Mike Hughes: None declared, Francesco Del Galdo: None declared, Rosaria Itrace: None declared, Oliver Distler Grant/research support from: OD (last three years) has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Valeria Ricciari: None declared, Yannick Allanoire Speakers bureau: YA received personal fees from Boehringer, Sanofi, Menarini and Medsenic and grants from Alpine with regards to the management of systemic sclerosis, Grant/research support from: YA received personal fees from Boehringer, Sanofi, Menarini and Medsenic and grants from Alpine with regards to the management of systemic sclerosis, Ana Maria Gheorghiu: None declared, Elise Siegert: None declared, Jeska de Vries-Bouwstra: None declared, Eric Hachulla: None declared, Mohammed Tikly: None declared, Nemanja Damjanov: None declared, Francois Spertini: None declared, Luc Mouthon: None declared, Anna-Maria Hoffmann-Vold Speakers bureau: AMHV: received consulting fees from Actelion, ARXX, Bayer, Boehringer Ingelheim, Lilly, Medscape, Merck Sharp & Dohme and Roche; and grants from Boehringer Ingelheim., Consultant of: AMHV: received consulting fees from Actelion, ARXX, Bayer, Boehringer Ingelheim, Lilly, Medscape, Merck Sharp & Dohme and Roche; and grants from Boehringer Ingelheim., Grant/research support from: AMHV: received consulting fees from Actelion, ARXX, Bayer, Boehringer Ingelheim, Lilly, Medscape, Merck Sharp & Dohme and Roche; and grants from Boehringer Ingelheim., Armando Gabrielli: None declared, Serena Guiducci: None declared, Marco Matucci-Cerinic Speakers bureau: has received consulting fees or honorarium from Actelion, Janssen, Inventiva, Bayer, Biogen, Boehringer, CSL Behring, Corbus, Galapagos, Mitsubishi, Samsung, Regeneron, Acceleron, MSD, Chemomab, Lilly, Pfizer, Roche, Grant/research support from: has received consulting fees or honorarium from Actelion, Janssen, Inventiva, Bayer, Biogen, Boehringer, CSL Behring, Corbus, Galapagos, Mitsubishi, Samsung, Regeneron, Acceleron, MSD, Chemomab, Lilly, Pfizer, Roche, Daniel Furst: None declared, Silvia Bellando Randone: None declared

DOI: 10.1136/annrheumdis-2021-eular.3048

POS0318

CLINICAL PHENOTYPE IN SCLERODERMA PATIENTS WITH ANTI-TOPOISOMERASE I POSITIVITY AND LIMITED CUTANEOUS FORM: DATA FROM THE EUSTAR DATABASE

E. Zanatta¹, D. Huscher², P. Airo³, A. Balbir-Gurman⁴, E. Siegert⁵, A. Ortolan¹, M. Matucci-Cerinic⁶, F. Cozzi⁷, G. Riemekasten⁸, A. M. Hoffmann-Vold⁹, O. Distler¹⁰, A. Gabrielli¹¹, S. Heitmann¹², N. Hunzelmann¹³, C. Montecucco¹⁴, J. Morovic-Vergles¹⁵, C. Ribi¹⁶, A. Doria¹, Y. Allanoire¹⁷ on behalf of on behalf of EUSTAR collaborators. ¹University Hospital of Padova, Department of Medicine, Rheumatology Unit, Padova, Italy; ²Charité-Universitätsmedizin, Institute of Biometry and Clinical Epidemiology and Berlin Institute of Health, Berlin, Germany; ³Spedali Civili, Rheumatology and Clinical Immunology, Brescia, Italy; ⁴Rappaport Faculty of Medicine, B. Shine Rheumatology Institute Rambam Health Care Campus, Technion, Haifa, Israel; ⁵Charité-Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany; ⁶University of Florence, Department of Experimental and Clinical Medicine, Division of Rheumatology, Florence, Italy; ⁷Ospedale Classificato Villa Salus, Internal Medicine Unit, Venice, Italy; ⁸Universitätsklinikum Schleswig Holstein-Campus Lubeck, Department of Rheumatology, Lubeck, Germany; ⁹Oslo University Hospital, Department of Rheumatology, Oslo, Norway; ¹⁰University Hospital Zurich, University of Zurich, Department of Rheumatology, Zurich, Switzerland; ¹¹Università Politecnica delle Marche, Dipartimento di Scienze Cliniche e molecolari, Ancona, Italy; ¹²Marienhospital Stuttgart Böhmeinstrasse, Department of Rheumatology, Stuttgart, Germany; ¹³University of Cologne, Department of Dermatology, Köln, Nordrhein-Westfalen, Germany; ¹⁴IRCCS Policlinico San Matteo Foundation, Department of Rheumatology, Pavia, Italy; ¹⁵Dubrava University Hospital, Department of Internal Medicine, Division of Clinical Immunology, Allergology and Rheumatology, Zagreb, Croatia; ¹⁶Lausanne University Hospital and University of Lausanne, Department of Rheumatology, Clinical Immunology and Allergy, Lausanne, Switzerland; ¹⁷Cochin Hospital, University of Paris Descartes, Department of Rheumatology, Paris, France

