lung function is impaired. It is unclear whether the presence of dyspnoea is associated with a worse course of SSC-ILD or with response to therapy.

**Objectives:** To investigate the rate of decline in FVC in patients with SSC-ILD in the SENSCIS trial in subgroups by patient-reported dyspnoea at baseline.

**Methods:** The SENSCIS trial enrolled patients with SSC-ILD with first non-Raynaud symptom within ≤7 years before screening, extent of fibrotic ILD ≥10% on HRCT and FVC ≥40% predicted. Patients were randomised to receive nintedanib or placebo until the last patient reached week 52. In post-hoc analyses, we analysed the rate of decline in FVC (mL/year) over 52 weeks in patients with and without dyspnoea at baseline based on the question about dyspnoea in the St. George's Respiratory Questionnaire (SGRQ). Patients who reported having shortness of breath “most days a week,” “several days a week” or “a few days a month” (rather than “only with chest infection” or “not at all”) over the last month were considered to have dyspnoea at baseline. A random slope and intercept model was used to assess the rate of decline in FVC (mL/year) and an interaction test was applied to assess potential heterogeneity in the treatment effect of nintedanib versus the subgroups.

**Results:** Of 576 patients, 69.8% had dyspnoea at baseline. In patients with and without dyspnoea, respectively, mean (SD) extent of fibrotic ILD on HRCT was 37.7 (21.7)% and 31.6 (19.4)% and mean (SD) FVC was 710 (16.3)% and 765 (16.8)% predicted; respectively. The rate of decline in FVC in the placebo group, the rate of decline in FVC in the placebo group was similar in patients with and without dyspnoea at baseline (Figure). The effect of nintedanib versus placebo on reducing the rate of decline in FVC (mL/year) was numerically more pronounced in patients without dyspnoea (difference: 79.8 [95% CI: 9.8, 149.7]) than with dyspnoea (difference: 25.7 [-19.9, 71.3]), but the exploratory interaction p-value did not indicate heterogeneity in the treatment effect between subgroups (p = 0.20).

**Conclusion:** In the SENSCIS trial, patients with SSC-ILD who had dyspnoea at baseline had a numerically greater effect of fibrotic ILD on HRCT and numerically lower FVC % predicted at baseline. The rate of decline in FVC in the placebo group was similar in patients with and without dyspnoea. Nintedanib had a numerically greater treatment effect in patients without dyspnoea. These data suggest that the presence of dyspnoea should not be used as a criterion for starting nintedanib in patients with SSC-ILD.

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**Figure:** Rate of decline in FVC (mL/year) over 52 weeks in subgroups by dyspnoea at baseline in the SENSCIS trial.

**Table:** Rate of decline in FVC (mL/year) over 52 weeks in subgroups by dyspnoea at baseline in the SENSCIS trial.

**Disclosure of Interests:** R. Spera1, M. Kuwana2, D. Khamana3, L. Hummers4, T. Frech5, W. Stevens4, J. Gordon4, S. Katfaj6, M. Matouci-Cerinic7, O. Distler8, E. B. Lee9, V. Levy10, I. Jung11, S. Constantine11, N. Digncluck12, B. White12, D. Funk12, C. Denton12, 1Hospital for Special Surgery, Department of Medicine, New York, United States of America, 2Nippon Medical School Graduate School of Medicine, Department of Allergy and Rheumatology, Tokyo, Japan, 3University of Michigan School of Medicine, Sclerodema Program, Ann Arbor, United States of America, 4States of America, 5Ann Arbor, United States of America, 6Johns Hopkins University School of Medicine, Division of Rheumatology, Baltimore, United States of America, 7University of Utah, Division of Rheumatology, Salt Lake City United States of America, 8St. Vincent's Hospital, Department of Rheumatology, Melbourne, Australia, 9Hospital for Special Surgery, Department of Rheumatology, New York, United States of America 10Hospital for Special Surgery, Department of Medicine, New York, United States of America, 11University of California, Department of Rheumatology, Los Angeles, United States of America, 12University of Florence, Department of Experimental Rheumatology, Florence, Italy, 13University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland, 14Seoul National University Hospital, Division of Rheumatology, Seoul, Korea, Rep. of (South Korea), 15Israel Sackler School of Medicine, Tel Aviv University, Department of Internal Medicine, Tel Aviv, Israel, 16Hanyang University Hospital for Rheumatic Diseases, Department of Rheumatology, Seoul, Korea, Rep. of (South Korea), 17Corbus Pharmaceuticals, Clinical, Norwood, United States of America, 18Royal Free Hospital, University College London, Division of Medicine, London, United Kingdom

**Background:** Lenabasum is an oral CB2 agonist that attenuates inflammation and fibrosis in SSC animal models and showed clinical benefit with acceptable safety in a Phase 2 trial in dcSSc.

