Abstract SAT0474 – Figure 1. Kaplan-Meier curves with 95% CI of the first non-RP feature after RP onset according to racial group.

Patients who experienced their first non-RP feature of the disease before the onset of RP were included with a simultaneous onset.

Conclusions: Several clinical and serological differences were evident between the three racial groups. Asians had high prevalences of Scl-70, PH and of a reduced FVC. Black patients in contrast had fast disease onset and a high prevalence of diffuse skin involvement.

Disclosure of Interest: None declared

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SAT0475

ANTI-MDA5 (+) CLINICALLY AMYOPATHIC DERMATOMYOSITIS-ASSOCIATED RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE: ROLE OF HEMOPERFUSION WITH POLYMYXIN

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Background: Patients with clinically amyopathic dermatomyositis (CADM) with MDA5 positive autoantibodies may develop a severe pulmonary syndrome with rapidly progressive interstitial lung disease (RP-ILD) with a bad prognosis and high mortality.

Objectives: To analyse the efficacy of a therapeutic protocol that includes hemoperfusion with polymyxin B (PMX-HP) in addition to immunosuppressive treatment with tacrolimus and glucocorticoids, plasmapheresis and intravenous immunoglobulin (IVIG).

Methods: We retrospectively analysed 12 (10 male) patients diagnosed with anti-MDA5 (+) CADM associated RP-ILD between 1983 and 2018. Anti-MDA5 antibodies were determined by ELISA and confirmed by blot. RP-ILD was defined as a worsening of radiologic interstitial changes with progressive dyspnoea and hypoxemia within 1 month after the onset of respiratory symptoms. From 2014 to 2018, patients (Group 1) were treated with the following protocol: pulses of methylprednisolone (500 mg/day for 3 consecutive days), tacrolimus 2 mg/12 hour, PMX-HP (Toraymyxin 20R, Toray Medical Co., Tokyo, Japan) at a flow of 100 ml/

h for 3 hour once daily on two successive days, and a plasmapheresis scheme with replacement of 3.5 l of seroalbumin 5% followed by IVIG infusion (0.4 mg/kg) during 3 consecutive days and then in alternate days for 7 days more. A comparison was performed with anti-MDA5 (+) CADM associated RP-ILD patients from a historical group (Group 2). PaO₂/FiO₂ (P/F) ratio was measured before and after PMX therapy. A composite endpoint that included mortality due to respiratory failure or lung transplantation was defined. Differences between pre- and post-PMX P/F values were evaluated using paired sample t-test.

Results: Mean (SD) age at diagnosis was 49 (3.5) yrs, with a mean (SD) follow-up of 13 (3.9) months. Comparison between both Groups showed that 3 out of 6 (50%) patients from the Group 1 in comparison with 5 out of 6 (83.3%) from the historical group (Group 2) reached the composite endpoint. Mean (CI 95%) values of P/F after PMX treatment showed a significantly improvement when compared with the pre-PMX values (240 [85–396] vs. 125, ^{60–189} p=0.038)

Conclusions: Our protocol seems to be useful at some extent in anti-MDA5 (+) CADM associated RP-ILD patients. A transient but significant improvement can be attributed to PMX-HP. Adsorption and elimination of inflammatory cytokines, mediators and activated leukocytes, as well as anti-MDA5 antibodies could be the rationale of its efficacy.

Disclosure of Interest: None declared

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SAT0476

INCIDENCE, PREVALENCE, MORTALITY AND PERFORMANCE OF THE ACR/EULAR 2013 CLASSIFICATION CRITERIA IN PHYSICIAN DIAGNOSED SYSTEMIC SCLEROSIS: RESULTS FROM A POPULATION BASED US COHORT (1980–2016)

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Background: Systemic Sclerosis (SSc) is a complex and heterogenous chronic inflammatory disease characterised by widespread fibrosis of the skin and visceral organs, microvascular injury and evidence of immune system activation. Diagnosis can be challenging in the absence of specific laboratory markers or diagnostic criteria.

Objectives: To determine the incidence, prevalence and mortality of physician diagnosed SSc in a population based US cohort and evaluate the performance of the ACR/EULAR 2013 Classification criteria in comparison to the 1980 ACR criteria in classifying patients with SSc.

