Abstract 102 Table 2 Comparision of the levels of reduced glutathione and lipid peroxidation in Kidney, liver, lung and spleen at 0 month, 6 month pristane treatment and after resveratrol treatment. Values are expressed as Mean±SEM.

		Kidney	Liver	Lung	Spleen
Reduced Glutathione (µmoles/mg protein)	0 month	4.53 ± 0.37	5.71 ± 0.46	9.67 ± 1.35	8.83 ± 2.10
	6 month	2.23 ± 0.37	2.03 ± 0.86	3.21 ± 0.99	4.91 ± 0.91
	Resveratrol	5.13 ± 0.57	5.45 ± 0.21	5.59 ± 0.1	9.88 ± 0.46
Lipid Peroxidation (µmoles MDA/mg protein)	0 month	1.35 ± 0.17	2.34 ± 0.5	1.58 ± 0.52	1.58 ± 0.27
	6 month	7.56 ± 0.78	10.62 ± 1.08	5.01 ± 0.53	6.27 ± 0.48
	Resveratrol	2.78 ± 0.16	4.22 ± 0.53	4.29 ± 0.84	3.74 ± 0.69

Methods Fifty-eight patients were enrolled at initiation of belimumab and followed longitudinally for up to 53 months. Surveillance outcomes included the SLE Disease Activity Index 2000 (SLEDAI-2K), 100 mm Visual Analogue Scales for Physician's Global Assessment (PGA), fatigue, pain and general health, and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI). Assessment of treatment response included the SLE responder index (SRI). B lymphocyte stimulator (BLyS) levels were determined using ELISA.

Results SLEDAI-2K (median baseline score: 8.0; IQR: 4.0–13.8), PGA and corticosteroid use decreased during therapy, and patients reported improvements on fatigue, pain, and general health ($p<0.0001$ for all). SDI scores remained stable ($p=0.08$). Patients with baseline SDI scores>1 showed decreased probability and prolonged time to attain SRI response (HR: 0.449; 95% CI: 0.208–0.967), as did current smokers compared with non-smokers (HR: 0.103; 95% CI: 0.025–0.427). In contrast, baseline BLyS levels≥1.2 ng/mL predicted increased probability and shorter time to attain SRI response (HR: 2.566; 95% CI: 1.222–5.387).

Conclusions Disease activity and corticosteroid usage decreased, patient-reported outcomes improved, and no significant organ damage was accrued during follow-up. Smoking and organ damage predicted reduced treatment efficacy. These findings might contribute to a better selection of patients who are likely to benefit from belimumab.

104 A MASS CYTOMETRY (CYTOF) APPROACH TO STUDY B CELL ALTERATIONS DURING BAFF BLOCKADE TREATMENT WITH BELIMUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and aims Belimumab is a monoclonal antibody that inhibits soluble B lymphocyte stimulator (BLyS, also known as BAFF), approved for the treatment of systemic lupus erythematosus (SLE). Here, we sought to identify B cell alterations during belimumab treatment.

Methods Twenty-three SLE patients treated with belimumab were enrolled. Peripheral blood mononuclear cells were collected and cryopreserved at treatment initiation and at regular follow-up visits for up to 3 years. The samples were simultaneously assayed using mass cytometry. Cell counts were adjusted for total lymphocyte counts.

Results $CD20^+$ B cells decreased over time ($p<0.0001$). We observed a rapid reduction of naïve ($CD19^+CD20^+IgD^+IgM^+CD27^-$) and age-associated B cells ($CD19^+CD20^+CD11c^+CD21^-$) already at the first follow-up visit (month 3), followed by a continuous decrease ($p<0.0001$ for both subsets), while double-negative memory B cells

($CD19^+CD20^+IgD^-CD27^-$) declined significantly first at month 6 ($p=0.033$) and pre-switching B cells ($CD19^+CD20^+IgD^+CD27^+$) showed a trend towards a decrease ($p=0.052$). Plasma cells ($CD138^+CD38^+CD27^+CD19^+CD3e^-CD20^-$) and switched memory B cells ($CD19^+CD20^+CD27^+IgD^-$) remained stable during the study period, as did T cells and monocytes ($p>0.2$). Despite continuously decreasing SLE Disease Activity Index, immunological changes correlated with clinical improvements only during early time points (month 0–3). Interestingly, high baseline B cell counts were predictive of non-attaining Lupus Low Disease Activity State at month 24 (area under the ROC-curve: 0.95).

