and 77% in N and E groups, respectively) and of IV cyclophosphamide (81 and 77%, respectively).
During the *first year*, mean (SD) uP/C decreased statistically more in group E compared to group N (p=0.028 by ANOVA), with striking differences at month 3 (N: 1.73±1.87; E: 0.96±1.34; p=0.038 by unpaired t-test). This difference at month 3 was also noticed for group P patients (0.85±0.76; p=0.02 by unpaired t-test). Interestingly, the mean MP dose at month 3 was statistically higher in group E (19±8) and P (20±9) compared to group N (15±6) (p=0.005 by unpaired t-test).
At *last follow-up*, serum creatinine was statistically lower in E and P patients compared to N patients. Eight of the 11 patients from the T group suffered form a renal relapse, justifying restart of GC, after a median time of 30 months. Importantly, SLICC/ACR-DI was significantly lower in E and P patients, compared to N patients (p=0.0068 and 0.0027, respectively).
Conclusions: In half of LN patients, complete GC withdrawal is achievable and in one third it can be maintained long term. As expected, patients able to stop GC display less damage at last followup. Patients who were able to stop GC decreased their proteinuria much more promptly during the first year of treatment. Interestingly, they received more GC within the first 3 months of therapy, thereby suggesting that a higher dose of GC during the first 3 months of treatment might be associated with a higher probability of later GC withdrawal.
Disclosure of Interest: None declared
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SAT0239 LATE-ONSET NEUTROPENIA FOLLOWING RITUXIMAB TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS – A ROLE OF THE BAFF/APRIL PATHWAY

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Background: Rituximab-mediated late-onset neutropenia (LON) has been studied in various diseases, but data from systemic lupus erythematosus (SLE) are limited.
Objectives: To study the prevalence and contributing factors for LON following treatment with rituximab in patients with SLE, including B cell related cytokines and growth factors of the myeloid lineage.
Methods: Patients from the Karolinska SLE cohort treated with rituximab (n=107) were enrolled in this observational study. Rituximab was given according to the lymphoma course (weekly for four weeks), the arthritis course (at week 0 and 2), or as a single infusion, with or without concomitant pulses of cyclophosphamide. LON was defined as an absolute neutrophil count $<$1,500 cells/μL, occurring four weeks to two years after initiation of rituximab treatment, provided that other apparent causes were excluded. Neutropenia occurring later than two years after treatment initiation but during sustained B cell depletion were also considered LON. B lymphocyte stimulator (BLyS/BAFF), a proliferation-inducing ligand (APRIL), interleukin 6 (IL-6), granulocyte colony stimulating factor (G-CSF) and granulocyte-macrophage colony stimulating factor (GM-CSF) were measured by ELISA prior to treatment (n=70) and either at the incidence of LON in patients who developed LON or after approximately the same median time following rituximab treatment in patients who did not develop LON (n=52).
Results: Thirty-four of 107 patients developed LON after a median time of 222 days (IQR: 105–355 days). BLyS levels increased from baseline (median: 0.62 ng/mL; IQR: 0.42–1.07 ng/mL) through the post-treatment measurement, both in patients who developed LON (median: 1.73 ng/mL; IQR: 1.03–2.13 ng/mL; P=0.005) and patients who did not (median: 1.03; IQR: 0.67–1.56 ng/mL; P$<$0.001), but the increase was greater in patients who developed LON, resulting in significantly higher post-treatment BLyS levels (P=0.029). BLyS levels did not differ between the two groups at baseline (P=0.745). We observed a numerical increase in APRIL levels from baseline (median: 1.29 ng/mL; IQR: 0.85–2.3 ng/mL) through the post-treatment measurement in patients who developed LON (median: 2.39; IQR: 1.08–5.16 ng/mL; P=0.074) and a numerical decrease in patients who did not (median: 1.11 ng/mL; IQR: 0.77–1.64 ng/mL; P=0.064), resulting in significantly higher post-treatment APRIL levels in the LON group (P=0.032), from being similar at baseline (P=0.125). We found no difference in levels of G-CSF, GM-CSF or IL-6 between patients who developed LON and patients who did not, either at baseline or at the post-treatment measurement. Higher prednisone dose administered concomitantly to rituximab (P=0.003) and younger age (P=0.001) were found to be associated with the development of LON, whereas neither the use nor the doses of cyclophosphamide were found to have any impact.
Conclusions: The prevalence of rituximab-mediated LON within the SLE patients of the current study (31.8%) was higher compared to previous reports on patients with lymphoma (3–27%), ANCA-associated vasculitis (11.9%) and rheumatoid arthritis (3%). Our results imply a role of the BAFF/APRIL pathway in the immunologic mechanisms underlying this phenomenon and demonstrate that LON following rituximab treatment is a common complication in SLE patients.
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SAT0240 PHASE 3 TRIAL RESULTS WITH BLISIBIMOD, A SELECTIVE INHIBITOR OF B-CELL ACTIVATING FACTOR, IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Targeted, biologic inhibitors of B-cell Activating Factor (BAFF) have been evaluated in Phase 3 trials in over 5000 patients with SLE. Post hoc analyses of these studies identify lower placebo response and greater treatment effect using more stringent endpoints in patients entering with higher disease activity, greater corticosteroid doses, and/or anti-double-stranded DNA (dsDNA) and low complement C3 or C4[1,2].
Objectives: The Phase 3 CHABLIS-SC1 trial evaluated blisibimod, an inhibitor of B-cell activating factor (BAFF), in a "responder population" identified from prior studies with this drug class.
Methods: 442 SLE patients with anti-nuclear antibodies or anti-dsDNA, SELENA-SLEDAI score $\geq$10 on standard of care medications were randomized to receive weekly subcutaneous blisibimod (200 mg) or placebo. Corticosteroid taper was encouraged from Week 8 with the goal to reach $\leq$7.5 mg prednisone/day. The primary endpoint at Week 52 was the SLE Responder Index-6 (SRI-6): $\geq$6-point improvement in SELENA-SLEDAI, no new BILAG 1A or 2B domain scores, and $<$0.3-point increase in Physician's Global Assessment.
Results: This study did not meet its primary endpoint at Week 52. Response rates to blisibimod were equivalent to past trials of BAFF inhibitors, but the placebo response was greater. A slightly higher proportion of subjects on blisibimod met the SRI-6 and SRI-4 criteria at most timepoints and more blisibimod-treated subjects achieved corticosteroid taper to prednisone $\leq$7.5 mg/day from Week 40 through Week 52 (p=0.04 at Week 44). Reductions in peripheral B cell lineages, anti-dsDNA, anti-phospholipid antibodies, and serum immunoglobulins, and increases in complement C3 and C4 were observed with blisibimod (see Table).
Blisibimod was well-tolerated. The most common adverse events were upper respiratory tract infection (10.6% vs 14.3% on placebo), urinary tract infection (6.9% vs 10.7%), injection site erythema (7.8% vs 2.0%), injection site reaction (7.3% vs 2.6%), and diarrhea (7.3% vs 2.6%).

