Table . Comparison of patients undergoing 2nd RB according to development of renal failure

	Renal failure (n=26)	No renal failure (n=69)*	p
Total FU (years), mean (SD)	21 (10.4)	16.5 (9.39)	0.002
SCr (mg/dl) at 2° RB, mean (SD)	1.7 (1)	0.98 (0.35)	0.001
Proteinuria (g/24h) at 2° RB, mean (SD)	4.7 (3.9)	2.99 (2.63)	0.022
Class IV and IV+V at 2° RB, %	76.9	54.5	0.07
Hypertension at onset, %	84.6	32.4	<0.001
HCQ intake at 2° RB, %	9.5	52	<0.001
Glucocorticoids at 2° RB %	84	87	ns
Immunosuppressants at 2° RB %	40	58	ns
AI at onset, mean (SD)	7.14 (3.95)	7.02 (3.86)	ns
AI at 2° RB, mean (SD)	5.37 (4.12)	4.02 (3.71)	ns
CI at onset, mean (SD)	2.05 (1.88)	1.56 (1.64)	ns
CI at 2° RB, mean (SD)	3.87 (3.08)	3.52 (2.16)	ns
Years between 2° RB and end of FU, mean (SD)	14.1 (10.5)	9.3 (8.84)	ns

*Group 1 excluded

RB, renal biopsy; AI, activity index; CI, chronicity index; SCr serum creatinine; FU, follow-up; SD, standard deviation.

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THU0250 URINE AND SERUM S100 PROTEINS ASSOCIATE WITH LUPUS NEPHRITIS AND RESPONSE TO TREATMENT

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune/inflammatory disease. Approximately 30% of SLE patients develop lupus nephritis (LN) that affects treatment and prognosis. Easily accessible biomarkers do not exist to reliably predict renal disease[1]. Recently, calcium-binding S100 proteins have been suggested as biomarkers in systemic inflammatory conditions, including SLE[2,3].

Objectives: The MASTERPLANS Consortium aims to identify indicators of treatment responses in SLE. This study tested the applicability of S100 proteins in serum and urine as biomarkers for disease activity and response to treatment with rituximab in LN.

Methods: S100A8/A9 and S100A12 proteins were quantified in the serum and urine of 243 SLE patients from the BILAG-BR study and 48 matched controls using MSD technology to determine whether they perform as biomarkers for active LN (n=85 SLE patients) and/or may be used to predict response to treatment with rituximab. Renal disease activity and response to treatment was based on BILAG-BR scores and changes in response to treatment[4,5].

Results: Serum S100A12 (p<0.001), and serum and urine S100A8/A9 (p<0.001) are elevated in SLE patients. While serum and urine S100 levels do not correlate with global SLE disease activity (SLEDAI), levels in urine and urine/serum ratios are elevated in SLE patients with active LN (S100A8/A9: urine p>0.005, urine/serum p<0.05; S100A12: urine p<0.05, serum/urine p<0.005). S100 proteins perform better as biomarkers for active LN involvement in SLE patients positive for anti-dsDNA antibodies. Lastly, binary logistic regression and AUC analysis suggests the combination of serum S100A8/A9 and S100A12 to predict response to RTX treatment in LN after 6 months.

Conclusion: Findings from this study show promise for clinical application of S100 proteins to predict active renal disease in SLE and response to treatment with rituximab. Significantly overlapping values between groups currently prohibit the definition of cut-off values and prospective studies are required to validate findings.

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THU0251 IMMUNOPHENOTYPIC CLUSTERS OF SLE PATIENTS REVEAL SUBGROUPS WITH SEVERE DISEASE RESISTANT TO CONVENTIONAL THERAPY

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Background: Biomarkers to predict response to rituximab include plasmablasts and, in the current MASTERPLANS consortium, Sm/U1RNP antibodies and high expression of IFN Score B (a subset of interferon-stimulated genes that predict more clinical outcomes than a classic interferon signature). The relationships amongst these biomarkers and their association with response to conventional therapies are less well described.

Objectives: To analyse the inter-relationships amongst immune biomarkers in two independent SLE cohorts in association with disease activity and stage of therapeutic pathway.

Methods: CONVAS is a cohort of unselected SLE patients; data available include current and historic disease activity, use of biologic therapy, flow cytometry, gene expression (IFN Score A and IFN Score B), and immunoprecipitation for autoantibodies (n=91). BILAG-BR is a British registry study for SLE patients commencing biologics; data available include current and historic disease activity, gene expression (IFN Score A and IFN Score B) and immunoprecipitation for autoantibodies (n=112). In both cohorts, biologics were only prescribed to patients with active disease (BILAG 1 x A or 2 x B) and failure of either cyclophosphamide or mycophenolate. Given the mixture of continuous and categorical variables, data were clustered using Gower distance and Partitioning Around Medioids. K was chosen using silhouette coefficient and clusters visualised with t-Distributed Stochastic Neighbor Embedding (t-SNE).

Results: There were 6 clusters. In rituximab-naïve patients:

1. Sm/U1RNP+, Ro60-, highest IFN Score A, low $CD4^+$ T cells, low NK cells, high plasmablasts
2. Sm/U1RNP-, Ro60+, medium IFN Score A, low $CD4^+$ T cells, high NK cells, high plasmablasts
3. Sm/U1RNP-, Ro60-, lowest IFN Score A, high $CD4^+$ T cells, low NK cells, low plasmablasts

Other antibody subtypes and flow cytometric markers did not improve the accuracy of clustering. In rituximab-treated patients, 3 equivalent clusters for antibody subtypes and IFN Score A were observed but differentiated due to flow cytometry findings, as expected after rituximab treatment. Overall, the patients in the cluster defined by Sm/U1RNP antibodies and high IFN Score A were notable for a higher rate of prior disease activity in the renal, neurological and general BILAG domains (Table 1).

Table 1 : Clinical features in unselected SLE patients (CONVAS)

System affected (ever)	Sm/U1RNP & high IFN Score A (n=27)	Other (n=92)	*p* value
General	14/27 (52%)	24/92 (26%)	0.02
Mucocutaneous	23/27 (85%)	73/92 (79%)	0.50
Neuro	10/27 (37%)	17/92 (19%)	0.04
MSK	25/27 (93%)	83/92 (90%)	0.71
Cardiorespiratory	9/27 (33%)	20/92 (22%)	0.22
Renal	12/27 (44%)	15/92 (16%)	0.005
Haematology	25/27 (93%)	67/92 (73%)	0.03