patients being able to restart HCQ after ophthalmologic examination in this study shows that it is important to perform multimodal imaging techniques in patients with retinal toxicity diagnosis. Since macular pathology can have a different etiologic background, an initial ophthalmologic examination is also necessary. Lack of difference in the duration of HCQ exposure and drug-free time between patients who restarted treatment and who could not may be a sign of personal sensitivity to HCQ toxicity.

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SAT0179

ADHERENCE TO HYDROXYCHLOROQUINE INFLUENCES THE INCIDENCE OF ORGAN DAMAGE DURING FOLLOW-UP IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

J. H. Kang¹, S. E. Choi¹, H. Xu¹, D. J. Park¹, S. S. Lee¹. ¹Chonnam National University Medical School & Hospital, Gwangju, Korea, Rep. of (South Korea)

Background:

Objectives: Hydroxychloroquine (HCQ) is a cornerstone drug in patients with systemic lupus erythematosus (SLE), decreasing the risk of flares and comorbidities and improving survival. This study investigated the effects of HCQ adherence on clinical manifestations, disease activity, and organ damage in Korean patients with SLE.

Methods: Data on 299 SLE patients were obtained from the Korean Lupus Network registry. Demographic variables, clinical manifestations, laboratory findings, PGA, and SLEDAI-2000 and SLICC damage index scores were recorded at the time of enrollment and repeated annually for 4 consecutive years. Patients were divided into two groups according to the level of HCQ adherence. Adherence was defined by the medication possession ratio and dichotomized as $\leq 80\%$ vs. $> 80\%$. Univariate and multivariate analyses were performed to assess the impact of adherence to HCQ on clinical outcomes.

Results: Of the 299 patients, 31 (10.4%) showed poor drug adherence during the follow-up period. Patients with poor HCQ adherence were older ($P=0.011$), less insured ($P=0.024$), experienced lower employment ($P=0.033$), and had a higher rate of comorbidities such as hypertension ($P=0.048$) and depression ($P<0.001$). The non-adherent group had higher mean and changed SLICC damage index scores than the adherent group across all 4 years. In the multivariate analysis, HCQ non-adherence was significantly associated with older age (OR, 1.043; 95% CI, 1.006–1.081; $P=0.021$), depression (OR, 11.98; 95% CI, 1.099–130.6; $P=0.042$), and an annual increase in the SLICC damage index score (OR, 2.275; 95% CI, 1.369–3.779; $P=0.002$).

Conclusion: HCQ adherence might be influenced by age and depressive mood. Additionally, the poor adherence to HCQ in SLE patients was correlated with higher cumulative organ damage. Therefore, patients with SLE should be educated to take HCQ appropriately to improve their clinical outcome in clinical practice.

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SAT0180

ANTIMALARIAL DRUGS ASSOCIATED RETINOPATHY IN SYSTEMIC LUPUS ERYTHEMATOSUS

X. E. Larco Rojas¹, A. Crespo Golmar¹, C. Moriano¹, A. López Robles¹, E. Díez Alvarez¹, T. Pérez Sandoval¹. ¹Hospital Universitario de León, Rheumatology, León, Spain

Background: The antimalarials remain to be the main treatment for Systemic Lupus Erythematosus (SLE). Its most important limitation when you want to increase dose or remain using them is the occurrence of retinal toxicity, which appears in a small number of patients. Since the lesions can progress even with drug withdrawal is important to perform a screening for an early diagnosis.

Objectives: To describe ocular toxicity in patients with SLE treated with antimalarials that attended the rheumatology office and to identify possible associated risk factors.

Methods: We performed a cross-sectional, retrospective study of SLE patients diagnosed of antimalarial drugs associated retinopathy, that were included in the data base of the Rheumatology department in León's Hospital between 2014-2019. Multiple clinical and therapeutic factors potentially associated with retinal toxicity were analyzed including: age, chronic kidney disease (CKD), liver failure, smoking, hypertension, Diabetes mellitus, presence of previous retinopathy, type of treatment, duration, daily dose and cumulative dose and tamoxifen intake. The diagnosis of retinopathy was performed by the Ophthalmology department. The dose of hydroxychloroquine (HCQ) used was of 400mg/day and chloroquine (CQ) 250mg/day.

Results: 437 medical records were analyzed, 20 patients diagnosed of antimalarial retinopathy were included (4.57%), 90% of them were women. The age of

diagnosis was more than 40 years in 18 patients (90%) and more than 60 years in 10 (50%) with a median of 60 years (IQR: 32,25).

The duration of treatment was ≤ 5 years in 10 patients (50%), between 6-10 years in 6 (30%), between 11-15 years in 2(10%) and between 16-20 years in 2 (10%) with a median of exposure of 5,5 years (IQR: 6,5); 15 patients (75%) were in treatment with HCQ, with CQ 2 patients (10%) and with both of them sequentially 3 patients (15%).