Table of Results

	Blisibimod (N=245)	Placebo (N=197)
Disease characteristics at baseline		
SELENA-SLEDAI mean score	13.4	13.5
Low C3/C4 & anti-dsDNA, %	62.4	61.7
Proteinuria $\geq$0.5 g/g, %	32.7	27.9
Mean prednisone dose, mg	15.6	15.6
Oral immunosuppressant use, %	42.4	41.6
Antimalarial use, %	61.2	62.2
Results at Week 52 (*p$<$0.05, **p$<$0.01)		
SRI-6 (primary), %	46.9	42.3
SRI-4, %	56.7	52.0
Taper to $\leq$7.5 mg prednisone/day, %	23.3	16.9
Total B cell change from baseline, counts	-3.30**	-1.58
Anti-dsDNA change from baseline, IU	-134.8	-75.5
C3 and C4 change from baseline, mg/dL	0.11**, 0.03**	0.03, -0.002
Anticardiolipin IgG % change from baseline	-12.7*	9.3

Conclusions: With a deliberate focus on a "responder population" for whom lower placebo rates were observed in previous trials, much higher placebo response rates were observed in the CHABLIS-SC1 trial. Modest benefits of blisibimod were observed on serological effects and corticosteroid tapering.
References:
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SAT0241 EARLY RESPONSE TO BELIMUMAB IN SLE-RELATED JOINT INVOLVEMENT EVALUATED BY ULTRASONOGRAPHIC ASSESSMENT

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Background: Belimumab (BLM), a fully human monoclonal antibody directed against B lymphocyte stimulator (BLyS), is currently the only biological drug