

placebo in patients with systemic lupus erythematosus, few studies renewed interest for this molecule.

We hypothesised that applying new SLE response criteria in EXPLORER study, we could show rituximab efficacy. Our objective was to reanalyze EXPLORER trial's data using four newly described SLE response criteria.

**Methods** In our reanalysis, rituximab efficacy was assessed at week 52 using 4 criteria: SRI-4 (Systemic lupus erythematosus Responder Index) with and without a concomitant oral corticosteroid tapering objective of <10 mg at months 6 (SRI-4 with or without OCS tapering), Lupus Low Disease Activity Score (LLDAS) and BILAG-based Combined Lupus Assessment (BICLA).

**Results** Data from all 257 patients were available. There was 234 women (91%) with a mean age of 40, 3 years among which 177 (69%) received hydroxychloroquine.

At week 52, SRI-4 response rate was 27,2% in the rituximab group vs 22,7% in the placebo group ( $p=0.43$ ); SRI-4 with OCS tapering was 16% in the rituximab group vs 13.6% in the placebo group ( $p=0.62$ ); LLDAS was 16% in the rituximab group vs 12.5% in the placebo group ( $p=0.46$ ) and BICLA was 15.4% in the rituximab group vs 15.9% in the placebo group ( $p=0.91$ ).

Subgroup analyses demonstrated a trend for better efficacy of rituximab compared to placebo in the subgroup of patients co-treated with methotrexate: SRI-4 of 30.6% in the rituximab group vs 12% in the placebo group ( $n=74$ ,  $p=0.08$ ). This trend was not found in the subgroup of patients co-treated with azathioprine or mycophenolate. In the subgroup of patients with an BILAG A/B in haematological system or vasculitis at baseline, there was a significantly higher SRI-4 response rate with rituximab: 28,6% vs 5,3% in the haematological group ( $p=0.047$ ) and 39,3% vs 0% in the vasculitis group ( $p=0.037$ ).

**Conclusions** Our study confirms the results from the original EXPLORER Study. However, subgroup analysis suggests that patients with haematological or vasculitis involvement might benefit from rituximab. Efficacy in the subgroup treated with methotrexate is likely to be due to a lesser bias of concomitant immunosuppressive medication compared to azathioprine and mycophenolate.

## S6d – Immunopathogenesis II

### S6D:4 ANTIBODIES TO MYELIN OLIGODENDROCYTE GLYCOPROTEIN IN PATIENTS WITH SLE ARE ASSOCIATED WITH CENTRAL NERVOUS SYSTEM INVOLVEMENT: AN UNBIASED PILOT STUDY OF THE SWISS SLE COHORT STUDY (SSCS)

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**Background** Nervous system involvement in systemic lupus erythematosus (SLE) is mediated either through autoimmune

vascular or inflammatory processes. The aetiology leading to inflammatory processes to date remains largely elusive. Given that the pathophysiologic hallmark of SLE is B cell hyperactivity, we hypothesised that antibodies against components of the central and peripheral nervous system might be present in the serum and contribute to inflammation/demyelination in these patients.

**Purpose** To determine the prevalence of a broad panel of novel and known nervous system (NS)-directed antibodies in a large, unbiased cohort of patients with systemic lupus erythematosus (SLE) in the Swiss Lupus Erythematosus Cohort Study (SSCS).

**Methods** This retrospective pilot study included 174 patients in a cross-sectional analysis and 104 patients in a longitudinal study. Antibodies against 12 NS-antigens (myelin oligodendrocyte glycoprotein (MOG), neurofascin 186 (NF186), aquaporin-4 (AQP4), N-methyl-D-aspartate receptor (NMDAR), AMPA-receptor subunit 1 and 2 (AMPA), gamma-aminobutyric acid B receptor (GABABR), Glycine-receptor (GlyR), metabolic glutamate receptor 5 (mGluR5), glutamate decarboxylase 65 (GAD65), voltage-gated potassium channel (VGKC)-complex antibodies (contactin-associated protein-like 2 (CASPR2), Leucine-rich glioma inactivated 1 (LGI1)), and dipeptidyl-peptidase-like protein 6 (DPPX) were screened with cell-based assays and correlated with clinical and diagnostic findings.

**Results** 23/174 patients harboured antibodies against MOG ( $n=14$ ), NF186 ( $n=6$ ), GAD65 ( $n=2$ ), AQP4 and GlyR ( $n=1$ ), of which 13 showed clinical symptoms of NS involvement that resembled the syndrome associated with the antibody. Nine patients harbouring antibodies have remained clinically asymptomatic to date, while another patient was lost to follow-up. Antibodies against MOG were those found most frequently (8%) and their titer correlated with the severity of neurologic involvement. The frequency of neuropsychiatric SLE (NPSLE) was much higher in the NS-antibody-positive patients (43%, 83%, 100%, 0% versus 14%).

**Conclusions** Antibodies against MOG, NF186, GAD65, AQP4 and GlyR are found in patients with SLE and NS involvement, of which MOG-antibodies are the most prevalent. This is the first large, unbiased study to screen for a broad panel of anti-NS antibodies. Screening for these antibodies could serve as a predictor and biomarker for inflammatory NS involvement in NPSLE and potentially aid in tailored treatment decisions.

### S6D:5 ANTIPHOSPHOLIPID ANTIBODIES DIFFERENTIALLY REGULATE THE EXPRESSION & ACTIVITY OF THE LYSOSOMAL PROTEASES WITH EFFECTS UPON MONOCYTE AUTOPHAGY

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**Purpose** Antiphospholipid antibodies (aPL) activate monocytes in antiphospholipid syndrome (APS), although the precise mechanisms by which this activation occurs are not fully understood. We have identified several novel protein targets using proteomic analysis of human monocytes treated with APS-IgG. Amongst these novel targets lysosomal proteases cathepsin B and D were identified. The balance between different cathepsins is important in protein degradation,