(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.

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TOLL-LIKE RECEPTOR 7-, BUT NOT TOLL-LIKE RECEPTOR 9-, MEDIATED INTERFERON- α 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.

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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 (113750/NCT01345253) randomised (2:1) subjects (≥ 18 years) with SLEDAI ≥ 8 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 (25 th , 75 th percentile), mg*	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 (25 th , 75 th percentile) ^c	0 (0, 172.0)	0 (0, 213.5)
p-value ^b	0.0288	
Prednisone reduction by $\geq 25\%$ from baseline to ≤ 7.5 mg/day during Weeks 40–52, n (%) ^c	20 (10.9)	55 (15.6)
p-value ^d	0.0721	

*Daily dose imputed after dropout/treatment failure; ^brank ANCOVA;

^camong subjects with prednisone dose >7.5 mg/day at baseline; ^dlogistic regression; ANCOVA, analysis of covariance; SD, standard deviation.