Background: There is renewed interest in the role of autoantibodies to predict outcomes in systemic sclerosis (SSc). Among the newly identified subsets, patients with limited cutaneous form (lcSSc) but anti-topoisomerase I antibodies (Scl70) positivity draw particular attention, and namely, assessing the risk of developing interstitial lung disease (ILD)—the main cause of death in SSc—to improve the management of Scl70-lcSSc patients.

Objectives: We aimed to characterize patients with Scl70-lcSSc in the large multicenter European Scleroderma Trial and Research (EUSTAR) cohort.

Methods: The EUSTAR database was locked in July 2019. We included all patients fulfilling 1980 ACR and/or 2013 ACR/EULAR criteria for SSc, with disease duration at database entry ≤ 3 yrs and known and stable skin form during the first 3 yrs. Patients with lcSSc were compared: Scl70-lcSSc (target group) vs. ACA-lcSSc and ANA-lcSSc (Step 1); and Scl70-lcSSc vs. Scl70-dcSSc (Step 2). In the ANA subgroup we included ANA+ patients with negative SSc-specific antibodies (Scl70, ACA, RNA polymerase III). In each step, we performed 5 generalized mixed models (GMM) for the risk of the new onset of ILD (defined by imaging), primary myocardial involvement (PMI), pulmonary hypertension (PH), "any severe" (ILD+PMI+PH+scleroderma renal crisis) and all-cause-mortality. An additional GMM assessed the risk of forced vital capacity (FVC) decline $\geq 10\%$ vs. FVC value at ILD onset. Each GMM was adjusted for age, sex and confounders.

Results: Overall, 1285 SSc patients were included: 1068 (83%) females, 860 (67%) lcSSc and 425 (33%) dcSSc. Among patients with lcSSc, 537 (62%) had ACA+, 194 (23%) Scl70+ and 129 (15%) ANA+; 425 patients had dcSSc and Scl70+. Median follow-up was similar in all 4 groups: 7.2 to 8.1 yrs.

Step 1: At baseline, Scl70-lcSSc patients had significantly shorter time from Raynaud's phenomenon (RP) to SSc onset, higher mRSS (5.8 ± 4.8 vs. 4.3 ± 4 , $p=0.001$), and higher rate of articular and muscular involvement vs. ACA-lcSSc patients (Figure 1). No differences were found between Scl70-lcSSc and ANA-lcSSc comparing the aforementioned variables. ILD was more frequent in Scl70-lcSSc (46%) than in ACA-lcSSc (10%) and ANA-lcSSc (25%), as well as restrictive lung disease. GMM showed that Scl70-lcSSc carries a higher risk of ILD than both ACA-lcSSc (HR 4.55, 95%CI 3.23-6.67) and ANA-lcSSc (HR 2.17, 95%CI 1.39-3.45), with a rate of FVC decline $\geq 10\%$ over time similar to the other limited forms. In Scl70-lcSSc patients the risk of "any severe" organ involvement was similar to ANA-lcSSc and higher than ACA-lcSSc (HR 1.89, 95%CI 1.40-2.50). In particular, Scl70-lcSSc shows a risk of PMI similar to ANA-lcSSc and lower than ACA-lcSSc; no differences regarding PH risk. The mortality risk in patients with Scl70-lcSSc was similar to the other limited forms.

