therapies have been reported e.g. tofacitinib [3] and plasma exchange therapy (PE) [1, 4, 5].

Objectives: We evaluated the effect of plasma exchange (PE) on survival in patients with refractory RP-ILD who were positive for anti-MDA5 antibodies.

Methods: Among 167 patients newly diagnosed with PM/DM, clinically amyopathic DM, or cancer associated myositis from 2008 to 2019 at our hospital, 12 were diagnosed with refractory RP-ILD and were positive for anti-MDA5 antibodies. PE was used as an adjunct to standard therapy and consisted of fresh frozen plasma as replacement solution. The primary outcome was non-disease-specific mortality. anti-MDA5 antibody titres were measured by ELISA using the MESACUP anti-MDA5 test in 155 patients whose serum was frozen and stored at the time of diagnosis.

Results: Anti-MDA5 antibodies were detected in 35 patients, of whom 26 were diagnosed with RP-ILD and 11 were refractory to intensive immunosuppressive therapy. Seven patients received PE (PE group) and four did not (non-PE group). The 1-year survival rate of the PE group was higher than that of the non-PE group (100% and 25%, respectively, $P = 0.011$). Regarding adverse events associated with PE, two patients had anaphylactic shock, one had high fever due to fresh frozen plasma allergy and one had a catheter infection. All adverse events resolved with appropriate treatment.

Conclusion: We evaluated the association between 1-year survival rate and PE for refractory RP-ILD in patients positive for anti-MDA5 antibodies. Intensive immunosuppressive therapy improved the survival rate in RP-ILD patients with anti-MDA5 antibodies, but 20-30% of cases were still fatal. PE could be administered to patients with active infectious disease who were immunocompromised by intensive immunosuppressive therapy. PE may be considered in refractory RP-ILD patients positive for anti-MDA5 antibodies.

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Acknowledgments: Funding: This work was supported by Japan Society for the Promotion of Science KAKENHI Grant Number JP18K15433.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1920

THU0338 THE CIRCULATING CD19-POSITIVE LYMPHOCYTES IN PATIENTS WITH SYSTEMIC SCLEROSIS: MODULATION WITHIN A YEAR AFTER THE INITIATION OF RITUXIMAB THERAPY

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Background: Significant disorders of B-cell homeostasis have been detected in systemic sclerosis (SSc) [1,2]. The improvement of the disease with anti-CD20 monoclonal antibody rituximab (RTM) has been shown in SSc [3]. There are limited data on change in circulating B lymphocytes count after RTM treatment in patients with SSc.

Objectives: To investigate the modulations in absolute and relative numbers of circulating CD19-positive B lymphocytes (B-lymph) in patients with SSc within a year after the initiation of RTM therapy.

Methods: 71 pts with SSc were included in the prospective study. Mean age was 46 ± 13 yrs., 83% were women, 59% had diffuse subset. Duration of SSc from the first non-Raynaud's symptom was 5.6 ± 4.4 yrs. All pts received low doses of glucocorticoids and 45% - immunosuppressive medications. The average follow-up of patients was 13.2 ± 2.0 (11-18) months. The mean dose of RTM for the period of follow up was 1.43 ± 0.60 grams, 48 patients received < 2 g of RTM (group 1, mean of 1.1 ± 0.1 g) and 23 patients received ≥ 2 grams of RTM (group 2, mean dose of 2.2 ± 0.6 g). Peripheral blood CD19-positive cell count was obtained by flow cytometry in patients and in 20 healthy persons, comparable in sex and age. Data are presented as the percentage (P %) and absolute number (AN) of B-lymph per ml of blood. In patients, the number of B-lymph was determined before (n=67 pts), within first month after the first introduction of RTM (n=66), 6 months later (n=34) and at the end of the study (n=71).

Results: At baseline, the AN and P% of B-lymph in pts did not differ from the healthy control. In pts with short disease duration (≤ 3 yrs.) the number of B-lymph before treatment with RTM was the higher (compared with longer duration > 3 yrs.) those who was ill ≥ 3 yrs.) and there was negative correlation between B-lymph count and duration of the disease (R - 0.36, $p=0.003$ for AN and R - 0.48, $p=0.001$ for P %). The number of B-lymph was significantly lower in patients receiving cyclophosphamide (Cyc) before being started with RTM. There was a negative correlation between the AN of B-lymph and the cumulative dose of Cyc (R - 0.293, $p=0.016$). In 1 month after the initiation of RTM a complete depletion of B-lymph was observed in all pts and in six months it persisted in 79% of cases, the rest began to repopulate (15%) or reached a normal levels (6%). At the end of the follow up the number of B-lymph was significantly lower than before treatment and a complete (n=41 pts) or partial (n=23) depletion of B-lymph remained, and only in 7 (10%) pts the count of this cells was normalized. We revealed a negative correlation between the AN of B-lymph and the cumulative dose of RTM (R-0.237, $p=0.048$). Higher doses of RTM in group 2 induced a more significant depletion than in group 1. Change in forced vital capacity and diffusing capacity of the lung (% predicted) during follow up were less pronounced for pts in group 1 compared with group 2 (Δ FVC 2,4% and 7,5% $p=0,01$; Δ DLCO -0,35% and 5,05%, $p=0,001$, respectively).

