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SAT0251 PREDICTING AND MANAGING PRIMARY AND SECONDARY NON-RESPONSE TO RITUXIMAB USING B-CELL BIOMARKERS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Rituximab (RTX) is the most commonly used biologic for the treatment of SLE. However, there is are no clinically applicable predictors of response, which is of particular importance in this heterogeneous disease with other biologics being restricted to certain subgroups.
Objectives: To assess factors associated with primary and secondary non-response to RTX in SLE in order to develop more targeted and effective B-cell therapy.
Methods: A prospective observational study was conducted in 125 SLE patients treated with RTX in Leeds for over 12 years. A major clinical response was defined as improvement of all active BILAG-2004 domains to grade C/better and no A/B flare. Partial responders were defined by 1 persistent BILAG B. B-cell subsets were measured using highly sensitive flow cytometry. Predictors of response were analysed using logistic regression analysis.
Results: 117 patients had evaluable data. In cycle 1 (C1), 96/117 (82%) achieved BILAG response [major=50%,partial=32%]. In MVA, younger age & B-cell depletion at 6 weeks increased the odds of major response (Table 1). Complete depletion was predicted by normal complement & lower pre-RTX plasmablasts. 77 (with data on 72) C1 responders were retreated on clinical relapse. Of these, 61/72 (85%) responded in C2. Of 11 C2 non-responders, 9 met secondary non-depletion non response (2NDNR) criteria, as defined by *infusion reaction & defective depletion (*incidence=12%) and tested positive for anti-RTX antibodies. Lack of concomitant immunosuppressant & higher pre-RTX plasmablasts predicted 2NDNR.
Conclusions: B-cell subsets should be monitored in the routine care of SLE patients receiving RTX and should aim to achieve complete depletion. About 1 in 8 SLE patients lose depletion on repeat cycles and this is associated with anti-RTX antibodies. Clinical trials using more intensive RTX treatment regimens in those predicted not to completely deplete, or alternatively use of humanised anti-CD20mAbs are likely to increase clinical response rates to B-cell depleting agents.
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SAT0252 THE NUMBER OF TREG CELLS IN PERIPHERAL BLOOD IN PSS PATIENTS IS DECREASED AND LOW DOSE IL-2 CAN PROMOTE ITS PROLIFERATION

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Background: PSS is a kind of autoimmune disease without clear pathogenesis. Treg cell plays an important role in autoimmune disease. However, opinions about change of amount of Treg cells in peripheral blood in autoimmune disease are various. Besides, the researches mainly focus on RA and SLE but not PSS.
Objectives: To explore the change of the number of Th17 and Treg (CD4+CD25+Foxp3+T cells) cells in peripheral blood in PSS and the effects of low dose IL-2 therapy on the balance of Treg and Th17 cells.
Methods: One hundred and ninety two PSS patients in our department, and 30 healthy controls were put in the research. The amount of Th17 cells and Treg cells were calculated by flow cytometry. Eighty eight in 192 were given low-dose IL-2 (50 WIU/day for 5 days) by hypodermic injection combined with standard therapy which includes glucocorticoid, immune-suppressants, biological agents or combination of them, while others (12 in 69) were given standard therapy only. The amount of these cells were calculated again after therapy.
Results: There was significant decrease in the absolute number of Treg cells and significant increase of the ratio of Th17/Treg cells in PSS patients when compared with healthy controls. There was no significant difference in absolute number of Th17 cells between PSS patients and healthy controls. Further, the number of Treg cells were negatively relative to ESSDAI. Traditional DMARDs had no obvious impact on Treg and Th17 cells. The amount of Treg cells significantly increased after the treatment of IL-2 by 1 week. But there was no significant improvement in clinical manifestations in the short time when comparing combinational treatment of IL-2 and classical drugs with classical therapy. No obvious adverse reactions were observed.

Table 1. Absolute number and percentage of CD4+T subsets in peripheral blood in PSS patients and Healthy controls.

