Methods: SLE patients fulfilling the 1982 ACR classification criteria who received RTX treatment at the Karolinska University Hospital during the years 2001–2015 were included. Stored serum samples obtained prior to and after six months from initiation of treatment were analysed for the detection of ADA using a GSK-developed and validated electrochemiluminescence assay. Disease specific screening and confirmation cut-point for SLE samples (1.44 AU and 29% respectively) were used. Clinical and laboratory data were retrieved from electronic medical charts. SLE activity was measured using SLE disease activity index 2000 (SLEDAI-2K). We defined treatment response according to the SLE responder index (SRI).²

Results: Thirty-eight patients (89.5% females, median age 35.0 years; IQR: 27.7–55.0) were included in this retrospective analysis. The median disease duration was 6.2 years (IQR: 2.1–11.6) and the baseline median SLEDAI-2K was 6.9 (IQR: 7.0–16.5). The indications for RTX were active lupus nephritis (65.8%), CNS involvement (10.5%), arthritis (13.2%), haematological manifestations (7.9%), or mucocutaneous involvement (2.6%). Twenty-six patients (68.4%) received RTX according to the lymphoma regimen (375 mg/m² at day 1, 7, 14, 28) while 12 (31.6%) according to the arthritis regimen (2 infusions at a dose of 1 g, 14 days apart). Intravenous corticosteroids and cyclophosphamide were given in 65.8% and 63.2% of the patients, respectively.

ADA were detected in 18 patient samples (47.4%) at follow-up and stratified into reactive samples (confirmed positive but with a titer <2 AU/mL; n=3), low positive (2–10 AU/mL; n=6), medium positive (11–50 AU/mL; n=4), and high positive (>51 AU/mL; n=5).

We found no association between the occurrence of ADA and either SRI response (p=0.26, Fisher exact test) nor the concomitant use of high dose IV 6-methylprednisolone (p=0.56, c²test) or IV cyclophosphamide (p=0.11, c²test). At follow-up, patients positive for ADA had higher levels of CD19 +B cells (median: 0.03 × 10⁹ cells/L; IQR: 0.01–0.13) compared to negative patients (median: 0.01 × 10⁹ cells/L; IQR: 0.005–0.01; p=0.007, Mann-Whitney test).

Conclusions: ADA to RTX in SLE are more frequent than in RA and MS and occur irrespective of treatment response and cotreatments, but are associated with higher counts of CD19 +B cells at follow-up. Such finding could reflect either incomplete B-cell depletion in ADA positive patients, or earlier repopulation. Further studies should address the relation between ADA titers and clinical outcomes as well as immunological consequences.

REFERENCES:

- [1] Dunn N, et al. *Mult Scler* 2017.
- [2] Navarra SV, et al. *Lancet* 2011.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6817

AB0513 B AND T LYMPHOCYTES MODIFICATIONS AFTER BELIMUMAB TREATMENT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

F. Regola¹, S. Piantoni^{1,2}, R. Reggia¹, R. Kumar¹, L. Andreoli¹, F. Franceschini¹, A. Tincani¹, P. Airo¹. ¹*Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia*; ²*Molecular and Translational Medicine, University of Brescia, Brescia, Italy*

Background: B- and T-cell hyper-activation is one of the pathogenic mechanisms of systemic lupus erythematosus (SLE). SLE patients have a severe defect in the B cell tolerance check, resulting in high numbers of autoreactive mature naïve B-cells (CD19 +CD27-IgD+) and of peripheral transitional B-cells (CD19 +38high24high). On the other hand, in patients with active SLE a reduced thymic output with a decreased number of recent thymic emigrants T-cells (RTE; CD4 +CD31+) was demonstrated, whereas repeated antigenic stimulation drives modifications in T-cells subpopulations, with enhanced differentiation into effector memory cells (CCR7-CD45RA-).¹

Belimumab is a monoclonal antibody against soluble BLyS used in the treatment of severe SLE. Although B cells are the main target of this treatment, a BLyS-dependent T-cell activation pathway has also been demonstrated.² However, few data are available on the effects of belimumab on circulating B- and T-cell subsets.

Objectives: The aim of this study was to characterise B and T-cell phenotype in a cohort of patients with SLE, and to analyse their modifications during belimumab therapy.

Methods: Phenotypic analysis of peripheral blood B and T lymphocyte subsets was made by flow-cytometry in 14 SLE patients before the first infusion of belimumab, and after 12 months of treatment. SLEDAI 2K-score was used to determine disease activity: a score ≥6 indicated high disease activity. Sex and age-matched healthy controls were enrolled for the comparisons.

