Results: As compared with those of HCs, patients with SLE had lower absolute numbers of total T, NK, and CD4⁺T but higher proportions of all lymphocyte subpopulations except NK, CD4⁺T cells ($P < 0.001$) (Figure 1 A, C). Notably, the absolute numbers and proportions of Tregs as well as Th1 in CD4⁺T subsets were decreased ($P < 0.05$) (Figure 1 B, D). Further, there was a significant increase in the ratio of Tregs/Tregs such as Th1/Tregs, Th2/Tregs and Th17/Tregs ($P < 0.05$) (Figure 1 E). After receiving immunoregulatory combination therapies, the absolute numbers and proportions of T, NK, CD4⁺T, and CD8⁺T were increased, while the proportion of B cells was decreased (Figure 2 A, C); the absolute numbers of most CD4⁺T subsets as well as the proportions of only Th1 and Tregs were significantly increased ($P < 0.001$) (Figure 2 B, D). The ratios of Th1/Th2 and Th1/Tregs increased while that of Th17/Tregs and Th2/Tregs decreased ($P < 0.01$) (Figure 2 E).

Conclusion: Quantitative and functional alterations of peripheral lymphocyte subsets, especially reduced Tregs, play crucial roles in the pathogenesis of the patients. Immunoregulatory combination therapies mainly promote the proliferation and functional recovery of Tregs to rebalance pro- and anti-inflammatory T cells in patients with SLE for patients' symptoms remission.

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Figure 1: Comparison of absolute numbers of lymphocyte subsets in peripheral blood between healthy individuals ($n=206$) and SLE patients ($n=985$). All the lymphocytes subsets were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean±SD and statistical analysis was determined by two-tailed unpaired t-test. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

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SAT0182 THE ASSOCIATION BETWEEN AUTOANTIBODIES AND RITUXIMAB RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic Lupus Erythematosus (SLE) is clinically and immunologically heterogeneous with a variable response to treatment. MASTERPLANS is an MRC-funded consortium that seeks to identify immunophenotypic subgroups of patients that predict response to therapy. Autoantibody profiles can differentiate subgroups of patients and have potential to predict response to treatment.

Objectives: To determine whether known and novel autoantibodies are associated with response to rituximab (RTX), and analyse the association between these antibodies and disease involvement in various organ systems.

Methods: Serum was obtained from 224 SLE patients in the BILAG Biologics Registry who received rituximab according to NHE England criteria (2). Patients were recruited if they were starting a first cycle of rituximab for active SLE (BILAG A or 2xBILAG B) despite previous cyclophosphamide or mycophenolate mofetil.

Evidence of any single organ system involvement previous or current was taken as having a BILAG score of A-D but not E. Disease activity was measured using BILAG-2004. Clinical response was defined as improvement by ≥ 1 grade in active BILAG-2004 systems with no worsening in other systems. Autoantibodies were measured by immunoprecipitation of proteins by sera from ³⁵S-labelled K562 cell lines, followed by SDS-PAGE separation and autoradiography. Autoantibodies not able to be detected by this technique (anti-Ro52, anti-dsDNA and aCL) were measured by ELISA. Autoantibody data was analysed in IBM SPSS and GraphPad Prism v8.2. Association between autoantibodies and RTX response was analysed using binary logistic interaction terms and Pearson's Chi-Square test.

Results: Of the 224 patients (201 female, 23 male, median age 40 years) the most common system involvement from the 9 BILAG domains was musculoskeletal (164 patients) and the least ophthalmic (11 patients). Patients with anti-Ro52 and anti-U1RNP/Sm had more frequent involvement of mucocutaneous ($p < 0.036$, $p < 0.012$) and musculoskeletal domains ($p < 0.015$ for U1RNP) respectively. There were 136 patients with sufficient data to define as either responders ($n=67$) or non-responders ($n=69$) to RTX at 6 months. RTX responders had a higher frequency of anti-U1RNP/Sm compared to non-responders (Figure 1). Further Pearson's Chi-Square analysis showed a significant association between presence of anti-U1RNP/Sm and better response to RTX ($p < 0.018$).

Figure 2: Changes of peripheral lymphocyte subsets after immunomodulatory combination therapy ($n=795$). Data were presented as mean±SD and statistical analysis was determined by two-tailed paired t-test. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Conclusion: Our findings suggest that the presence of U1RNP/Sm autoantibodies in a cohort of patients who have received treatment with RTX is associated with more frequent musculoskeletal and mucocutaneous involvement and predicts a more favourable response to treatment.

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SAT0183 STATUS OF LYMPHOCYTE SUBSETS IN PERIPHERAL BLOOD OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME AND THEIR CHANGES AFTER RECEIVING OUR NEW IMMUNOREGULATORY COMBINATION THERAPY: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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Background: Primary Sjögren's syndrome (pSS) is a chronic inflammatory autoimmune disease mainly involving exocrine glands and involving multiple organs and systems¹. Recent studies have reported that peripheral lymphocyte subsets such as Th1, Th2, Th17, and regulatory cells (Tregs), have been implicated in the pathogenesis of pSS². However, the detailed statuses of lymphocyte subsets of pSS patients remain to be clearly evaluate and effects of immunomodulatory therapies on the lymphocyte subsets are unknown.