Of the group of patients treated with HCQ 35 % were above the global accumulated recommended dose (1000g) and 71% of them were on treatment more than 10 years. In the group treated with CQ none were above the global recommended dose (460g). Of the 3 patients that took both drugs, two were above the recommended dose for HCQ.

25% of the patients had CKD and 10% liver failure, 20% of the patients were active smokers and 15% ex-smokers.

10% of the sample had previous retinopathy related with other comorbidities (age related retinopathy and diabetes), associating hypertension and diabetes mellitus in the same percentage (15%).

Severe retinopathy was found in 1 patient (5%), mild-moderate in 9 patients (45%), retinopathy stages were not specified in 10 patients (50%).

Conclusion: In our sample we observed a prevalence of antimalarials retinopathy of 4.57%, similar of what is found in the literature. Half of the patients had retinopathy in a period of treatment ≤ 5 years, being a described risk factor the duration of treatment of more than 6 years. This early manifestation could be related to the presence of other comorbidities like hypertension, diabetes and CKD.

Dose readjustment should be considered in patients with a period of treatment of more than 10 years. Age seems to be an associated factor for the development of antimalarials retinopathy and to perform a screening in the first year of treatment is important to rule out basal disease related with more risk to develop ocular toxicity.

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SAT0181

ALTERATIONS OF PERIPHERAL LYMPHOCYTE SUBSETS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND THEIR CHANGES AFTER OUR NEW IMMUNOREGULATORY COMBINATION THERAPIES

J. Q. Zhang¹, S. X. Zhang¹, L. Xue², J. Qiao¹, M. T. Qiu¹, R. Zhao¹, M. J. Chang¹, Y. Li¹, J. Luo¹, G. Y. Liu¹, C. Gao³, X. Li¹. ¹The Second Hospital of Shanxi Medical University, Rheumatology, Taiyuan, China; ²The Second Hospital of Shanxi Medical University, Rheumatology, Taiyuan, China; ³Brigham and Women's Hospital, Harvard Medical School, Boston, United States of America

Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by abnormal activation of circulating lymphocytes and overproduction of autoantibodies¹. Breakdown of self-tolerance is considered as a critical cause in the development of SLE². However, the quantitative changes of lymphocyte subsets in SLE are unclear. Since low-dose IL-2 and several drugs have been used to promote the proliferation of regulatory T cells (Tregs)³, we developed immunoregulatory therapies using these drugs to rebalance effector T cells with Tregs and test whether they are benefit to remission disease activity of SLE.

Objectives: To observe the different levels of peripheral lymphocyte subsets at the first laboratory examination of SLE patients with those of healthy controls (HCs) and to evaluate the effect of immunoregulatory combination therapies on levels of lymphocyte subsets in patients with SLE.

Methods: From September 2014 to December 2019, a total of 985 diagnosed patients with SLE (878 females, 107 males, mean age 42.99 ± 13.37 years) and 206 healthy adults were enrolled in this retrospective cross-sectional study. And 795 patients with SLE (711 females and 84 males, mean age 38.26 ± 15.242 years) were received the immunomodulatory drugs (IMiDs) such as low-dose interleukin-2, rapamycin, metformin, retinoic acid, coenzymes Q10 or other immunomodulatory treatments. The absolute numbers of T, B, NK, CD4⁺T, CD8⁺T, Th1, Th2, Th17 and CD4⁺CD25⁺Foxp3⁺T regulatory cells (Tregs) in peripheral blood (PB) of these individuals were measured by Flow Cytometer (FCM) combined with standard absolute counting beads.

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

D. Li¹, H. Lu¹, J. Dunphy², T. Smith¹, E. Vital^{3,4}, I. N. Bruce⁵, N. Mchugh¹. ¹The University of Bath, Pharmacy and Pharmacology, Bath, United Kingdom; ²Royal United Hospital Bath NHS Foundation Trust, Bath, United Kingdom; ³The University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Disease, Leeds, United Kingdom; ⁴Leeds Teaching Hospitals NHS Trust, NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom; ⁵The University of Manchester, Centre for Epidemiology Versus Arthritis, Faculty of Biology Medicine and Health, Manchester, United Kingdom

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

J. Y. Yang¹, S. X. Zhang², L. Hao², Q. Y. Su¹, J. Bai¹, S. J. Guo¹, J. Luo², G. Y. Liu², C. Gao³, X. Li². ¹Shanxi Medical University, Taiyuan, China; ²The Second Hospital of Shanxi Medical University, Taiyuan, China; ³Brigham and Women's Hospital, Harvard Medical School, Boston, United States of America

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.