+ and aβ2GPI+ IgG/IgM (24)	Group 4: aPS/PT+ and/or aβ2GPI+ IgM low titres (15)
APS clinical manifestations				
Thrombosis (Y/N), n (%)	14 (87,5%)	16 (80%)	21 (87,5%)	13 (86,6%)
N of thrombotic events	21	23	36	15
Arterial thrombosis (Y/N), n (%)	10 (62,5%)	9 (45%)	14 (58,3%)	11 (73,3%)
Arterial events, n	13	10	21	12
Venous thrombosis (Y/N), n (%)	6 (37,5%)	10 (50%)	11 (45,8%)	3 (20%)
Venous events, n	9	13	15	3
Pregnancy morbidity, n (%)	3 (18,8%)	4 (20%)	3 (12,5%)	2 (13,3%)
Recurrent thrombosis (Y/N), n (%)	3 (18,8%)	3 (15%)	7 (29,1%)	0
Livedo reticularis, n (%)	1 (6,2%)	1 (5%)	4 (16,6%)	0
Thrombocytopenia, n (%)	4 (25%)	4 (20%)	6 (25%)	2 (13,3%)
Valvular, n (%)	1 (6,2%)	0	2 (8,3%)	0
Peripheral artery disease, n (%)	0	3 (15%)	4 (16,6%)	0
Diffuse alveolar hemorrhage, n (%)	0	0	1 (4,1%)	0

Figure 1. Graphical representation of the differences between TGA and LA profiles between groups.**Disclosure of Interests:** None declared**DOI:** 10.1136/annrheumdis-2021-eular.2341

POS0173

METABOLOMIC PROFILING AND SYMPTOM BURDEN IN BLACK WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Black individuals with systemic lupus erythematosus (SLE), who are predominantly women, have disproportionately poorer health outcomes across the trajectory of their disease including increased mortality, higher symptom burden, and poor quality of life than non-Hispanic Whites. The heterogeneity of immunopathology and biochemical complexity of SLE create major knowledge gaps around the mechanisms of disease and differences in SLE symptom

expression. Metabolomics may reveal biochemical dysregulation that underlies SLE symptoms and provide novel metabolic targets for precision symptom interventions.

Objectives: We conducted untargeted metabolomic plasma profiling of Black females with SLE and Black female non-SLE controls to gain insight into metabolic disturbances associated with SLE.

Methods: We analyzed blood specimens collected from 23 Black female patients with diagnosis of SLE during a routine outpatient rheumatology visit and from 21 Black female non-SLE controls whose data were collected as part of another study of obese caregivers. Data collection for both cases and controls was completed with harmonized protocols. Clinical data for cases were obtained via chart review and both cases and controls completed identical, reliable and valid measures of fatigue, depression, anxiety, and sleep disturbance. A commercial metabolomics analysis company within the US conducted untargeted metabolomics on the 44 plasma samples using ultrahigh performance liquid chromatography/tandem mass spectrometry along with metabolite identification and quantification to examine differences between SLE/non-SLE groups.

Results: All SLE subjects met 2019 EULAR/ACR criteria (Aringer et al., 2019). SLE subjects were significantly ($p < .05$) younger (42.5 ± 12.2 vs. 63.2 ± 6.4), had a lower BMI (30.3 ± 9.4 vs. 34.9 ± 4.1), and greater co-morbidities (2.3 ± 1.3 vs. 1.1 ± 1.3) than non-SLE controls. SLE subjects reported higher symptoms than controls across all measures, but differences were not statistically significant. Metabolomics analysis revealed 290 biochemicals that were statistically significant ($p \leq .05$) between SLE and non-SLE groups. Random Forest analysis had a predictive accuracy of 91% in differing between the two groups using out-of-bag sampling. Significant metabolic differences between groups were noted in biochemicals associated with glycolysis, the TCA cycle (see Table 1), fatty acid metabolism, branched chain amino acids, sterol levels, heme catabolism, and potential markers of renal impairment. Overall, the differences would suggest reduced energy production among SLE patients compared to controls.

