antihypertensive and corticosteroids. The immunosuppressant treatment used was: mycophenolate mofetil, azathioprine, cyclophosphamide, tacrolimus and rituximab. Considering that the time of follow-up of patients varies, each temporary space was analyzed according to the number of patients. Figure 1 shows that at 6 months, 38% of patients had an improvement >50% and 7.7% of patients achieved remission. After one year of treatment, 42% of patients presented improvement >50% and 17% achieved remission but in 23% of patients two changes of immunosuppressive treatment was needed. At 24 months, 50% of patients improved >50% and 25% achieved remission; in 13% of patients it was necessary to make another treatment change. Finally, after 24 months, it was observed that 50% of patients achieved remission, 33% of patients presented an improvement >50% and only 17% presented renal failure, and it was necessary to make another treatment change. Globally, in 36% of patients 1 or more changes of immunosuppressive treatment were necessary to achieve improvement >50% or remission.

Conclusions Patients who do not experience an improvement >50% in a period of 6 months are more likely to improve if a change in immunosuppressive treatment is made. It is necessary to extend the series to reach conclusions with statistical value.

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DAMAGE ACCRUAL IN SWEDISH SYSTEMIC LUPUS ERYTHEMATOSUS: SECONDARY SJÖGRENS SYNDROME IS AMONG THE FACTORS ASSOCIATED WITH INCREASED RISK

¹Martina Frodlund*, ²Sarah Reid, ¹Jonas Wetterö, ¹Örjan Dahlström, ¹Christopher Sjöwall, ²Dag Leonard. ¹Linköping University; ²Uppsala University

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Background Although the expected survival of patients with systemic lupus erythematosus (SLE) has improved during the last 50 years, accrual of damage remains a critical concern. Acquired damage is tightly linked to decreased quality-of-life

and premature death, and could be due to raised disease activity, drug-related side-effects or co-morbidities.

Methods Accumulation of organ damage was studied in 543 well-characterized and from 1998 and onwards consecutively recruited prevalent/incident SLE cases meeting the 1982 American College of Rheumatology (ACR82) and/or the 2012 SLICC criteria. The SLICC/ACR damage index (SDI) was used to estimate damage. Disease variables were evaluated regarding association with damage accrual, and time to first damage. Detailed information on clinical and immunological features, as well as damage in each SDI domain, where at hands. Standardized mortality rate was calculated and causes of death recorded. Comparisons between groups were performed using Chi-square- or Mann-Whitney U-tests, p-values<0.05 were considered significant.

Results 59% of the patients had an SDI score 1% and 25% had extensive damage defined as SDI 3. Patients with presence of damage (SDI 1) were significantly older at disease onset, had longer SLE duration and fulfilled further classification criteria. Caucasian ethnicity was more common among cases with damage. Having ACR82-defined neurologic disorder, antiphospholipid syndrome (APS), any antiphospholipid antibody (positive IgG anti-2-GPI or a lupus anticoagulant test, separately) as well as concomitant comorbidities such as hypertension, hyperlipidemia, diabetes, depression and secondary Sjögrens syndrome were associated with presence of damage (SDI 1). In addition to factors associated with SDI 1, serositis, renal and hematological disorder as well as interstitial lung disease and positive IgG anti-cardiolipin were associated with extensive damage (SDI 3). Time to first damage was significantly shorter for males and for cases with a positive lupus anticoagulant test, whereas APS patients were borderline significant. Cases with malar rash and anti-La/SSB antibodies had significantly longer time to first damage. Malignancy was the most common cause of death.

Conclusions Despite that Swedish health care is tax-funded and offers universal access, a considerable number of patients are affected by irreversible damage over time. We confirm previous observations for several damage associations and

Abstract 264 Figure 1 Distribution of organ damage

report secondary Sjögrens syndrome to be associated with an increased risk of organ damage in SLE.

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ASSOCIATION OF PCSK9 SERUM LEVELS WITH LIPID METABOLISM DYSREGULATION, ACTIVITY/DAMAGE SCORES AND SUBCLINICAL ATHEROSCLEROSIS IN SLE PATIENTS

¹Ivan A Ferraz-Amaro*, ¹Hurma Sanchez, ²Juan Carlos Quevedo-Abeledo, ³Iñigo Rúa-Figueroa, ⁴Beatriz Tejera-Segura, ⁵Antonia De Vera-Gonzalez, ⁵Alejandra González-Delgado, ⁵Laura De Armas-Rillo, ⁵Federico Díaz-González. ¹Servicio de Reumatología; ²Hospital Dr. Negrín; ³Department of Rheumatology, Dr Negrín General University Hospital, Las Palmas de Gran Canaria; ⁴Hospital Insular; ⁵Hospital Universitario de Canarias

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Background SLE patients are characterized by a lipid metabolism dysregulation. Proprotein convertase subtilisin/kexin type 9 (PCSK9) regulates cholesterol metabolism through low-density-lipoprotein (LDL) receptor degradation. PCSK9 has been linked to cardiovascular risk (CVR) in general population. The purpose of this study is to examine whether PCSK9 levels are related to disease activity, damage and severity scores; abnormalities in the lipid profile; and the subclinical atherosclerosis that occur in SLE patients.

