categorically. Furthermore, potentially severe lupus manifestations, such as hemolytic anemia are not scored in SLEDAI.
Objectives: To evaluate the performance of SLEDAI-2K to detect a clinically meaningful change in SLE disease activity.
Methods: Prospective cohort study of SLE patients followed at a tertiary care lupus clinic from January 2014 to December 2016. Consecutive patients fulfilling the ACR'97 and/or the SLICC'12 classification criteria were included. At each outpatient visit, disease activity from the last 30 days was scored in the Physician Global Assessment (PGA) (0–3 cm scale) and in SLEDAI-2k. The association between PGA and SLEDAI-2K at each visit was tested with Spearman's Correlation. A clinically meaningful change in SLE disease activity was defined as difference in PGA $\geq$0.3 cm at follow-up compared to the baseline visit. Performance of change in SLEDAI-2K was tested in two models: against worsening and improvement in PGA $\geq$0.3 cm from baseline using Receiver Operating Characteristic (ROC) curve analysis. Sensitivity, specificity, positive and negative predictive values (PPV, NPV) of SLEDAI-2k to change in PGA was calculated. Statistical significance was set at 0.05.
Results: We included 334 patients (87.1% female, mean age at baseline - 44.8±14.5 years). At baseline, median PGA and SLEDAI-2k score was 0.2 points (range 0–2.5) and 2 points (range 0–19), respectively. Eighty-three patients (24.8%) had a PGA $\geq$0.4 points at baseline. During follow-up of 36 months, 2129 visits were performed. PGA and SLEDAI-2K scores presented a high correlation (rho=0.82, $p<0.0001$) (fig. 1). Reductions in SLEDAI-2K presented in ROC analysis an area under curve (AUC) of 0.697 [95% CI (0.628–0.766), $p<0.0001$] for an improvement in PGA$\geq$0.3. For a worsening of PGA$\geq$0.3 points, increase in SLEDAI-2K presented an AUC of 0.877 [95% CI (0.822–0.932), $p<0.0001$]. Estimated sensitivities, specificities, PPV and NPV are presented in table 1.

Table 1. Performance of Sledai-2K to detect a clinically meaningful change in PGA, using cut-offs of decrease and increase (for a clinical improvement and worsening, respectively) in SLEDAI-2K $\geq$1 and $\geq$4 points

	Δ SLEDAI-2K≥1				Δ SLEDAI-2K≥4			
	Sens.	Spec.	PPV	NPV	Sens.	Spec.	PPV	NPV
Improvement PGA≥0.3	0.7	0.571	0.397	0.825	0.288	0.929	0.622	0.763
Worsening PGA≥0.3	0.725	0.903	0.627	0.936	0.353	0.996	0.947	0.873

Sens: Sensitivity; Spec: Specificity; PPV: Positive predictive value; NPV: Non predictive value.

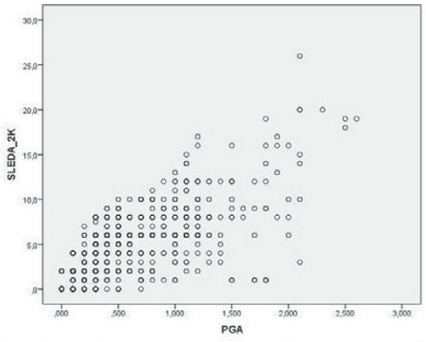

Fig. 1 Scatter diagram showing linear positive correlation between PGA and SLEDAI-2K scores (Spearman's correlation coefficient (rho) = 0.82, p <0.0001).

Conclusions: SLEDAI-2K presents a limited performance in detecting a clinically meaningful change in SLE disease activity, failing to identify more than a quarter of cases with clinically meaningful improvement or worsening. There is a need to optimize SLE disease activity measures.
Disclosure of Interest: None declared
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THURSDAY, 15 JUNE 2017

Joint EULAR - EFIS session: tilting the balance: from disease to tolerance induction

OP0207 B CELL DEPLETION INCREASES REGULATORY T CELLS AND AMELIORATES SKIN AND LUNG FIBROSIS IN A BLEOMYCIN-INDUCED SYSTEMIC SCLEROSIS MODEL MOUSE