Step 2: At baseline, time from RP to SSc onset was longer in patients with Scl70-lcSSc, with less frequent joint synovitis and tendon friction rubs vs. patients with Scl70-dcSSc. Conversely, the frequency of muscular, cardiac and pulmonary involvement was similar. The risk of ILD in Scl70-lcSSc patients was similar to Scl70-dcSSc, with a lower risk of FVC decline $\geq 10\%$ over time. The risk of "any severe" involvement (HR 0.66, 95%CI 0.49-0.83), PMI and PH was lower and the mortality risk tended to be lower (HR 0.57, 95%CI 0.33-1.01, $p=0.053$) vs. Scl70-dcSSc.

Conclusion: In our large multicenter EUSTAR cohort one quarter of lcSSc patients were Scl70+. We show a ranking for major organ involvement within lcSSc: Scl70 the most severe, ANA+ intermediate and ACA the milder form. Scl70-dcSSc patients present the most severe phenotype, and Scl70 positivity, more than the cutaneous subset, is strongly predictive of ILD, whereas other variables may influence progression. These results may provide new insight to improve the management of Scl70-lcSSc patients.

Figure 1. Baseline clinical features and organ involvement in the 3 groups of patients with limited cutaneous systemic sclerosis (lcSSc) (step 1)

ACA, anticentromere antibodies; ANA, antinuclear antibodies; CK, creatine kinase; GI, gastrointestinal involvement; ILD, interstitial lung disease; PMI, primary myocardial involvement; PH, pulmonary hypertension; Scl70, anti-topoisomerase I; SRC, scleroderma renal crisis.

Disclosure of Interests: Elisabetta Zanatta: None declared, Dörte Huscher: None declared, Paolo Airo: None declared, Alexandra Balbir-Gurman: None declared, Elise Siegert: None declared, Augusta Ortolan: None declared, Marco Matucci-Cerinic: None declared, Franco Cozzi: None declared, Gabriela Riemekasten: None declared, Anna-Maria Hoffmann-Vold: None declared, Oliver Distler Speakers bureau: has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac,

Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Consultant of: has/had consultancy relationship and/or has received research funding in the area of potential treatments for systemic sclerosis and its complications from (last three years): Abbvie, Acceleron Pharma, Amgen, AnaMar, Arxx Therapeutics, Baecon Discovery, Blade Therapeutics, Bayer, Boehringer Ingelheim, ChemomAb, Corbus Pharmaceuticals, CSL Behring, Galapagos NV, Glenmark Pharmaceuticals, GSK, Horizon (Curzion) Pharmaceuticals, Inventiva, iQvia, Italfarmaco, iQone, Kymera Therapeutics, Lilly, Medac, Medscape, Mitsubishi Tanabe Pharma, MSD, Novartis, Pfizer, Roche, Sanofi, Serodapharm, Topadur, Target Bioscience and UCB. Patent issued "mir-29 for the treatment of systemic sclerosis" (US8247389, EP2331143)., Grant/research support from: Kymera Therapeutics, Mitsubishi Tanabe, Armando Gabrielli: None declared, Stefan Heitmann: None declared, Nicolas Hunzelmann: None declared, Carlomaurizio Montecucco: None declared, Jadranka Morovic-Vergles: None declared, Camillo Ribì: None declared, Andrea Doria: None declared, Yannick Allanore: None declared
DOI: 10.1136/annrheumdis-2021-eular.3048

POS0319

PERFORMANCE OF PATIENT REPORTED OUTCOMES (PROS) IN SCLERODERMA PATIENTS WITH REDUCED LUNG FUNCTION IN AN OBSERVATIONAL COHORT

M. G. Lazzaroni¹, G. Abignano^{2,3}, M. Wilson², V. Kakkar², F. Del Galdo². ¹ASST Spedali Civili di Brescia, University of Brescia, Rheumatology and Clinical Immunology, Brescia, Italy; ²University of Leeds, Institute of Rheumatic and Musculoskeletal Medicine and NIHR Biomedical Research Centre, Leeds, United Kingdom; ³Azienda Ospedaliera San Carlo, Rheumatology, Potenza, Italy

Background: Patient Reported Outcomes (PROs) are used to capture disease impact on patients' Health Related Quality of Life (HRQoL) and they have been increasingly used as endpoints in clinical trials for Systemic Sclerosis (SSc). The DeSSciper project within the EUSTAR group highlighted dyspnea as one of the factors more strongly related with the highest SHAQ scores (1). Nevertheless, the SENSICIS trial in SSc-ILD (2) showed the efficacy of Nintedanib in reducing the annual rate of FVC loss, as compared to placebo, without significant changes in the PROs used as secondary endpoints (St. George's Respiratory Questionnaire and the FACIT-Dyspnoea questionnaire). Since patient's perspective is a crucial determinant to define the overall relevance of an intervention, the performance of PROs in reflecting different lung functional stages is a relevant issue in SSc.

