FVC were considered, the 5-year extrapolated survival was increased to 86.3% (Figure 2).

Conclusion: Long-term experience of nintedanib treatment in SSc-ILD patients is lacking so far, therefore we modeled and extrapolated the 52-week treatment efficacy of nintedanib on the long-term FVC course and survival in SSc-ILD patients from the EUSTAR database. We could demonstrate a significant reduction of FVC decline by extrapolating the annual treatment effects of nintedanib from the SENSICIS trial from 1 to 5 years in EUSTAR. Translating these reductions of FVC decline into survival, the 5-year mortality rate was reduced from 18% to 13%.

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POS0317

THE PERFORMANCE OF DIFFUSING CAPACITY FOR MONOXIDE CARBON (DLCO) AND FORCED VITAL CAPACITY (FVC) IN PREDICTING THE ONSET OF SYSTEMIC SCLEROSIS (SSC)-INTERSTITIAL LUNG DISEASE (ILD) IN THE EUROPEAN SCLERODERMA TRIALS AND RESEARCH (EUSTAR) DATABASE

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Background: In SSc, ILD is a major cause of morbidity and mortality. High resolution computed tomography (HRCT) is the gold standard for the diagnosis. Predictors of ILD onset are eagerly awaited to improve SSc-ILD management. Pulmonary function test (PFTs) are routinely performed to measure lung function changes.

Objectives: Our aim was to investigate the performance of DLCO (diffusing capacity of lung carbon monoxide) and FVC (forced vital capacity) in predicting the development of SSc-ILD.

Methods: The longitudinal data of DLCO, FVC and ILD on HRCT of SSc patients from the EUSTAR database were evaluated at baseline (t_0), after 12 (± 4) (t_1) and 24 (± 4) (t_2) months. Patients with negative HRCT for any sign of ILD both at t_0 and t_1 were included. Patients who presented or developed pulmonary hypertension during the study period were excluded. At baseline, demographic data, disease duration from Raynaud's onset, disease subsets, autoantibodies and other laboratory and instrumental data were recorded.

Results: 474/17805 patients were eligible for the study (403 females, 71 males): 26.0% dcSSc, 58.3% lcSSc, 220 (48.0%) patients with positive anticentromere antibodies (ACA) and 117 (25.4%) with positive antitopoisomerase I antibodies (Topo-I abs). Among all enrolled patients, 46 (9.7%) developed HRCT signs of ILD at t_2 . Patients with Topo-I abs showed an association with ILD development at t_2 (16.7% vs 7.8%, $p=0.0031$), contrarily ACA positive patients were negatively associated with ILD appearance after 2 years of follow-up (4.4% vs 14.4%, $p=0.0001$). Positive t_2 HRCT patients had a significant lower value of DLCO and FVC at all three assessments when compared to patients with a negative HRCT at t_2 (Table 1) and both t_0 DLCO and FVC values negatively correlated with ILD development (Table 1). The mean t_0 to t_1 change (Δ) of DLCO in patients with negative t_2 HRCT and positive t_2 HRCT were $-0.5 (\pm 12.6)$ and $-1.0 (\pm 15.1)$, respectively. The mean t_0 to t_1 Δ FVC in patients with negative t_2 HRCT and positive t_2 HRCT were $-0.2 (\pm 10.6)$ and $0.1 (\pm 11.5)$, respectively. None of them predicted the appearance of ILD at t_2 (ADLCO: OR (IC) 0.997 (0.97-1.02), $p=0.8024$; Δ FVC OR (IC) 1.002 (0.97-1.03), $p=0.8664$). The data showed an association between t_0 DLCO value <80% and ILD appearance after 2 years of follow-up [OR(IC): 3.09 (1.49-6.40), $p=0.0023$]. Such association was not observed for t_0 FVC value <80% [OR(IC): 1.95 (0.81-4.68), $p=0.1329$]. The predictive capability of t_0 DLCO <80% was moderate but stronger than FVC <80% [AU ROC: 0.62 (0.56-0.69), 0.53 (0.48-0.59) respectively, $p=0.0205$].

Conclusion: Our data suggest that an impaired baseline DLCO (<80%) may have a predictive value for the development of ILD on HRCT after 2 years of follow-up. Further rigorous prospective studies are warranted to understand the role of DLCO evaluation in the course of SSc.

Table 1. DLCO and FVC values at t_0 , t_1 and t_2 values in patients with positive or negative HRCT for ILD at t_2 and their statistical differences.

	Patients without ILD at t_2 (mean $\pm$ SD)	Patients with ILD at t_2 (mean $\pm$ SD)	OR (95%CL)	p-value
DLCO at t_0	79.0 $\pm$ 16.6	69.9 $\pm$ 17.4	0.97 (0.95 - 0.99)	0.0006
DLCO at t_1	78.4 $\pm$ 16.8	68.9 $\pm$ 18.6	0.97 (0.95 - 0.98)	0.0005
DLCO at t_2	78.0 $\pm$ 17.0	65.1 $\pm$ 19.1	0.95 (0.93 - 0.97)	<0.0001
FVC at t_0	102.2 $\pm$ 17.3	94.6 $\pm$ 16.2	0.97 (0.96 - 0.99)	0.0052
FVC at t_1	101.9 $\pm$ 17.9	94.7 $\pm$ 16.5	0.98 (0.96 - 0.99)	0.0092
FVC at t_2	101.6 $\pm$ 17.6	94.5 $\pm$ 20.0	0.98 (0.96 - 1)	0.0126

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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

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POS0318

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

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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.

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