Disclosure of Interests: Victoria Werth Grant/research support from: Investigator for Corbus Pharmaceuticals and received funding to conduct trials, Josef Concha: None declared, Julie Burroughs: None declared, Joyce Okawa: None declared, Rui Feng: None declared, Anisha Jobanputra: None declared, Robert Borucki: None declared, Kathleen Hally Employee of: Employee of Corbus Pharmaceuticals, Emily Hejazi: None declared, Michael Tillinger Employee of: Employee of Corbus Pharmaceuticals, Scott Constantine Employee of: Employee of Corbus Pharmaceuticals, Nancy Dreyfueck Employee of: Employee of Corbus Pharmaceuticals, Barbara White Employee of: Employee and stockholder of Corbus Pharmaceuticals

DOI: 10.1136/annrheumdis-2021-eular.2048

POS0316

MODELLING SHORT-TERM FVC CHANGES FROM SENSICS TO LONG-TERM FVC COURSE IN SSC-ILD DEMONSTRATES CLINICALLY MEANINGFUL REDUCTION OF FVC DECLINE AND SURVIVAL BENEFITS


1Oslo University Hospital, Department of Rheumatology, Oslo, Norway; 2Charité-Universitätsmedizin, Institute of Biometry and Clinical Epidemiology, and Berlin Institute of Health, Berlin, Germany; 3Aust Institut für Herz- und Kreisläufe und Herz-Erkrankungen, Berlin, Germany; 4University of Padova, Rheumatology Unit, Department of Medicine, Padova, Italy; 512 October University Hospital, Department of Rheumatology, Madrid, Spain; 6Cochin Hospital, Department of Rheumatology, Paris, France; 7Justus Liebig University Giessen, Campus Kerckhoff, Department of Rheumatology and Clinical Immunology, Bad Nauheim, Germany; 8University of Verona, Rheumatology Section, Department of Medicine, Verona, Italy; 9University of Milan-Bicocca, Respiratory Unit, San Gerardo Hospital, Department of Medicine and Surgery, Monza, Italy; 10Università degli Studi di Parma, Division of Rheumatology, Department of Medicine, Curtiba, Brazil; 11Charles University, Department of Rheumatology, Praha, Czech Republic; 12Geneva University Hospitals and University of Geneva, Rheumatology Unit, Geneva, Switzerland; 13Poznan University of Medical Sciences, Department of Rheumatology, Rehabilitation and Internal Medicine, Poznan, Poland; 14Università Politecnica delle Marche, Dipartimento di Scienze Cliniche e Molecolari, Ancona, Italy; 15Boehringer Ingelheim International GmbH, TA Inflammation Med, Ingelheim am Rhein, Germany; 16University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland

Background: Nintedanib has shown to slow FVC decline by 41ml over 52 weeks in systemic sclerosis-associated interstitial lung disease (SSc-ILD). However, the long-term effect of nintedanib treatment on ILD progression and mortality in SSc patients is so far unknown.

Objectives: Here, the 52-week treatment efficacy of nintedanib was modeled and extrapolated on the long-term FVC course and survival in SSc-ILD patients from the European Scleroderma Trial and Research (EUSTAR) database.

Methods: SSc patients from the EUSTAR database fulfilling the inclusion criteria of the SENSICS trial (SSc classification criteria, ILD confirmed by imaging, disease duration of <7 years, FVC>40%pred, diffusion capacity of the lung for carbon monoxide (DLCO) 30-89%pred) and matched for baseline characteristics as well as matched for the 52-week FVC change of SENSICS patients were included (n=236). Linear mixed models including time, risk factors at baseline (sex, age, dyspnea class, DLCO%, CRP modified Rodnan skin score, SSC subtype, SSC auto-antibodies, disease duration, synovitis and muscle weakness) were used to estimate the natural FVC course over time. On this natural course of FVC, the observed effect from the SENSICS trial representing the absolute 52-week difference of FVC decline between the nintedanib and the placebo group was applied as continuous annual effect (SENSICS effect model). Survival was estimated for both the natural course as well as the SENSICS effect model using Cox regression.

Results: Of the 236 included patients, 75% were females, 65% had diffuse cutaneous SSc. Mean age was 50.6 years, mean FVC 78.2%pred and DLCO 56.3%pred at time of inclusion. Mean FVC change after 12±2.3 months was -2.3 ±6.9%pred. These parameters were largely similar to the characteristics of the SENSICS population. In the longitudinal follow up of this population, the natural course of FVC showed a total FVC decline of -16.3%pred over 5 years. With assumed SENSICS effects (effects of nintedanib treatment reported in SENSICS), the 5-year FVC decline was reduced to -10.3%pred (Figure 1).