Results: At baseline, SLE patients had lower numbers of B- (82 vs 153 cell/μl; p=0.05), T- CD4+ (365 vs 1131 cell/μl; p<0.01), T- CD8+ (340 vs 516 cell/μl; p=0.01), and RTE (95 vs 240 cell/μl; p=0.03) than healthy donors.

After treatment there was a decrease of total B lymphocytes (82 vs 19 cell/μl; p<0.01), and particularly of naïve (45 vs 19% of CD19+; p<0.01) and transitional cells (1 vs 0.2 cell/μl; p=0.03). The absolute number of unswitched memory B cells decreased (2.2 vs 1.4 cell/μl; p=0.05), whereas the percentage of switched memory B cells increased (16 vs 44% of CD19+; p<0.01). The absolute number of CD8 +effector memory cells was also reduced (61 vs 53 cell/μl; p=0.05), as well as percentages of RTE (20 vs 10% of CD4+; p=0.01).

After 1 year therapy in the only 2 patients with persistent high disease activity the percentages of transitional B cells and unswitched memory cells were higher than in 7 patients in which an initially high disease activity decreased below SLEDAI=6 (9% vs 1%; p=0.03; and 29% vs 6%; p=0.04, respectively).

Conclusions: The effects of belimumab on B cell subpopulations are likely to be directly explained by the blockage of soluble BLyS. On the other hand, the effects on the phenotype of T cells are modest and it cannot be excluded that they are indirectly explained by the reduction of disease activity obtained through the therapy. The number of certain circulating B cell subsets might be a marker of response to treatment.

REFERENCES:

- [1] Piantoni S, et al. *Lupus* 2017.
- [2] Jacobi AM, et al. *Arthritis Rheum* 2008.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3150

AB0514 THE EFFECT OF HYDROXYCHLOROQUINE ON REDUCING PROTEINURIA IN STABLE SLE PATIENTS

H. Takahashi, Y. Nasa, E. Takamasu, S. Sugii, N. Yokogawa. *Rheumatology, Tokyo Metropolitan Tama Medical Hospital, Fucyu Tokyo, Japan*

Background: It is thought that hydroxychloroquine (HCQ) reduces proteinuria by preventing endothelial dysfunction in mouse models, but the effects in systemic lupus erythematosus (SLE) patients are not known.

Objectives: To investigate the effects of HCQ on proteinuria in stable SLE patients.

Methods: This was a single-centre, retrospective cohort study. We included stable SLE patients who met the updated or revised American College of Rheumatology 1997 criteria for SLE or the 2012 Systemic Lupus International Collaborating Clinics criteria, and had no active organ dysfunction that needed an increase in immunosuppressive therapy. The subjects (HCQ group) were SLE patients with proteinuria >0.2 g/gCr who started HCQ between 11/1/2015 and 8/1/2017. The controls (non-HCQ group) were SLE patients with proteinuria >0.2 g/gCr seen between 5/1/2016 and 10/31/2016. The reduction in proteinuria over 6 months in the HCQ and non-HCQ groups was compared. The following patients were excluded from the analysis: those who had proteinuria of other aetiologies (diabetic nephropathy, etc.), those who increased the prednisolone (PSL) dose or started immunosuppressive agents, angiotensin converting enzyme inhibitors, or angiotensin II receptor blockers beginning 1 month before the observation period started until its end. Improvement was defined as a reduction in proteinuria ≥0.1 g/gCr. The statistical analysis was performed with the t-test and chi-square test.

Results: There were no significant differences in disease duration, sex, Systemic Lupus Erythematosus Disease Activity Index, or the use of immunosuppressants at baseline between the HCQ (n=16) and non-HCQ (n=14) groups. The respective mean PSL dose at baseline was 5.9±2.8 and 3.3±3.8 mg in the HCQ and non-HCQ groups (p=0.042). Patients in the HCQ group were younger (mean 47±12 vs. 63±14 years, p=0.005). The kidney pathology of the HCQ group was 6.25, 25, 6.25, 6.25, and 6.25% class I to V, respectively, compared with 7.14% class IV, 14.2% class V, and 14.2% class IV+V in the non-HCQ group. The other patients were diagnosed with lupus nephritis clinically.

Proteinuria was significantly lower in the HCQ group than in the non-HCQ group (-0.170±0.343 g/gCr vs. +0.129±0.401 g/gCr, p=0.036). The mean proteinuria at baseline and 6 months later was 0.501±0.276 and 0.331±0.274 g/gCr, respectively, in the HCQ group, and 0.587±0.409 and 0.717±0.720 g/gCr in the non-HCQ group. The proportion of patients who improved in the HCQ and non-HCQ groups was 68.7% (11/16) and 28.5% (4/14), respectively (p=0.028).

Conclusions: HCQ may reduce proteinuria in SLE patients. This suggests that HCQ administration protects the kidneys of SLE patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2249