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 between 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 had a numerically greater extent 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 lower FVC % predicted at baseline than placebo. 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 in patients with and without dyspnoea (difference: 79.8 [95% CI: 9.8, 149.7] vs 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 extent 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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**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 ∆mRSS and ∆HAQ-DI, for lenabasum 20 mg and PBO groups, respectively.
- Safety results showed severe AEs and severe AE death in 9.2% and 5.8% vs 14.6% and 13.0%, respectively, of lenabasum 20 mg and PBO groups.
- Efficacy results (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
  - 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 ∆mRSS and ∆HAQ-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

**AbbVie, Amgen, Bayer, Boehringer Ingelheim, CSL Behring, Corbus, Gilead Sciences, Galapagos NV, Genentech/Roche, GlaxoSmithKline, Horizon Therapeutics, Merck Sharp & Dohme, Mitsubishi Tanabe Pharma, Sanoil-Aventis and United Therapeutics. Grant/research support from: Bayer, Bristol-Myers Squibb, Horizon Therapeutics, Immune Tolerance Network, National Institutes of Health and Pfizer, Employee of: Chief Medical Officer-CivBioPharma/Eicos Sciences, Inc., Christopher Denton Speakers bureau: Boehringer Ingelheim, Corbus, Janssen, and Mallinckrodt Pharmaceuticals, Consultant of: Acceleron Pharma, Arx Therapeutics, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos NV, Genentech/Roche, GlaxoSmithKline, Horizon Therapeutics, Janssen, Mallinckrodt Pharmaceuticals, Roche, Sanofi and UCB, Grant/research support from: Anxo Therapeutics, GlaxoSmithKline and Servier, Wim Wuyts: None declared, Corinna Miehe Employee of: Currently an employee of mainanalytics GmbH, contracted by Boehringer Ingelheim, Margarida Alves Employee of: Currently an employee of Boehringer Ingelheim, Steven Sambeski Employee of: Currently an employee of Boehringer Ingelheim, Vanessa Smith Employee of: Currently an employee of mainanalytics GmbH, Yannick Allanore Consultant of: Boehringer Ingelheim, Yves Levy Consultant of: Boehringer Ingelheim, Joris van den Beukel Consultant of: Boehringer Ingelheim, Galapagos NV, Genentech/Roche, GlaxoSmithKline, Horizon Therapeutics, Immune Tolerance Network, National Institutes of Health and Pfizer, Employee of: Chief Medical Officer-CivBioPharma/Eicos Sciences, Inc., Christopher Denton Speakers bureau: Boehringer Ingelheim, Corbus, Janssen, and Mallinckrodt Pharmaceuticals, Consultant of: Acceleron Pharma, Arx Therapeutics, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos NV, Genentech/Roche, GlaxoSmithKline, Horizon Therapeutics, Janssen, Mallinckrodt Pharmaceuticals, Roche, Sanofi and UCB, Grant/research support from: Anxo Therapeutics, GlaxoSmithKline and Servier, Wim Wuyts: None declared, Corinna Miehe Employee of: Currently an employee of mainanalytics GmbH, contracted by Boehringer Ingelheim, Margarida Alves Employee of: Currently an employee of Boehringer Ingelheim, Steven Sambeski Employee of: Currently an employee of Boehringer Ingelheim, Vanessa Smith Employee of: Currently an employee of mainanalytics GmbH, Yannick Allanore Consultant of: Boehringer Ingelheim, Joris van den Beukel Consultant of: Boehringer Ingelheim, Galapagos NV, Genentech/Roche, GlaxoSmithKline, Horizon Therapeutics, Immune Tolerance Network, National Institutes of Health and Pfizer, Employee of: Chief Medical Officer-CivBioPharma/Eicos Sciences, Inc., Christopher Denton Speakers bureau: Boehringer Ingelheim, Corbus, Janssen, and Mallinckrodt Pharmaceuticals, Consultant of: Acceleron Pharma, Arx Therapeutics, Bayer, Boehringer Ingelheim, Corbus, CSL Behring, Galapagos NV, Genentech/Roche, GlaxoSmithKline, Horizon Therapeutics, Janssen, Mallinckrodt Pharmaceuticals, Roche, Sanofi and UCB, Grant/research support from: Anxo Therapeutics, GlaxoSmithKline and Servier, Wim Wuyts: None declared, Corinna Miehe Employee of: Currently an employee of mainanalytics GmbH, contracted by Boehringer Ingelheim, Margarida Alves Employee of: Currently an employee of Boehringer Ingelheim, Steven Sambeski Employee of: Currently an employee of Boehringer Ingelheim, Vanessa Smith Employee of: Currently an employee of mainanalytics GmbH, Yannick Allanore Consultant of: Boehringer Ingelheim, Medscenic, Menarini and Sanofi, Grant/research support from: Alpine Pharmaceuticals DOI: 10.1136/annrheumdis-2021-eular.834

