Results The ITT population of ADDRESS II included 306 patients; 158 of whom met the predefined high disease activity (HDA) criterion (SLEDAI-2K≥10 at Screening). Of the 262 patients who completed the ADDRESS II, 253 entered the LTE. At 24 weeks in the PBO-controlled trial, cumulative incidence of severe flare was significantly reduced with atacicept 75 mg vs PBO by BILAG A (HR 0.24; p=0.0186), and with atacicept 150 mg vs PBO by SFI (HR 0.18; p=0.002). There was no difference in moderate-to-severe flare by BILAG A/2B. In the HDA subpopulation, incidence of severe flare at 24 weeks was significantly reduced with both atacicept doses vs PBO by BILAG A (75 mg HR 0.08, p=0.002; 150 mg HR 0.32, p=0.038) and SFI (75 mg HR 0.33, p=0.029; 150 mg HR 0.19, p=0.004). Incidence of moderate-to-severe flare by BILAG A/2B was significantly reduced with atacicept 150 mg vs PBO (HR 0.34, p=0.032). At 48 weeks, risk of severe flare by SFI was significantly lower with atacicept 150 mg vs the PBO/150 mg in both the ITT and HDA populations (figure 1); significant flare reductions were seen with atacicept 75 mg by BILAG A, and with both atacicept doses by BILAG A/2B vs PBO/150 mg, in the HDA subpopulation.

Conclusions In this 24 week, double-blind, PBO-controlled trial, atacicept treatment was associated with significant flare reductions compared with PBO. Rates of flare continued to be low in atacicept-treated patients between weeks 24–48. Most flares occurred in HDA patients in the PBO group.

S7A:5 SRI RESPONSE, ATTAINMENT OF LOW DISEASE ACTIVITY AND SAFETY IN PATIENTS WITH SYSTEMIC LUPUS TREATED WITH ATACICEPT IN A PHASE IIB STUDY (ADDRESS II)

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Purpose Atacicept targets B-cell stimulating factors, BLyS and APRIL. ADDRESS II (NCT01972568) investigates the efficacy and safety of atacicept in SLE.

Methods In this Phase IIb multicenter study, patients with active (SLEDAI-2K≥6), autoantibody-positive SLE on standard of care therapy received weekly SC injections of atacicept (75 or 150 mg) or placebo (PBO) for 24 weeks. The primary endpoint was proportion of patients achieving SLE responder index (SRI)−4 response at week 24. Other endpoints included SRI-5 through SRI-8 response and low disease activity (LDA) attainment, defined as LDA-1 (SLEDAI-2K≤2), LDA-2 (SLEDAI-2K≤2 and prednisone-equivalent ≤7.5 mg/day), or LLDAS (SLEDAI–2K≤4 without major organ activity, no new disease activity vs previous visit, Physician's Global Assessment≤1,

Abstract S7A:5 Table 1 Clinical response endpoints at week 24 for the HDA subpopulation

	PBO	Atacicept 75 mg	Atacicept 150 mg
	n=52	n=55	n=51
SRI response, n (%)			
SRI-4	22 (42.3)	33 (60.0)	32 (62.7)*
SRI-5	15 (28.8)	24 (43.6)	28 (54.9)†
SRI-6	15 (28.8)	24 (43.6)	28 (54.9)†
SRI-7	11 (21.2)	20 (36.4)	22 (43.1)*
SRI-8	11 (21.2)	19 (34.5)	22 (43.1)*
LDA			
LDA-1, n (%)	7 (13.5)	11 (20.0)	19 (37.3)
OR (95% CI)		1.61 (0.57, 4.52)	3.82 (1.44, 10.15) †
LDA-2, n (%)	4 (7.7)	4 (7.3)	11 (21.6)
OR (95% CI)		0.94 (0.22, 3.98)	3.30 (0.98, 11.17)
LLDAS, n (%)	3 (5.8)	10 (18.2)	12 (23.5)
OR (95% CI)		3.63 (0.94, 14.03)	5.03 (1.32, 19.06)*

CI, confidence interval; LDA, low disease activity; LLDAS, Lupus low disease activity state; OR, odds ratio; PBO, placebo; SLE, systemic lupus erythematosus; SRI, SLE responder index
LDA-1: SLEDAI-2K ≤2
LDA-2: SLEDAI-2K ≤2 and Prednisone-equivalent ≤7.5 mg/day
LLDAS: SLEDAI–2K ≤ 4 without major organ activity, no new disease activity compared with previous visit, Physician's Global Assessment (0–3) ≤1, prednisone-equivalent ≤7.5 mg/day, and stable maintenance doses of immunosuppressants
*p<0.05; †p<0.01

prednisone-equivalent ≤7.5 mg/day, and stable maintenance doses of immunosuppressants). A pre-defined subset of patients was also evaluated, with high disease activity (HDA: SLEDAI-2K≥10 at Screening). Differences in clinical response between patients treated with atacicept and PBO at Week 24 were analysed using odds ratio estimated from logistic regression.