Conclusion: RTM may be more effective at the early stage of the disease, when the level of B-lymph is the highest. In SSc, the repopulation of B-lymph after depletion with RTM develops slowly. There were a more significant depletion of B-lymph and a more pronounced improvement in pulmonary function with the higher dose of RTM to compare with the lower one. This results indicate the option of a flexible dosing regimen of RTM.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1419

THU0339 THE INFLUENCE OF SKIN CALCINOSIS ON THE PROGNOSIS OF DIGITAL ULCERS IN PATIENTS WITH SSC.

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Background: Digital ulcers (DUs) are one of the main burdens in patients with systemic sclerosis (SSc) as they have a major impact on quality of life and prognosis. Some DUs are associated with the presence of subcutaneous calcinosis (SC) that may worsen their management, and the prognosis of these DUs is still not well defined.

Objectives: To define the characteristics of SSc patients with DUs related to SC and analyze the impact on prognosis and on healing time.

Methods: We prospectively collected data from DUs of the hands evaluated in our dedicated wound-care outpatient clinic from October 2018 to August 2019. Fifty-five patients were enrolled (50 females, 18 with limited-SSc and 37 with diffuse-SSc, mean age 62.3 ± 17.2 years). For every DU we collected: presence/absence of calcinosis, pathogenesis (spontaneous, post-traumatic), area of DU, location (fingertip, periungual area, metacarpophalangeal, proximal/distal interphalangeal-PIP/DIP), VAS-pain at the baseline and after two weeks, local signs of infection (edema, redness), deep wound swab results and time to the healing. Additionally, we calculated the wound-bed score (WBS), at the baseline and we correlated the total score with the time of healing. All the ulcers were managed with weekly treatment following a definite protocol: wound cleansing, disinfection, mechanic debridement, application of antiseptic dressing.

Results: Out of 98 DUs evaluated, 24 (24.5%) were associated with SC. Patients with SC were older than those without calcinosis (67.1 ± 16.9 vs 59.4 ± 16.9 $p < 0.05$) and were more frequently affected by lc-SSc (18 – 75% vs 6 – 25% $p < 0.001$). There were no significant differences between the mean areas of DUs (SC 22 mm^2 vs non-calcinosis 30.8 mm^2) neither in the localization of the ulcers: fingertip (14-61% vs 34-49.3%), periungual area (4-17.4% vs 16-23.2%), PIP (2-9% vs 13-18.9%), DIP (2-9% vs 9-13%) and MCP (1-4% vs 4-5.8%). The VAS-pain was not statistically different at the baseline (6.0 for SC vs 5.4), neither after 2 weeks (3.8 vs 3.2). Although the presence of local signs of infection was similar (5-20.8% vs 14-18.9%), the positivity for the wound swab was higher in SC compared with those without calcinosis (6-26.1% vs 9-11.5%; $p = 0.05$).

All the DUs treated in our outpatient clinic healed but those with SC required more weeks (10.4 ± 7.9 vs 7.13 ± 5.7 ; $p = 0.03$). The WBS was similar in the two groups (8.96 ± 0.46 in SC vs 9.43 ± 0.33) and was negatively correlated with the time of healing ($r = -0.24$, $p = 0.02$).

Conclusion: Although DUs with calcinosis have a different pathogenesis compared to those without SC, the location, dimensions and DU-related pain are similar in both groups. Despite these aspects, DUs associated with calcinosis are more prone to be infected and require more time to heal; the WBS may represent a simple, easy-calculated score to predict the time for DUs healing. The presence of calcinosis may represent a negative prognostic factor in the management of SSc-DUs.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.4234

THU0340 DURATION AND SYSTEMIC SCLEROSIS SUBTYPE ARE ASSOCIATED WITH DIFFERENT GUT MICROBIOME PROFILES

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Background: A growing body of evidence suggests that the gut microbiota plays a significant role in the development of autoimmune diseases. Altered microbiota composition was associated with gastrointestinal and extraintestinal features in systemic sclerosis (SSc) patients.

