Purpose Long term immunosuppressive therapy (IST) in systemic lupus erythematosus (SLE) requires constant adjustment according to severity and organ involvement. This ongoing study aims to implement hydroxychloroquine therapy, reduce unnecessary IST, while achieving disease remission without worsening damage.

Methods A 3Rs strategy (Reduction, Replacement and Refinement) was implemented and therapy adjusted considering overall disease activity and safety profile. SLE patients from a single centre were followed between January 2013 and July 2017. Inclusion criteria: ACR criteria fulfilment; diagnosis from >1 year. Demographic and clinical features were registered at inclusion; SLEDAI-2K, therapy and flares recorded at inclusion and at each visit. SLICC damage index was calculated at inclusion and at the end. Data were analysed using SPSS.

Results At inclusion (n=79), 94% were females, median age 45 (IQR 36–57), mostly Caucasians (89%). Median disease duration was 13 (IQR 7–20). SLEDAI-2K at inclusion was <3 (inactive disease) in 63 (80%). Patients with active disease (SLEDAI-2K>3) at baseline were younger, with less disease duration, not enriched for a specific phenotype. Percentages of azathioprine and mycophenolate were reduced from 35 and 8 to 23 and 6, respectively, similar to interim results (39 months); hydroxychloroquine use remained >70% (10 discontinuations due to retinopathy). In contrast, steroids were steadily reduced from 68% to 42% and are now used at <6 mg/day in 22/33 patients. Importantly, steroid reduction or withdrawal rate was significantly higher in inactive disease group. Belimumab was maintained in 8 patients. Flare occurrence was higher in active disease patients (73% vs 17%, overall 27%). Most episodes were mild. Patients with flares were younger, with higher SLEDAI-2K and steroid dose at inclusion. No treatment discontinuation was associated with flare, except for azathioprine, mostly stopped due to safety profile. During the study, median SLICC damage index augmented from 0 to 1, frequently in the ophthalmological domain. Three patients died and ten were lost to follow-up from 39 to 54 months.

Conclusions The 3Rs strategy allowed to reduce unnecessary IST, especially in low disease activity group. Flares rates were in accordance to recent reports. In a long term perspective, our quest to reduce steroid burden seems promising.

S6A:6 SCREENING IN PATIENTS AT HIGH RISK OF HYDROXYCHLOROQUINE RETINAL TOXICITY

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Background/purpose Despite effectiveness and favourable safety profile, antimalarials have the potential to cause irreversible macular retinopathy. Screening methods have evolved over the last decade and the optimal dose of hydroxychloroquine (HCQ) is now set at under 5 mg/kg real body weight. HCQ in Portugal comes only as a 400 mg pill and in 10 pills per package, which is neither friendly for optimising safe dosing nor for promoting compliance. This study aims to test the frequency of retinal hydroxychloroquine toxicity in a single-centre cohort.

Methods Cross-sectional study conducted between January-2016 and May-2017, of a convenience sample of chronically compliant and well characterised patients. The screening strategy consisted of automated threshold visual fields and objective test: spectral-domain optical coherence tomography, fundus autofluorescence and multifocal electroretinogram. Toxicity was diagnosed on the basis of compatible visual fields defects together with at least one positive objective test. Univariate statistical analysis was performed using the Wilcoxon Mann-Whitney (WMW) and Chi-Square (CS) tests for non-parametric distributed data.

Results Of the 62 patients screened, 32 (51%) had no prior ophthalmological examination. Median age was 46 years (y), IQR 37–60; range 27–83; 59 (95%) were female; the majority, 28 (45%) took HCQ due to SLE, 4 (6%) for Sjögren syndrome, 12 (19%) for UCTD, 11 (18%) for incomplete/cutaneous forms of lupus and 7 (11%) for other CTD. No patient had concomitant renal or liver disease. Median duration and cumulative dose were respectively 8 y (IQR 3–12; range 0.4–31) and 1168 g (IQR 584–2044; range 36–8760). Retinal toxicity was confirmed in 6 SLE and 1 non-SLE patient; in all HCQ was stopped (2/7 screen-naïve; 1/7 on tamoxifen; 1/7 with visual loss). Toxicity correlated to disease (p=0,003) and HCQ therapy (p=0,002) duration, cumulative HCQ dose (p=0,001) and SLE (p=0,04). Table 1 dose adjustments were performed in 13 patients.

Conclusion Using a standardised referral protocol for HCQ retinopathy screening led to cessation of therapy due to toxicity (11%) and adjustment of daily dosing (21%). This study highlights that regular adjustment of dose and retinal toxicity screening is mandatory in patients on prolonged HCQ therapy and reinforces lobbying for more flexible dosages. In addition, HCQ toxicity raises the need for alternative therapies in patients with CTD.

Abstract S6A:6 Table 1 Univariate analysis comparing patients according to retinal toxicity

Characteristic	Retinal toxicity (n=7)	No Retinal toxicity (n=55)	P value (*sig)	Statistical test
Age y (mean±SD)	50±11	49±16	0,764	WMW
Non-Caucasian (n, %)	1 (14)	7 (13)	1,000	CS
Disease duration y (mean±SD)	21±9	10±7	0,003*	WMW
Duration HCQ therapy y (mean±SD)	17±7	8±6	0,002*	WMW
Current HCQ > 5 mg/kg (n, %)	6 (86)	38 (69)	0,06	CS
Cumulative HCQ g (mean±SD)	2976±1381	1253±1339	0,001*	WMW
SLE (n, %)	6 (86)	22 (40)	0,04*	CS

S6A:7 EXPLORER STUDY: RITUXIMAB USE IN SYSTEMIC LUPUS ERYTHEMATOSUS, A NEW LOOK ON OLD DATA

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Background Even if randomised trials EXPLORER and LUNAR failed to prove the superiority of rituximab versus

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,