Conclusions B cell alterations betided in two distinct phases, a rapid early and a gradual late phase. Late clinical improvements might reflect preceding immunological changes, implying that early treatment evaluation and discontinuation might underestimate delayed improvements reflecting the late B cell changes.

105 TOLL-LIKE RECEPTOR 7-, BUT NOT TOLL-LIKE RECEPTOR 9-, MEDIATED INTERFERON-A PRODUCTION FROM PLASMACYTOID DENDRITIC CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and aims Aberrant and persistent production of type I interferon (IFN) is known to play a pivotal role in the pathogenesis of systemic lupus erythematosus (SLE), and plasmacytoid dendritic cells (pDCs) are the major source of type I IFN upon toll-like receptor 7 (TLR7) and TLR9 stimulation. However the respective impacts of TLR7 and TLR9 responses on type I IFN production in SLE has not been addressed.To investigate the precise function of pDCs in SLE patients, we shed light upon the differential regulation of TLR7/9 responses during type I IFN production from pDCs.

Methods PBMCs from SLE patients and healthy controls were analysed in the presence of a TLR7 agonist loxoribine and a TLR9 agonist CpG2216. The IFN-α production in Lin-HLA-DR+CD123+CD11c- pDCs was detected by flow cytometry.

Results We demonstrated that TLR7-mediated IFN-α production were up-regulated and were positively correlated with disease activity, conversely, TLR9-mediated IFN-α production were down-regulated in SLE. The differential regulation of TLR7/9 responses of pDCs was not dependent on expression levels of TLR7/9. Furthermore, *in vitro* experiments revealed that up-regulation of TLR7 response was caused by pre-treatment with type I IFNs, conversely, down-regulation of TLR9 response was caused by pre-treatment with type II IFN.

Conclusions This is the first report demonstrated the differential regulation of TLR7- and TLR9- mediated IFN-α production from pDCs in SLE, namely, caused by priming effects of type I and type II IFNs. Taken together, TLR7-, but not TLR9-, mediated IFN-α production contributes the pathogenesis of SLE, and TLR7 could be a potential therapeutic target for SLE.

106 EFFECTS OF BELIMUMAB ON CORTICOSTEROID USE IN A PIVOTAL PHASE III, RANDOMISED, PLACEBO CONTROLLED STUDY IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN NORTH EAST ASIA

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Background and aims Steroid reduction is an important treatment goal in systemic lupus erythematosus (SLE). The steroid-sparing effects of belimumab were investigated in subjects in North East Asia.

Methods This multicentre, 52 week study (1 13 750/NCT01345253) randomised (2:1) subjects (≥18 years) with SELENA-SLEDAI 38 to intravenous belimumab 10 mg/kg or placebo every 28 days, plus standard SLE therapy. Multiple measures of steroid use (prednisone equivalent) were made, including a secondary endpoint of reduction in dose over 52 weeks among subjects receiving >7.5 mg/day at baseline

Abstract 106 Table 1 Prednisone dose over 52 weeks

All subjects (N=677)	Placebo (n=226)	Belimumab 10 mg/kg (n=451)
Baseline prednisone dose (all subjects), mean (SD), mg/day	17.2 (10.82)	16.0 (10.66)
Cumulative prednisone dose over 52 weeks (all subjects), median (25th, 75th percentile), mg[a]	4758.1 (3597.5, 6695.0)	4190.0 (3090.0, 5475.0)
p-value[b]	0.0005	
Number of subjects with baseline prednisone dose >7.5 mg/day, n (%)	184 (81.4)	352 (78.0)
Number of days that prednisone was reduced to ≤7.5 mg/day and/or by 50% from baseline over 52 weeks, median (25th, 75th percentile)[c]	0 (0, 172.0)	0 (0, 213.5)
p-value[b]	0.0288	
Prednisone reduction by ≥25% from baseline to ≤7.5 mg/day during Weeks 40–52, n (%)[c]	20 (10.9)	55 (15.6)
p-value[d]	0.0721	

[a]Daily dose imputed after dropout/treatment failure; [b]rank ANCOVA; [c]among subjects with prednisone dose >7.5 mg/day at baseline; [d]logistic regression; ANCOVA, analysis of covariance; SD, standard deviation.