Objectives: To explore the pathogenesis and evaluate the therapeutic effect of immunomodulatory drugs (IMiDs) by comparing the changes of lymphocyte subsets in peripheral blood (PB) before and after treatment.

Methods: This study included 1,221 pSS patients and 206 healthy controls (HCs). Among these patient, 759 patients were received our new immunoregulatory therapies such as low-dose interleukin-2, rapamycin, metformin, retinoic acid etc. The absolute numbers of T, B, NK, CD4⁺T, CD8⁺T, Th1, Th2, Th17 and Tregs in PB of these subjects were detected by flow cytometry combined with standard absolute counting beads. Data were expressed as mean $\pm$ standard deviation to the distribution. Independent-samples T test and paired-samples T test were applied. *P* value <0.05 were considered statistically significant.

Results: The absolute numbers of circulating Tregs as well as T, NK cells in pSS patients were significantly lower than those of HCs (*P* <0.05). After immunoregulatory combination treatments, the number of Tregs was significantly increased (*P* <0.05). Though the absolute numbers of T, NK, CD4⁺T, CD8⁺T, Th1, and Th17 cells were also increased to some degree (*P* <0.05), the increased amount of Tregs was much more than other cells, resulting a new balance between pro- and anti-inflammatory lymphocyte homeostasis.

Conclusion: The decrease of peripheral Tregs played an important role in the pathogenesis of primary Sjögren's syndrome. Immunoregulatory combination therapies promoted the increase of Tregs and might help for the recovery of pSS.

Figure 1

Figure 1: Comparison of peripheral blood lymphocyte subsets between healthy patients (n=206) and pSS patients (n=1221). All the lymphocytes subsets were analyzed by detected by flow cytometry combined with standard absolute counting beads. Data were presented as mean $\pm$ SD and statistical analysis was determined by two-tailed unpaired t-test. (**P* < 0.05, ***P* < 0.01, ****P* < 0.001).

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Figure 2: Changes of peripheral lymphocyte subsets after immunoregulatory combination treatment (n=79). Data were expressed as mean $\pm$ standard deviation to the distribution.

Independent-samples T test and paired-samples T test were applied. *P* value <0.05 were considered statistically significant. (**P* <0.05, ***P* <0.01, ****P* <0.001)

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SAT0184 MAINTENANCE THERAPY WITH AZATHIOPRINE ASSOCIATED WITH HIGHER RISK OF FLARE IN PROLIFERATIVE LUPUS NEPHRITIS

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Background: Goals of lupus nephritis (LN) maintenance treatment include prevention of LN flares and long-term preservation of renal function, while minimizing drug iatrogenicity. There is an unmet need for identifying predictors of LN flare in order to guide optimization of maintenance immunosuppression.

Objectives: To identify predictors of LN flare after attainment of complete renal response (CRR) in patients with proliferative LN.

Methods: Retrospective cohort study over 36 months including patients with SLE fulfilling the ACR'97 and/or the SLICC'12 classification criteria, enrolled in the CHUC Lupus Cohort between 1999 and 2018, with a biopsy-proven proliferative LN (class III/IV) and who attained CRR (proteinuria <0.5g/day and normal renal function, according to EULAR/ERA-EDTA definition) following induction treatment. Only proteinuric flares were considered and defined as doubling of proteinuria to >1g/day. Clinical-analytic characteristics at baseline (time of first CRR attainment after induction) were compared using survival analysis for time-to-flare. Variables with *p* < 0.10 on univariate analysis with Log-Rank tests were further evaluated as predictors with multivariate Cox proportional hazards regression models (Backward Stepwise method, Wald-based), with estimation of hazard ratios (HR) with 95% confidence intervals (95%CI).

Results: A total of 50 patients in CRR were included in the analysis (78.4% female, age at baseline 30.0 $\pm$ 12.5 years-old). Over the follow-up period, 10 patients (20.0%) experienced a proteinuric flare, within a mean time of 29.1 months (95%CI 26.89-31.37). In univariate analysis, age <30 years (*p*=0.020), arterial hypertension (*p*=0.020) and presence of anti-RNP antibody (*p*=0.002) at baseline were associated with higher risk of LN proteinuric flares. In multivariate analysis, age <30 years (HR 26.56; 95%CI 1.93-365.08; *p*=0.014), arterial hypertension (HR 8.30; 95%CI 1.21-56.92; *p*=0.031), use of antihypertensive antiproteinuric drugs (angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers) (HR 11.18; 95%CI 1.24-100.66; *p*=0.031) and maintenance therapy with azathioprine (HR 6.23; 95%CI 1.51-25.66; *p*=0.011) (Figure 1) were predictors of LN proteinuric flares.