The reduced FVC progression translated into an improved survival. The natural 5-year survival of this SSc-ILD population was 88.2%. When extrapolating also a severe FVC decline early in the course, frequently terminated by early mortality of SSC patients excluding them from long-term outcome assessment, the estimated 5-year survival was reduced to 81.6%. When the SENSICS effects on
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


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 analyzed. We evaluated baseline (t0) after 12 (t1) and 24 (t2) months. Patients with negative HRCT for any sign of ILD both at t1 and t2 were included. Patients who presented or developed pulmonary hyper-tension 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% dSSC, 58.3% lcSSC, 220 (48.0%) patients with positive antitopomerase antibodies (ACA) and 117 (25.4%) with positive antitopomerase I antibodies (Topo-I abs). Among all enrolled patients, 46 (9.7%) developed ILD signs on HRCT at t1. Patients with Topo-I abs showed an association with ILD development at t1 (16.7% vs 7.8%, p=0.0031), contrarily ACA positive patients were negatively associated with ILD development with a HRCT positive rate of 15.1% (p=0.0001). Positive t1 HRCT patients had a significant lower value of DLCO and FVC at all three assessments when compared to patients with a negative HRCT at t1 (Table 1) and both t1 DLCO and FVC values negatively correlated with ILD development (Table 1). The mean t1, t2 change (Δ) of DLCO in patients with negative t1 HRCT and positive t1 HRCT were -0.5 (±12.6) and -10.1 (±15.1), respectively. The mean t1, t2 change (Δ) of FVC in patients with negative t1 HRCT and positive t1 HRCT were -2.0 (±10.9) and 0.1 (±15.1), respectively. None of them predicted the appearance of ILD at t2 (ΔDLCO: OR (IC 95%) =0.97 (0.97-1.02), p=0.8024; ΔFVC OR (IC 95%)=1.002 (0.97-1.03), p=0.8684). The data showed an association between t1 DLCO value≤80% and ILD appearance after 2 years of follow-up [OR (IC): 3.09 (1.49-6.40), p=0.0023]. The predictive capability of t1 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 t1, t2 and t3 values in patients with positive or negative HRCT for ILD at t1 and their statistical differences.

<table>
<thead>
<tr>
<th>Patients without ILD at Patients with ILD at t1 (mean±SD)</th>
<th>Patients without ILD at Patients with ILD at t2 (mean±SD)</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLCO at t1: 79.0 ± 16.0</td>
<td>69.9 ± 17.4</td>
<td>0.97 (0.95 - 0.99)</td>
<td>0.0006</td>
</tr>
<tr>
<td>DLCO at t2: 68.9 ± 16.8</td>
<td>68.9 ± 16.8</td>
<td>0.97 (0.95 - 0.98)</td>
<td>0.0005</td>
</tr>
<tr>
<td>DLCO at t3: 78.0 ± 17.0</td>
<td>65.1 ± 19.1</td>
<td>0.93 (0.93 - 0.97)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FVC at t1: 102.2 ± 17.3</td>
<td>94.6 ± 16.2</td>
<td>0.97 (0.96 - 0.99)</td>
<td>0.0052</td>
</tr>
<tr>
<td>FVC at t2: 101.9 ± 17.3</td>
<td>94.7 ± 16.5</td>
<td>0.96 (0.95 - 0.99)</td>
<td>0.0092</td>
</tr>
<tr>
<td>FVC at t3: 101.6 ± 17.3</td>
<td>94.5 ± 20.0</td>
<td>0.98 (0.96 - 0.99)</td>
<td>0.0126</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Gemma Lepri: None declared, Cosimo Bruni Speakers bureau: CB reports personal fees from Actelion, personal fees from Eli Lilly, Grant/ research support from: CB reports personal fees from Actelion, personal fees from Eli Lilly, grants from European Scleroderma Trial and Research (EUSTAR) group, grants from New Horizon Fellowship, grants from Foundation for Research in Pulmonary Fibrosis, grants from Fondo Ricerca Italiana per la Ricerca sul Trattamento delle Fibrosi Interstiziali (FIRAt), during the submitted work, Lorenzo Tofani: None declared, Alberto Moggi Pignone: None declared, Marta Orlandi: None declared, Tomasetti Sara Speakers bureau: Speaker’s fees for Roche and Boehringer Ingelheim,