Table 1- Comparison SLE (n= 23) and No SLE Subjects (n=21) on Biochemicals in the TCA Cycle

Pathway	Metabolite	SLE/ No SLE log ₂ fold change	p-value	FDR q-value
TCA Cycle	citrate	0.82	0.0005	0.008
	aconitate [cis or trans]	0.65	< 0.0001	0.001
	alpha-ketoglutarate	0.74	0.0017	0.017
	succinylcarnitine (C4-DC)	0.94	0.3558	0.362
	succinate	0.75	0.0001	0.003
	fumarate	0.64	0.0002	0.004
	malate	0.73	0.0149	0.057
	citraconate/glutamate	1.46	0.6843	0.507

Note: SLE= systemic lupus erythematosus. Welch's Two sample t-test used to compare groups. FDR= False discovery rate. Green color indicates value for SLE group significantly lower than non-SLE controls.

Conclusion: Black women with SLE had biochemical profiles consistent with reduced energy production which has implications for the high burden of fatigue and other symptoms in this population. Future work with larger sample sizes should involve integrating symptom and metabolomics data to identify potential biomarkers of symptom burden.

References: Aringer, M., Costenbader, K., Daikh, D. et al. (2019). 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Ann Rheum Dis*, 78,1151-1159.

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POS0174 IMMUNOPHENOTYPE OF SJÖGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IDENTIFIED TWO ENDOTYPES WITH POTENTIAL THERAPEUTIC IMPLICATIONS

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Background: Primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE) are chronic autoimmune rheumatic diseases (ARDs) that share a strong female gender bias, as well as genetic, clinical and serological characteristics. Although significant progress has been made in improving treatment and patient related outcomes in pSS and SLE, there is a need for improved early diagnosis, adequate therapy monitoring, treatment of refractory manifestations and strategies to address co-morbidities. However, the results of many clinical trials are disappointing, and nobiologic treatments are licensed in pSS, while few are available for SLE patients with refractory disease.

Objectives: Identifying shared immunological features between patients with pSS and SLE that could lead to better treatment selection using a stratification approach.

Methods: Immune-phenotyping of 29 immune-cell subsets in peripheral blood from patients with pSS (n=45), SLE (n=29) and secondary SS associated with SLE (SLE/SS) (n=14) with low disease activity or in clinical remission, and sex-matched healthy controls (n=31), was performed using flow cytometry. Data were analysed using logistic regression and multiple t-tests and supervised machine learning (balanced random forest-BRF, sparse partial least squares discriminant analysis-sPLS-DA). Patients were stratified by k-means clustering. Clinical trajectories were analysed over 5 year follow-up.

Results: Comparing the immune profile of pSS and SLE patients using a variety of statistical and machine learning (ML) approaches, identified very few statistically significant differences between the two cohorts despite patients having a different clinical presentation and diagnosis. Thus, we hypothesised that immune-based subtypes could be shared between pSS, SLE and SLE/SS patients. Unsupervised k-means clustering was applied to the immunological features of the combined patient cohorts and two distinct patient endotypes, were identified: Group-1 (n=49; pSS=24, SLE=19, SLE/SS=6) and Group-2 (n=39; pSS=21, SLE=10, SLE/SS=8). Significant differences in immune-cell phenotypes across B-cell and T-cell subsets were identified by logistic regression, BRF (AUC=0.9942, assessed by 10-fold cross-validation) and sPLS-DA analysis. Comparison of the multiple analysis approaches identified eight common immune-cell subsets, including total and memory CD4+ and CD8+ T-cell subsets but no B-cell subsets. Using this common immune-signature the stratification between the groups was maintained and slightly improved (AUC=0.9979 and accuracy 96.16%). Interestingly, patients in Group-2 had elevated disease activity measures at baseline and over a 5-year trajectory compared to Group-1. Finally, correlation analysis identified correlations between disease activity markers and the top ranked immune features from the ML models.