Methods: Medical records of patients with a diagnosis or suspicion of SSc in Olmsted County, Minnesota from January 1, 1980 to December 31, 2016 were reviewed to identify incident cases of SSc (defined by physician diagnosis). Prevalent cases of SSc in Olmsted County on January 1, 2015 were also identified. Incidence and prevalence rates were age and sex adjusted to the 2010 US white population. Survival rates were compared with the expected rates in the population of Minnesota. Fulfilment of the 1980 and 2013 classification criteria was ascertained.

Results: A total of 79 incident cases of SSc from 1980 through 2016 and 49 prevalent cases on Jan 1, 2015 were identified. Of these, 71 (90%) were females, 68 (87%) were caucasians, age at diagnosis 55.8±15.9 years (mean ±SD). The overall age- and sex- adjusted annual incidence for 1980–2016 was 2.7 (95% C.I. 2.1–3.3) per 1 00 000 population. The age-adjusted incidence was 4.6 (95% C.I. 3.5–5.7) per 1 00 000 for females and 0.6 (95% C.I. 0.2–1.1) per 1 00 000 for males, with no change in incidence over time. The age- and sex-adjusted prevalence on January 1, 2015 was 47.4 (95% C.I. 34.1–60.7) per 1 00 000 population.

64 of 79 (81%) patients fulfilled the 2013 classification criteria, while only 48% fulfilled the 1980 criteria. All but 1 patient that fulfilled the 1980 criteria, also fulfilled the 2013 criteria. All 79 patients had Raynaud's, 38 had cardiopulmonary involvement (pulmonary artery hypertension and/or interstitial lung disease), 33 had digital ulcers/pitting scars, 66 had telangiectasias and 69 had sclerodactyly. 66 patients had limited cutaneous SSc, 11 had diffuse cutaneous SSc and only 2 had Sine scleroderma. 39 patients had a positive autoantibody for SSc: anti-centromere in 29, anti Scl-70 in 8 and anti RNA-polymerase III in 2.

Mortality among SSc patients was significantly higher in comparison to the general population (standardised mortality ratio, 2.24; 95% C.I., 1.52–3.18). Figure 1 demonstrates survival of 79 Olmsted County residents with incident SSc compared to expected rates from Minnesota lifetables (observed: solid line; expected dashed line).

Conclusions: The average incidence of SSc in this population-based US cohort was 2.7 per 1 00 000 population with no change in incidence over the 36 year period of study. The new 2013 classification criteria perform significantly better than the 1980 criteria, but failed to classify 19% of patients in this cohort. Overall survival of patients with SSc is worse than the general population with no evidence of improved survival over time, indicating an unmet need for early diagnosis and more aggressive management.

Disclosure of Interest: None declared

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SAT0477

INTENSIFIED B-CELL DEPLETION THERAPY IN PROGRESSIVE SYSTEMIC SCLEROSIS PATIENTS: 24 MONTHS FOLLOW-UP

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Background: Systemic sclerosis (SSc) is a connective tissue autoimmune disease with systemic involvement and a serious medical condition with a high rate of mortality, especially due to interstitial lung disease (ILD). The exact pathophysiology is still unclear, but B cells seem to play a crucial role in the initiation and the progression of the disorder.¹ Therefore, the use of Rituximab (RTX) might have a rational in the treatment of SSc.

Objectives: We aimed to investigate the outcomes of SSc patients treated with RTX after a follow-up of 24 months.

Methods: We retrospectively collected data from SSc patients² resistant or intolerant to previous therapies, treated with intensified B-depletion therapy, between 2013 and 2016. Therapeutic protocol comprehends: RTX 375 mg/sm on days 1, 8, 15, 22, and two more doses after one and two months, associated with two intravenous administrations of 10 mg/kg of cyclophosphamide and three methylprednisolone pulses (15 mg/kg) followed by oral prednisone (0.8 mg/kg/day, rapidly tapered to 5 mg/day by the end of the 3rd month after RTX).

Results: The study included 20 SSc patients (18 females and 2 males; mean age 66.7±11.0 years). Patients presented with severe multiorgan involvement: ILD (19/20, 95%), pulmonary hypertension (12/20, 60%), and skin thickening (17/20, 85%). After a follow-up of 24 months, we observed a decrease in the levels of NT-proBNP (mean baseline: 385.4±517, mean at 24 months: 283±648, p<0.05), and in the Modified Rodnan Skin Score (mRSS) (mean mRSS baseline: 14.4±10.5, mean after 24 months of follow-up: 12.9±10, p<0.05). Four out of 19 (21%) patients experienced a significant improvement of ILD, as assessed by high-resolution computed tomography, while in 12/19 (63%) patients the intensified B-cell depletion therapy was associated with a stabilisation of the imaging features with no sign of progression. Three out of 19 (16%) patients showed a deterioration of the ILD.