**Objectives:** Test efficacy and safety of lenabasum in a Phase 3 trial in dcSSc.

**Methods:** Subjects ≥18 years old with disease duration ≤ 6 years were randomized 1:1:1 to lenabasum 5 mg, 20 mg, or placebo (PBO), all BID, with stable background immunosuppressant therapy (IST) allowed. The primary efficacy endpoint was ACR CRISS score, and secondary endpoints were ΔmRSS, ΔHAQ-DI, and ΔESR. Safety results showed no AEs and severe AEs occurred in 9.2% and 5.8% vs 14.6% and 13.0%, respectively, of lenabasum 20 mg and PBO groups, respectively. Efficacy (Table) demonstrated:

- No significant differences were seen in primary and secondary efficacy endpoints. Primary MMRM analyses with treatment-by-time-by-subgroup interactions showed that background mycophenolate (MMF) significantly influenced the outcome.
- Subjects on no IST with disease duration ≤3 years were only 7% of PBO subjects and showed little improvement on PBO, in line with other dcSSc trials in which IST was restricted. Post-hoc subgroup analyses of these subjects on no IST suggested improvement in ΔmRSS and ΔHAQ-DI, for lenabasum 20 mg vs PBO.
- Unexpectedly high improvement occurred in PBO subjects receiving IST, notably those on MMF started within 2 years of baseline.
- Post-hoc analyses of subjects on established IST (MMF or, if no MMF, ≥ 1 non-MMF IST started > 2 years before baseline)
Post-hoc comparisons, per protocol completers, LOCF

<table>
<thead>
<tr>
<th>IST Treatment</th>
<th>Phase I study (n=123)</th>
<th>ΔFVC (% mean (SD)) mean (SD)</th>
<th>ΔMDGA mean (SD)</th>
<th>ΔmRSS mean (SD)</th>
<th>ΔHAQ-DI mean (SD)</th>
<th>ACR CRISS median</th>
</tr>
</thead>
<tbody>
<tr>
<td>No IST Placebo</td>
<td>29</td>
<td>-10.7 (8.1)</td>
<td>-0.12 (0.456)</td>
<td>-6.7 (6.59)</td>
<td>-0.13 (0.468)</td>
<td>0.935</td>
</tr>
<tr>
<td>Established IST</td>
<td>97</td>
<td>-10.9 (8.1)</td>
<td>-0.17 (0.495)</td>
<td>-6.7 (6.2)</td>
<td>-0.15 (0.367)</td>
<td>0.931</td>
</tr>
</tbody>
</table>

Table 1. Primary and secondary efficacy endpoints and post-hoc analyses, Week 52

<table>
<thead>
<tr>
<th>Disease duration</th>
<th>ΔmRSS, mean (SD)</th>
<th>ΔFVC, mean (SD)</th>
<th>ΔmITT population, MMRM primary analysis method</th>
</tr>
</thead>
<tbody>
<tr>
<td>No IST Placebo</td>
<td>-10.7 (8.1)</td>
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<tr>
<td>Established IST</td>
<td>-10.9 (8.1)</td>
<td>-0.17 (0.495)</td>
<td>-6.7 (6.2)</td>
</tr>
</tbody>
</table>

Conclusion: Lenabasum was safely used in this study. Unexpected high improvement on background IST, especially MMF, has not been previously reported at this level. The primary endpoint was not met. Post-hoc analyses showed greater improvement in lenabasum vs PBO-treated subjects who were not on an established IST, including subjects with ILD.

Disclosure of Interests: No disclosures.

Background: Systemic sclerosis (SSc) is an autoimmune disease affecting multiple organs causing morbidity and mortality. Treatments targeting SSc skin often have limited success. The presence of CD30+ lymphocytes in skin biopsies and increased levels of serum CD30 have been reported in SSc patients. This could constitute a new therapeutic target.

Objectives: To explore the efficacy and safety of brentuximab vedotin, a chimeric anti-CD30 antibody drug conjugate, in patients with severe active diffuse cutaneous SSc who failed multiple treatments.

Methods: This Phase IIb, single center, open-label, investigator-initiated trial will recruit 10 patients. Brentuximab vedotin 0.6 mg/Kg was infused intravenously assuming stability in MRSS from week 24 to 48 in cases 5 and 6; 5 6 0.731 0.775 0.559 N/D 0.013 0.079

References: 1. Martucci, D. et al. Increased levels of serum CD30 have been reported in SSc patients. 2. Ouellette, C. et al. Scleroderma, Interim Results of a Phase IIb Open-Label Trial.

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