Conclusion: The identified immune-cell signatures could reflect the underlying disease pathogenesis that spans diagnostic criteria and could be used to select patients for targeted therapeutic approaches.

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POS0175 ASSOCIATION BETWEEN BIOMARKERS AND THERAPEUTIC PATHWAY IN PATIENTS WITH SLE

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Background: SLE is heterogeneous in clinical presentation, underlying immunology, and response to therapy. Patients with severe or resistant disease receive cyclophosphamide or rituximab. Although effective, late use of these therapies entails cumulative damage.

Emerging predictors of response to rituximab include demographics, IFN-Scores and autoantibodies. For such predictors to change treatment strategy we need to understand their association with the effectiveness of other therapeutic options at earlier decision points.

Prospective studies of treatment pathways are difficult to perform, requiring large populations followed for many years. We therefore investigated this question by analysing retrospective treatment pathways since diagnosis in patients whose biomarker status is subsequently known.

Objectives: To use interferon scores and other markers to;

- [1] identify SLE patients more likely to need escalation of therapy to either rituximab or cyclophosphamide, and
- [2] determine if this occurred sooner than in others.

Methods: In patients with established SLE, attending Leeds SLE clinic, we collected demographics, clinical characteristics and blood at a single timepoint. Two previously validated IFN-Scores[1,2] (IFN-Score A and IFN-Score B) were measured using Taqman. Autoantibodies were measured using immunoprecipitation. Treatment history covering all antimalarials, oral and intravenous immunosuppressants (agent, start and stop dates and reasons) since diagnosis was collected. Univariable and multivariable Cox proportional hazards models were used to test variables as predictors of the primary endpoint: time to cyclophosphamide/rituximab.

Results: 124 patients were included. Follow up since diagnosis was Median (IQR) 37.5 (27.4-52.3) years, total therapies per patient was 3 (1-4), therapies per year was 0.2 (0.1-0.3). 54/124 (44%) patients required cyclophosphamide/rituximab.

Results of Cox regression are shown in the table 1. There was a significant association between high expression of IFN-Score B and requirement for cyclophosphamide/rituximab as well as trends for age in the first quartile (<28 years), IFN-Score A and anti-Sm/U1RNP antibodies. Both age <28 and IFN-Score B retained trends as independent predictors in a multivariable model.

Table 1.

Characteristic	CYC/ RTX=Yes n(%)	CYC/ RTX = No n(%)	Univariable Hazard ratio (95% CI)	Univariable p value	Multivariable Hazard Ratio (95% CI)	Multivariable p value
Age						
-Q1: under 28	22 (71%)	9 (29%)	2.25 (0.99,5.12)	0.054	1.74 (0.95,3.18)	0.074
-Q2: 28 – 38	12 (39%)	19 (61%)	1.03 (0.41,2.56)	0.949	Not included	Not included
-Q3: 38 – 52	12 (39%)	19 (61%)	1.52 (0.62,3.72)	0.360	Not included	Not included
-Q4: over 52	8 (26%)	23 (74%)	reference	reference	Not included	Not included
Ethnicity						
-Caucasian	42 (48%)	46 (52%)	1.17 (0.58,2.35)	0.660	Not included	Not included
-AfroCaribbean, South Asian, East Asian, Other	10 (36%)	18 (64%)	reference	reference		
IFN Score A, mean (SD)	-2.59 (-2.67)	-3.84 (-2.71)	1.10 (0.98,1.24)	0.113	Not included	Not included
IFN Score B, mean (SD)	-2.61 (-1.16)	-3.53 (-1.76)	1.31 (1.05,1.64)	0.017	1.23 (0.98,1.55)	0.079
Anti-Sm/U1RNP Ab positive	17 (61%)	11 (39%)	1.50 (0.84,2.67)	0.171	Not included	Not included
Anti-Ro(60) Ab positive	14 (45%)	17 (55%)	0.88 (0.47,1.65)	0.686	Not included	Not included