Study Participants	Health	PSS	Untreated PSS
Th17	6.44 (5.10, 8.55)	7.09 (4.05, 11.48)	6.08 (4.30, 12.60)
Treg	36.20 (27.82, 47.02)	28.24 (15.89, 41.36)*	27.30 (17.43, 39.87)*
Th17%	0.96 (0.67, 1.33)	1.26 (0.77, 1.95)*	1.26 (0.86, 1.92)^
Treg%	4.80 (4.19, 6.37)	4.64 (3.10, 6.44)	4.70 (2.52, 6.91)
Th17/Treg	0.18 (0.14, 0.29)	0.27 (0.15, 0.43)*	0.28 (0.15, 0.47)^

Median (range, cells/μl). ^P<0.1, *p<0.05, **p<0.01, ***p<0.0001 vs Healthy controls.

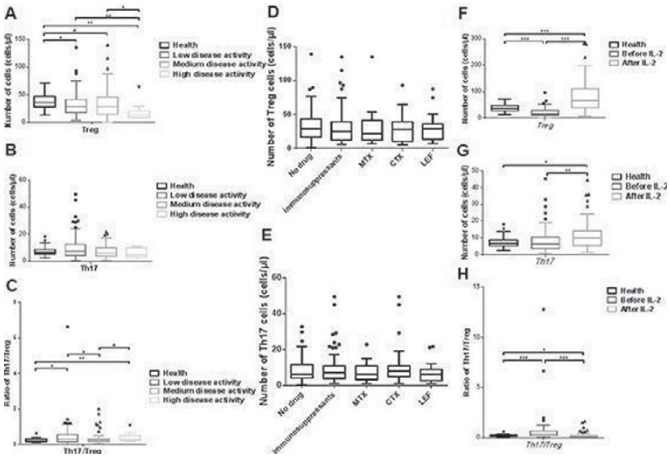

Figure 1

Conclusions: The number of CD4+CD25+Foxp3+T cells in peripheral blood was decreased obviously and was inversely related to ESSDAI. While there was no significant difference of Th17 cells between PSS patients and healthy controls. And there was no correlation between the number of Th17 cells and ESSDAI. So the imbalance of Th17/Treg is due to the decrease of Treg cells not increase of Th17 cell which indicates that the pathogenesis of PSS maybe mainly because of shortage of autoimmune tolerance. Low dose IL-2 therapy can effectively promote proliferation of Treg cells by which low dose IL-2 may induce and restore autoimmune tolerance to benefit disease control.
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Abstract SAT0251 – Table 1

	Non/Partial Response (n=59)	Major Clinical Response (n=58)	UVA OR (95% CI), P-value	MVA OR (95% CI), P-value
Age, mean (SD) years	43 (17)	37 (14)	0.97 (0.95–0.99), p=0.031 per year	0.97 (0.94–0.99), **p=0.037**
White, N (%)	43 (73)	37 (64)	1.53 (0.70–3.34), p=0.292	0.93 (0.34–2.54), p=0.882
Anti-dsDNA, mean (SD) IU/ml	147 (230)	142 (230)	1.00 (0.99–1.00), p=0.913 per unit	1.00 (0.99–1.00), p=0.518
Anti-ENA positivity, N (%)	40 (68)	38 (66)	0.93 (0.42–2.06), p=0.860	1.00 (0.39–2.57), p=1.00
Low C3 and/or C4, N (%)	25 (42)	24 (41)	0.97 (0.46–2.06), p=0.945	1.33 (0.46–3.80), p=0.599
ESR, mean (SD) mm	40 (32)	41 (36)	1.00, (0.99–1.01), p=0.901 per unit	1.00 (0.97–1.00), p=0.349
Concomitant DMARDs,N (%)	41 (69)	35 (60)	0.67 (0.31–1.43), p=0.301	0.39 (0.16–1.00), p=0.051
Global BILAG, mean (IQR)	21 (8)	24 (13)	1.03 (0.99–1.07), p=0.093 per point	1.03 (0.98–1.08), p=0.191
Total B-cell counts x 1000 mean (IQR)	101 (95)	138 (150)	1.00 (1.00–1.01), p=0.169 per unit	1.00 (1.00–1.01), p=0.103
B-cell depletion at 6 weeks, N (%)	29 (49)	39 (68)	2.15 (0.98–4.71), p=0.056	3.44 (1.25–9.48), **p=0.017**