Methods Cross-sectional study that encompasses 195 SLE patients. PCSK9 and lipoproteins serum concentrations were assessed. Activity (SLEDAI), severity (Katz) and damage (SLICC) index scores, and carotid ultrasound sonography were evaluated. A multivariable analysis was performed to evaluate the association of PCSK9 with SLE related dyslipidemia, subclinical atherosclerosis and activity/damage status

Results In the univariate analysis, body mass index, waist circumference, traditional CVR factors and triglycerides were related with PCSK9 serum levels. On the contrary, HDL cholesterol and apolipoprotein A levels showed a negative association. LDL cholesterol exhibited a trend to a negative association (beta coeff. -0.30, 95% CI -0.67-0.07, p=0.11). Carotid plaques and cIMT were not associated with PCSK9 levels although a trend was observed. Patients with longer disease duration (beta coeff. 1.25, 95% CI 0.15-2.35, p=0.026) and higher C reactive protein levels (beta coeff. 1.42, 95% CI 0.61-2.22, p=0.00) disclosed higher PCSK9 levels. Prednisone intake was positively associated with PCSK9 (beta coeff. 35.48, 95% CI 14.29-56.6), p=0.001), and patients that were taking any DMARD or hydroxychloroquine disclosed significant lower levels of PCSK9 (beta coeff. -27.91, 95% CI -54.5--1.32, p=0.040 and beta coeff. -39.21, 95% CI -62.21--16.21, p=0.001 respectively). Higher values of SLICC (beta coeff. 9.66, 95% CI 4.47-14.84, p=0.000) and patients that were in the high/very high SLEDAI activity category (beta coeff. 62.98 95% CI 18.10-107.86, p=0.006) disclosed significant higher values of PCSK9. When multivariate analysis was performed these positive associations with both SLICC and SLEDAI and the use of prednisone were maintained, as well as negative associations with LDL levels and the use of hydroxychloroquine.

Conclusions PCSK9 serum levels are independently related to SLE activity and damage scores. This would imply that the mechanisms leading to lipid metabolism dysregulation in SLE patients may be mediated or be a consequence of PCSK9.

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ANTI-OVARIAN ANTIBODIES ARE NOT FOUND MORE COMMONLY AMONG SLE WOMEN WITH PRE-MATURE MENOPAUSE

¹Martha Tsalliki, ²Kristi A Koelsch, ³Eliza Chakravarty, ⁴Hal Scofield*. ¹University of Oklahoma Health Sciences Center; ²Oklahoma Medical Research Foundation; ³University of Oklahoma Health Sciences Center; ⁴Oklahoma Medical Research Foundation; ⁵University of Oklahoma; ⁶Oklahoma Medical Research Foundation; ⁷University of Oklahoma; ⁸Oklahoma City US Department of Veterans Affairs Medical Center

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Background Systemic lupus erythematosus (SLE) is commonly treated with broad immunosuppression, including cyclophosphamide. Use of this agent can result in ovarian toxicity leading to premature menopause. Ovarian failure is associated with concomitant hypothyroidism. We hypothesized that hypothyroidism might be a marker for ovarian autoimmunity because organ-specific autoimmune diseases tend to occur together. We undertook this study to determine whether anti-ovarian antibodies are associated with premature ovarian failure among SLE women who received cyclophosphamide.

Methods All SLE women with a history of cyclophosphamide therapy were identified in the Lupus Registry and Repository (LFRR). All subjects were shown to meet the revised ACR classification criteria. Premature menopause was defined as spontaneous lack of menstrual periods prior to age 45. Anti-ovarian antibodies were measured by ELISA (Anti-Ovarian Ab ELISA, IBL, Minneapolis, catalog # IB9184). Data were analyzed by Students T test and chi square testing. The protocol received ethical approval from the University of Oklahoma Health Sciences Center and Oklahoma Medical Research Foundation IRBs.

Results Among ~3000 SLE women enrolled in the LFRR who had received cyclophosphamide, we found 169 with menopause before age 45 along with 73 who underwent menopause after age 45 and 16 patients over age 45 who were still having menstrual periods at the time of evaluation. Thus, there were a total of 89 SLE women who did not have premature menopause. Mean anti-ovarian antibodies in the 169 with premature ovarian failure was 16.2 units (SD=20.3), while the mean among those without premature menopause was 17.4 units (SD=21.7). These values were not statistically different between the groups. 11 of 169 (6.5%) prematurely menopausal SLE women had a positive result and 8 of 89 (8.9%) without premature menopausal were positive (2=0.53, p=0.46, OR=1.02 (95% CI 0.95-1.1).

Conclusions Anti-ovarian antibodies were present at low levels (~10% positivity) among women with SLE. However, the presence of these antibodies was not related to premature ovarian failure after cyclophosphamide.