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Background: B cells play a critical role in systemic autoimmunity and disease expression through various functions such as cytokine production and induction of other immune cell activation. Recently, some clinical studies have shown that the efficacy of B cell depletion therapy with rituximab, a chimeric monoclonal antibody against human CD20, in systemic sclerosis (SSc) patients. However, it still remains unclear why B cell depletion can be an effective treatment for SSc.
Objectives: The purpose of this study is to assess the role of B cell depletion in SSc. We evaluated the skin and lung fibrosis of bleomycin (BLM)-induced SSc model mice treated with B cell depletion. Furthermore, we investigated the effect of B cell depletion on T cell cytokine profile.
Methods: To generate BLM-induced SSc model mice, 300 μg of BLM was injected subcutaneously into the shaved backs of the C57BL/6 mice every other day for 4 weeks. Anti-mouse CD20 monoclonal antibodies, which can deplete mouse B cells, were also injected every 2 weeks from 2 weeks later starting BLM treatment. After 4 weeks of BLM treatment, skin and lung fibrosis were assessed histopathologically. T cells and B cells were isolated from spleen using magnetic cell sorting system. Purified T cells ($5x10^5$ cells) were cultured with B cells ($5x10^5$ cells) in the presence of phorbol 12-myristate 13-acetate, ionomycin, and anti-CD3/CD28 antibodies. Cytokine expressions in the fibrotic skin and lung were quantified by real-time polymerase chain reaction. Cytokine production of T cells and B cells were analyzed by flow cytometric analysis.
Results: Dermal thickness and lung fibrosis score increased in BLM-treated mice compared with phosphate buffer saline (PBS)-treated control mice. Frequencies of interleukin (IL)-10 producing splenic B cells significantly decreased in BLM-treated mice compared with PBS-treated mice, while IL-6 producing B cell frequencies increased. Moreover, interferon (IFN)-γ, IL-4, or IL-17 producing T cell frequencies increased in BLM-treated mice. There were no significant differences in regulatory T cell frequencies between BLM-treated and PBS-treated mice. B cell depletion increased IL-10 producing regulatory T cell frequencies in BLM-treated mice. By contrast, frequencies of IFN-γ, IL-4, or IL-17 producing T cells were significantly decreased by B cell depletion in BLM-treated mice. In addition, fibrogenic cytokine mRNA expression levels of skin and lung decreased in BLM-treated mice with B cell depletion. To assess the role of B cells on T cell cytokine production, purified splenic B cells from BLM- or PBS-treated mice were cultured with naive T cells. T cells which were cultured with B cells from BLM-treated mice produced greater amounts of INF-γ, IL-4, and IL-17 than those cultured with PBS-treated mouse B cells. By contrast, B cells from PBS-treated mice induced a higher amount of IL-10 production from T cells than those from BLM-treated mice.
Conclusions: B cell depletion inhibited skin and lung fibrosis in BLM-treated mice. Furthermore, B cell depletion increased regulatory T cell frequencies in BLM-treated mice, though INF-γ, IL-4, and IL-17 producing T cell frequencies were decreased by B cell depletion. These results suggest that B cell depletion alters T cell cytokine profile, which results in inhibition of fibrosis in this model.
Disclosure of Interest: None declared
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OP0208 SYNOVIAL TISSUE OF RA PATIENTS IN REMISSION CONTAINS A UNIQUE POPULATION OF REGULATORY MACROPHAGES

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Background: The majority of RA treatments target inflammation or the adaptive immune response. Partial- or non-response is common and only a minority have sustained remission. There is a knowledge gap in understanding the mechanisms that could reinstate synovial homeostasis in RA. Tissue macrophages may have a role in this process; they are present in healthy synovium and aid resolution of the inflammation in experimental models of RA. However, little is known about the regulatory properties of human synovial tissue macrophages.
Objectives: Our hypothesis is that healthy and RA synovium in remission contain macrophages with anti-inflammatory/repair properties and identifying the effector pathways that drive their function could facilitate therapeutic restoration of synovial homeostasis in RA.
Methods: We developed a flow cytometry sorting strategy for harvesting tissue-resident macrophages obtained from digested synovial biopsies of RA patients (n=21, including in remission n=5; and active RA n=16). Cells were labelled with cell lineage-specific antibodies; then macrophages were gated based on their expression of $CD64^{pos}CD11b^{pos}MHCII^{pos}Lineage^{neg}$. The potential homeostatic/repair macrophage was preliminary identified by the presence of CD206 marker. $CD206^{pos}$ and $CD206^{neg}$ macrophages were sorted using a FACS Aria III and RNAseq performed to characterise their functional signature. In some experiment, macrophages were seeded on collagen-coated plates and production of TNFa evaluated.
Results: All synovial tissue macrophages from RA in remission were $CD206^{pos}$ whereas a substantial number of synovial macrophages from active RA tissue were $CD206^{neg}$. Gene expression analyses and functional assays suggest that these populations represent distinct phenotypes in the activation spectrum. $CD206^{neg}$ macrophages have high expression of microRNA-155, which drives production of inflammatory mediators *e.g.* TNFa. In contrast, $CD206^{pos}$ macrophages showed regulatory properties characterised by increased expression of soluble (*e.g. IL10, TGFB*), surface (*e.g. IL4/14R, TGFBR1/2*) and cellular (*e.g. SHIP1, TAM, SMAD2, STAT6*) inhibitors of inflammatory activation, and increased expression of repair markers (*e.g. ARG2 and CCL18*).
Conclusions: We propose therefore that anti-inflammatory/repair macrophages may be present in human synovial tissues in remission representing a hitherto unnoticed regulatory tissue mechanism.