Objectives: To look for differences in gut microbiota between SSc patients regarding disease duration, disease subset and occurrence of digital ulcers (DU).

Methods: SSc patients seen at our center were recruited in a prospective study. The exclusion criteria included antibiotic or probiotic treatment during the month prior to recruitment, recent hospitalization, BMI > 30, diabetes mellitus or concomitant inflammatory bowel disease. Fecal samples were processed and 16S rRNA gene sequences were analyzed using the QIIME2 package. Weighted (quantitative) and unweighted (qualitative) UniFrac distances, alpha diversity for richness and homogeneity, taxa plots for species and phyla and ANCOM analyses were performed.

Results: During July 2018-May 2019, 26 SSc patients (mean age [SD] $53[12.7]$ years) and disease duration $8.8[7.1]$ years) fulfilled the criteria and were willing to participate in the study. Thirteen patients had diffuse SSc, 16 patients had active DU, 8 patients had Raynaud's phenomenon only without DU, 2 patients had past DU. The microbiota was significantly more similar between patients without active DU compared to those with active DU ($P = 0.024$), but species richness did not differ. Patients with SSc duration less than 6 years had significantly different microbiota compared to long-lasting SSc (unweighted PCoA – $q = 0.031$). Significant variations concerning quantitative and qualitative UniFrac distances ($q = 0.063$, $q = 0.005$) and species richness ($q = 0.009$) were found among patients with diffuse compared to limited SSc. Limited SSc was

associated with greater species richness. Taxa plot analysis revealed higher relative abundance of Firmicutes in diffuse disease and of Actinobacteria and Bacteroidetes in limited SSc.

Conclusion: Disease duration, disease subset and active DU were associated with shifts in the microbiome of SSc patients. The impact of these changes on disease progression needs further elucidation.

Figure:

Disclosure of Interests: Yolanda Braun-Moscovici: None declared, Shira Ben Simon: None declared, Katya Dolnikov: None declared, Sami Giryas: None declared, Doron Markovits: None declared, Yonit Tavor: None declared, Kohava Toledano: None declared, Alexandra Balbir-Gurman Consultant of: Novartis, Omry Koren: None declared

DOI: 10.1136/annrheumdis-2020-eular.4865

THU0341 DIGITAL ARTERY VOLUME INDEX (DAVIX®) PREDICTS THE ONSET OF FUTURE DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Neointima proliferation is a key pathologic feature of Systemic Sclerosis (SSc), causing arterial vessel narrowing and being the recognised culprit pathological lesion in Digital Ulcers (DUs), pulmonary artery hypertension and renal crisis. Nevertheless, there are no validated imaging techniques to assess the severity of vascular involvement in SSc. Digital Artery Volume index (DAVIX®) is an MRI Time of flight angiography based quantitative score of digital arteries flow, without the need to administer contrast.

Objectives: To determine the value of DAVIX in predicting the onset of digital ulcers (DUs), the worsening of patient reported outcomes (PROs) and clinical parameters in SSc patients.

Methods: We enrolled 91 consecutive patients affected by Raynaud's phenomenon, 63 of which fulfilled the 2013 ACR/EULAR classification criteria for SSc and 28 had a score < 9. The data collected included: pulmonary function tests (PFTs), nailfold capillaroscopy, modified Rodnan Skin Score (mRSS), and Scleroderma Health Assessment Questionnaire Disability Index (sHAQ-DI). DAVIX of the dominant hand was calculated as % mean of the 4 fingers, employing IAG proprietary algorithm. The distribution was analysed with DAGostino-Pearson normality test. Medians were compared by Mann-Whitney-Wilcoxon test, correlation with clinical parameters was performed using Spearman's or Pearson test, as appropriate (Prism 7).

Results: 78/91 patients were females and median disease duration was 4 years (IQR 1.91-9). Complete historical and prospective follow-up data were available for 68 patients. DAVIX® correlated with mRSS ($r = -0.258$, $p = 0.017$), DLCO% ($r = 0.338$, $p = 0.008$) and capillaroscopy pattern ($r = -0.388$, $p = 0.001$). In patients with DUs, DAVIX® showed a stronger correlation with DLCO% ($r = 0.786$, $p = 0.048$). DAVIX® predicted the worsening of HAQ-DI ($r = 0.295$, $p = 0.029$), sHAQ ($r = -0.333$, $p = 0.029$) and VAS pain ($r = -0.269$, $p = 0.038$) independently of the presence of DUs. In the context of DU, 7 patients had DUs at baseline (5 with a positive history for DUs). 12 patients developed DUs within 12 months, 3 of them had DUs at baseline. 38 patients did not have either previous or current DUs, neither did they develop new DUs within 12 months. DAVIX of patients