Patients showed no significant decrease in forced vital capacity (FVC) (mean baseline FVC: 93.6±19.3, mean after 24 months of follow-up: 92.2±23.3), no significant decrease in forced expiratory volume in one second (FEV1) (mean baseline FEV1: 89.5±15.6, mean FEV1 at 24 months: 87±21.2), no significant decrease in diffusing capacity (DLCO) (mean baseline DLCO values: 58.8±8.6, mean at 24 months: 60.3±14), no significant change in the ejection fraction (EF)

(mean baseline EF values: 62.8±6.4, mean EF values at 24 months: 58.6±7.1) and in pulmonary artery pressure (PAP) (mean baseline PAP: 30.2±10.5, mean at 24 months: 31.1±11.05).

Conclusions: Despite recent advances in the treatment of SSc, ILD heavily affects prognosis and life expectancy of these patients. Our data suggest that the intensified B-depletion therapy protocol might represent a promising tool for the management of SSc in terms of controlling the progression of the disease, especially when considering pulmonary and skin manifestations. Further prospective studies are needed in order to confirm our results.

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SAT0478

DISEASE-SPECIFIC AUTOANTIBODIES ASSOCIATE WITH REMARKABLY DIFFERENT RISK OF DEVELOPMENT OF SIGNIFICANT LUNG FIBROSIS IN SYSTEMIC SCLEROSIS

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Background: Pulmonary fibrosis (PF) is an important complication of systemic sclerosis (SSc), being a leading cause of disease related death. Some studies suggest that the timing of PF development differs between patients with different autoantibodies.

Objectives: We set out to assess a large single-centre SSc cohort, focusing on the timing of clinically significant PF (csPF), and to compare this within subgroups with different disease-specific autoantibodies, in particular anti-centromere antibody (ACA), anti-topoisomerase I antibody (ATA) and anti-RNA polymerase antibody (ARA).

Methods: Patients with confirmed SSc and information on autoantibodies were included. PF was confirmed on high-resolution CT and defined as clinically significant based on at least one of the following: FVC <70%; a drop in FVC >15%; DLCO <70% with no pulmonary hypertension (PH) present; or a drop in DLCO >15% with no PH. Only subjects who had first available lung function test result within the first 3 years from onset were included. 1-Kaplan-Meier (1 KM) estimation was used to calculate cumulative incidence of csPF. To assess the timing of highest rates of csPF development, hazard rates were calculated within intervals of 12 months over the follow-up.

Results: A total of 450 subjects, 75 (16.7%) male, mean age of onset 47.4 years, were included in the study. Of those 225 (50%) had diffuse cutaneous SSc, 105 (23.3%) carried ACA, 113 (25.1%) ATA and 72 (16%) ARA. Mean follow-up was 12 years, interquartile range 8–16 years. Over the entire follow-up period, 196 (43.6%) of the subjects developed csPF.

Using 1 KM estimation, for the whole cohort, over the first 20 years of disease, approximately half of the patients developed csPF. Three quarters of the patients who developed csPF had reached this endpoint by 5 years (38.2%) with much lower incidence thereafter (at year 10, 15 and 20%–43%, 47% and 49.6%, respectively).

Analysis within subgroups showed that, ACA was associated with a very low risk of csPF development (cumulative incidence of 5.9%, 8.1%, 9.8% at 5, 10 and 15 years from SSc onset). On the other hand, ATA +patients had a remarkably high risk of csPF development, which ultimately occurred in the majority of cases, with cumulative incidence of 77.6% at 5 years, 82.7% at 10 years and 87.1% at 15 years. Rates of csPF development among ARA+patients were higher than those in ACA+, but still much lower than ATA+, and even after 20 years of follow-up, the cumulative incidence of csPF among them was less than a half of that among ATA+patients (23.7%, 33% and 41% at years 5, 10 and 15, figure 1).

The hazard of csPF among ACA+patients was highest in the second year from SSc onset (3%) and in the subsequent years varied between 0% and 1.8%. On the other hand, among ATA+patients hazard of csPF was 28.3% in year 1, 44.9% in year 2, peaked at 52.5% in year 3 and went down sharply thereafter. Although hazard was much lower among ARA+patients, this still peaked at year 3 (2.8%, 6.1% and 12.1% at year 1, 2 and 3 respectively) and declined after.