Objectives: To analyse in a prospective SSc cohort the inference of reduced lung function as measured by FVC on median PRO scores and the correlation among distinct commonly used PROs.

Methods: A cross-sectional study was performed on data exported from the STRIKE database regarding SSc patients followed in Leeds Scleroderma Programme for SSc. Data included records of periodical visits with scores of different PROs commonly used in SSc (Scleroderma-Health Assessment Questionnaire (SHAQ), Cochin Hand Function Scale (CHFS) and Borg dyspnoea scale) and FVC%-predicted (%pFVC) and DLCO%-predicted (%pDLCO). SHAQ score was calculated as the mean value of HAQ (0-3) with the average of the 7-VAS scores divided by 3.33. The 7-VAS (score 1-10) were 1: pain, 2: general function, 3: arthritis, 4: gastro-intestinal, 5: dyspnoea, 6: Raynaud Phenomena; 7: digital ulcers. The correlation of FVC with distinct PROs, and the inter-PRO correlation, were analysed through the non-parametric Spearman test.

Results: Complete data were available from 182 visits of 87 SSc patients (41 with diffuse and 46 with limited cutaneous involvement). Mean %pFVC was 95.16 ±24.93 (median 95) and mean %pDLCO was 59.31±16.51 (median 59). Overall, FVC and DLCO showed a moderate correlation with SHAQ ($r=-0.36$, $p<0.001$ and $r=-0.24$, $p<0.001$ respectively), while Borg score showed a stronger negative correlation with FVC and DLCO ($r=-0.42$ and $r=-0.38$, $p<0.001$ for both). In a sub-analysis of patients grouped by FVC, patients with FVC 50-70% showed a significant correlation of FVC with SHAQ ($r=-0.47$, $p<0.012$), which was not present in patients with FVC 70-90% ($r=0.23$, $p<0.13$). VAS-5 dyspnoea and Borg were not associated with FVC in these two subgroups of patients. Inter PROs analysis showed that CHFS score had a stronger correlation with SHAQ than Borg dyspnoea score in the overall population ($r=0.86$ vs. $r=0.57$, both $p<0.001$).

Conclusion: The analysis of a single centre prospective cohort of SSc patients, suggests a small inference of lung function in the overall SHAQ. The stronger correlation of SHAQ with CHFS, than with Borg score, suggests a higher weight of hand function on SHAQ in this population with relatively conserved lung function. In patients with %pFVC <70%, the correlation with SHAQ was stronger than in patients with %pFVC >70%, suggesting that mild reductions in FVC might not be perceived by the patients, or at least they might not modify HrQoL as measured by SHAQ.

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Disclosure of Interests: Maria Grazia Lazzaroni Grant/research support from: Boehringer-Ingelheim, Giuseppina Abignano: None declared, Michelle Wilson: None declared, Vishal Kakkar: None declared, Francesco Del Galdo Consultant of: Astra-Zeneca, Boehringer-Ingelheim, Mitsubishi-Tanabe, Capella Biosciences, Kymab, Actelion, Grant/research support from: Astra-Zeneca, Boehringer-Ingelheim, Mitsubishi-Tanabe, Capella Biosciences, Kymab, Actelion
DOI: 10.1136/annrheumdis-2021-eular.3505

POS0320

POOR PROGNOSIS PREDICTION IN ANTI-MDA5 POSITIVE DERMATOMYOSITIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE: THE CROSS-CAR DECISION TREE MODEL