Results The ITT population included 306 patients, and 158 had HDA. There was a trend towards improved SRI-4 response with atacicept vs PBO at Week 24 (p=ns in primary analysis; screening visit as baseline, BL). In a pre-specified sensitivity analysis using study day 1 as BL, a significantly larger proportion of patients on atacicept achieved SRI-4 response at week 24. In the HDA subpopulation, there were significant improvements in SRI-4,–5, −6,–7 and −8 response rates and attainment of LDA with atacicept 150 mg vs PBO (table 1). Atacicept was associated with increased serum C3 and C4, and decreased IgG, IgA, IgM and anti-dsDNA antibodies over time. Rates of treatment emergent adverse event (TEAE) and serious TEAEs were similar among groups. The most frequent serious TEAEs were infections but the incidence was not increased in the atacicept groups vs PBO.

Conclusions Atacicept showed evidence of efficacy in SLE with a dose-dependent reduction of SLE disease activity in patients with HDA. Atacicept was associated with an acceptable safety profile. These results also suggest that more discriminatory endpoints will be useful for future SLE clinical trials.

S7A:6 BASELINE SERUM LEVELS OF BAFF OR APRIL ARE INDEPENDENT PREDICTORS OF SLEDAI RESPONSE AFTER 12 MONTHS OF TREATMENT WITH BELIMUMAB IN PATIENTS WITH REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Belimumab, a monoclonal antibody targeting BlyS (B lymphocyte stimulator), is used in refractory Systemic Lupus Erythematosus (SLE). Pivotal clinical trials showed that SLE patients with positive anti-dsDNA antibodies and reduced levels of C3 and/or C4 fractions were those more likely to be responders to treatment. Our study aims at exploring predictors of response to Belimumab in the post-marketing experience in consecutive SLE patients treated at a single centre.

Methods Twenty-one patients received Belimumab intravenously at standard regimen (10 mg/kg at 0–15–30 days and then every 4 weeks). Anti-dsDNA were tested by Farr assay and C3/C4 levels by nephelometry. Biomarkers belonging to the TNF superfamily and related to B cell activity (BAFF, APRIL, sBCMA, sCD40L, sTACI, TWEAK) were tested by ELISA. All laboratory parameters were tested at baseline and every 6 months afterwards. SLE disease activity was assessed by SLEDAI-2K score. General linear modelling and correlation analysis were performed using SPSS.

Results Enrolled patients were 2 males and 19 females with a median (25th-75th percentile) age of 38 (31–42) years. The disease duration at time of Belimumab start was 12 (8–19) years. The baseline SLEDAI score was 6 (4–9), the anti-dsDNA level was 26 (11–99) UI/ml, and their C3 and C4 level was 72 (56–86) and 9 (7–15) mg/dL, respectively.

All the parameters of the TNF superfamily showed moderate/strong correlation (r values ranging from 0.543 and 0.989, p<0.01). With and without correction for different variables, BAFF and APRIL serum levels measured at the start of Belimumab treatment were the most robust predictors of relative SLEDAI reduction after 12 months of treatment (table 1).

In contrast, C3, C4, anti-dsDNA, and SLEDAI were less likely to predict relative SLEDAI change at 12 month of Belimumab treatment (uncontrolled model: C3 p=0.410; C4 p=0.778; anti-dsDNA p=0.412) in this cohort of patients preselected for the treatment with Belimumab.

Conclusions In this preselected 'real-life' cohort of refractory SLE patients fulfilling the requirements for Belimumab treatment baseline serum levels of BAFF or APRIL are independent predictors of response to treatment. Therefore, BAFF and APRIL could be useful for response estimation in patients qualifying for Belimumab treatment.

S7A:7 ADMINISTRATION OF SERPINB3 DELAYS GLOMERULONEPHRITIS AND ATTENUATES THE LUPUS-LIKE DISEASE IN LUPUS MURINE MODELS BY AN IMMUNOMODULATORY EFFECT

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10.1136/lupus-2018-abstract.44

Background Abnormal apoptosis and clearance of cellular debris concur to development of systemic lupus erythematosus (SLE). SERPINS (serin-protease inhibitors) are ancient molecules regulating immune homeostasis. SERPINB3 modulates apoptosis and is hypoexpressed on SLE B cells.

Aim To explore the effects of SERPINB3 administration in murine lupus models, focusing on glomerulonephritis.

Abstract S7A:6 Table 1 General linear modelling to calculate predictive value of baseline BAFF and APRIL levels for the relative change of SLEDAI at 12 month

General linear modeling (GLM), ANOVA	Baseline APRIL as predictor of SLEDAI change at 12 month BELIMUMAB	Baseline BAFF as predictor of SLEDAI change at 12 month BELIMUMAB
uncontrolled	F= 8.289; p < 0.001	F= 8.195; p < 0.001
controlled for initial AGE, LEUCOCYTES, CRP	F= 7.272; p = 0.007	F= 7.647; p = 0.006
controlled for initial AGE, LEUCOCYTES, CRP, SLEDAI	F= 5.929; p = 0.019	F= 6.624; p = 0.015