L. Wang¹, C. Lv¹, F. Yuan², J. Li³, M. Wu⁴, Z. Da⁵, H. Wei⁶, L. Zhou⁷, S. Yin⁸, J. Wu⁹, W. Tan¹. ¹The First Affiliated Hospital of Nanjing Medical University, Department of Rheumatology, Nanjing, China; ²The Affiliated Wuxi People's Hospital of Nanjing Medical University, Department of Rheumatology, Wuxi, China; ³Huai'an First People's Hospital, Department of Rheumatology, Huai'an, China; ⁴The Third Affiliated Hospital of Soochow University, Department of Rheumatology, Changzhou, China; ⁵Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China; ⁶Northern Jiangsu People's Hospital, Department of Rheumatology, Yangzhou, China; ⁷Changzhou Second People's Hospital Affiliated to Nanjing Medical University, Department of Rheumatology, Changzhou, China; ⁸Affiliated Hospital of Xuzhou Medical University, Department of Rheumatology, Xuzhou, China; ⁹The First Affiliated Hospital of Soochow University, Department of Rheumatology, Suzhou, China

Background: The prognosis of anti-melanoma differentiation-associated gene 5 positive dermatomyositis (anti-MDA5+ DM) – associated interstitial lung disease (ILD) is poor and heterogeneity.

Objectives: The aim of this study was to evaluate prognostic factors and to develop a simple and generally applicable bedside decision tree model for predicting outcomes in patients with anti-MDA5+ DM and to guide treatment.

Methods: We analyzed data for 246 anti-MDA5+ DM patients from Myositis Study Group-Jiangsu, a multicenter cohort across eighteen tertiary hospitals in Jiangsu province, from March 2019 to October 2020. The primary end point was all-cause death, and the secondary end point was occurring of rapidly progressive-ILD (rp-ILD). We used a multivariable Cox proportional hazards model to identify the independent prognostic risk factors of death and rp-ILD respectively. A decision-tree prediction model was developed by using data from 10 hospital of southern region (n=163), with validation by using contemporaneous data from northern region (n=83).

Results: To assess the risk of rp-ILD, we developed a combined risk score, the CROSS score, that included the following values and scores: C-reactive protein ($\leq 8\text{mg/L}$, 0; $>8\text{mg/L}$, 3), anti-Ro52 antibody (negative, 0; positive, 4), Sex (Female, 0; Male, 2) and Short course of disease (More than 3 months, 0; Less than 3 months, 2). The mortality risk was identified by the CAR score, including C-reactive protein ($\leq 8\text{mg/L}$, 0; $>8\text{mg/L}$, 1), Alanine Transaminase ($\leq 50\text{units/L}$, 0; $>50\text{units/L}$, 1) and rp-ILD (non-rpILD, 0; rp-ILD, 3). We divided patients into three risk groups according to the CROSS score: low, 0 to 3; medium, 4 to 7; and high 8-11. And then Use of a simple decision tree prediction model permitted stratification into three different outcome prediction groups. High-risk patients had significantly higher mortality rates than low- and medium-risk patients in both discovery and validation cohorts ($p < 0.0001$).

Conclusion: The CROSS-CAR decision tree model is easy to evaluate the poor prognostic risk in MDA5+ DM patients during any follow-up period. Unnecessary lung examination, such as chest CT scan and arterial blood gas analysis was avoided in low- and medium- rpILD risk patients. The special ambulance, with red cross sign tagged on car in China, may help to screen the high risk patients and to guide further treatment.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3514

POS0321

USE OF HYDROXYCHLOROQUINE AND SYSTEMIC SCLEROSIS: RESULTS FROM A PROSPECTIVE OBSERVATIONAL STUDY ON THE EUSTAR COHORT

S. Bellando Randone¹, H. Wilhelme², C. Bruni¹, E. Siegert³, P. Airò⁴, R. Irace⁵, O. Distler⁶, A. Doria⁷, L. P. Ananieva⁸, L. Cziráj⁹, C. Denton¹⁰, Y. Allanore¹¹, V. Riccieri¹², A. Vacca¹³, I. Foeldvari¹⁴, A. M. Hoffmann-Vold¹⁵, A. Gabrielli¹⁶, M. Matucci-Cerinic¹, D. Furst^{1,2} on behalf of EUSTAR. ¹AOU Careggi University of Florence, Division of Rheumatology, Florence, Italy; ²University of California at Los Angeles, Department of Medicine, Division of Rheumatology, Los Angeles, United States of America; ³Charité University Hospital, Rheumatology, Berlin, Germany; ⁴Spedali Civili di Brescia, Servizio di Reumatologia Allergologia e Immunologia Clinica, Brescia, Italy; ⁵II University of Naples,