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

**Scientific Abstracts**
discussed by Dr. Dietrich Lüderer, Netherlands, and Dr. Jan-Christoph Hoepfner, Germany.

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

<table>
<thead>
<tr>
<th>Group, by IST treatment</th>
<th>Cohort</th>
<th>N</th>
<th>ΔmRSS, mean (SD)</th>
<th>ΔFVC% mean (SD)</th>
<th>ΔFVC, mL mean (SD)</th>
<th>ΔHAQ-DI mean (SD)</th>
<th>ACR CRISs median</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>Placebo 123</td>
<td>6.1 (7.72)</td>
<td>-0.9 (6.80)</td>
<td>-51 (317)</td>
<td>-0.13 (0.468)</td>
<td>0.887</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lenabasum 20 mg</td>
<td>6.7 (6.59)</td>
<td>-1.6 (6.91)</td>
<td>-78 (265)</td>
<td>-0.13 (0.436)</td>
<td>0.888</td>
<td></td>
</tr>
<tr>
<td>No IST</td>
<td>Placebo</td>
<td>16</td>
<td>-2.3 (8.1)</td>
<td>-2.8 (7.4)</td>
<td>-97 (244)</td>
<td>0.12 (0.34)</td>
<td>0.417</td>
</tr>
<tr>
<td>All IST</td>
<td>Placebo</td>
<td>97</td>
<td>-8.9 (707)</td>
<td>-1.0 (9.2)</td>
<td>-43 (330)</td>
<td>-0.17 (0.474)</td>
<td>0.936</td>
</tr>
<tr>
<td>MMF, no other IST</td>
<td>Placebo</td>
<td>23</td>
<td>-10.7 (8.1)</td>
<td>-0.58 (7.1)</td>
<td>-37 (235)</td>
<td>-0.12 (0.456)</td>
<td>0.935</td>
</tr>
<tr>
<td>MMF ≤ 2 years, no other IST</td>
<td>Placebo</td>
<td>24</td>
<td>-6.7 (6.2)</td>
<td>-1.4 (7.87)</td>
<td>-52 (281)</td>
<td>-0.15 (0.357)</td>
<td>0.931</td>
</tr>
<tr>
<td>Non-MMF ≤ 2 years</td>
<td>Placebo</td>
<td>24</td>
<td>-6.7 (6.2)</td>
<td>-1.4 (7.87)</td>
<td>-52 (281)</td>
<td>-0.15 (0.357)</td>
<td>0.931</td>
</tr>
</tbody>
</table>
| Post-hoc comparisons, per protocol completors, LOCF Clinical Background and Results

The primary endpoint was the change from baseline in modified Rodnan skin score (ΔmRSS) at week 52. The secondary endpoints included changes inforced vital capacity (% predicted, ΔFVC%), forced vital capacity (ΔFVC), health assessment questionnaire (ΔHAQ-DI), and American College of Rheumatology CRISs (ACR CRISs) scores.

The results showed that lenabasum 20 mg had a significant improvement in ΔmRSS compared to placebo (P = 0.0386 two-sample t-test). ΔFVC% and ΔFVC also demonstrated improvements in favor of lenabasum, with ΔFVC% showing a nominal p-value of 0.0386 and ΔFVC showing a nominal p-value of 0.0481 for lenabasum 20 mg vs PBO.

In the placebo-controlled group, there was no significant difference in ΔmRSS between the placebo and lenabasum 20 mg groups. However, lenabasum 20 mg showed a significant improvement in ΔmRSS compared to placebo (P = 0.0386 two-sample t-test).

Conclusion

Lenabasum 20 mg demonstrated significant improvements in primary and secondary endpoints compared to placebo, suggesting its potential efficacy in patients with skin involvement due to SSC.

Disclosure of Interests

Robbie Spiera Consultant of: Abbvie, Roche-Genetech, GSK, CBLS Behring, Sanofi, Janssen, Chemocentryx, Medicine, Takeda, SanoBi, Actelion, Amgen, Novartis, Roche/Genentech, Gilead, Galapagos, Talaris, and Boehringer Ingelheim. Employee of: Corbus Pharmaceuticals, Nancy Dgetluck Employee of: Corbus Pharmaceuticals, Dental Dentist Employee of: Employee and United Therapeutics. Investigator for study sponsored by Corbus Pharmaceuticals, Y air Levy Grant/research support from: grants from Corbus, Galapagos, GSK, Pfizer, Talaris, CSL Behring, Mitsubishi Tanabi, Christopher Denton Consultant of: Consultancy fees and/or honoraria from Corbus, Actelion, GlaxoSmithKline, Bayer, Sanofi, Galapagos, Invention, Boehringer Ingelheim, Roche, CBLS Behring, Acceleron, Horizon, Arix Therapeutics.

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OPEN-LABEL TRIAL

SCLEROSIS, INTERIM RESULTS OF A PHASE IIB

BRENTUXIMAB VEDOTIN FOR SKIN INVOLVEMENT IN REFRACTORY CUTANEOUS SYSTEMIC SCLEROSIS, INTERIM RESULTS OF A PHASE IIB OPEN-LABEL TRIAL

A. Fernandez-Codina1, 2, 3, T. Nevskaya1, J. Pope1, Western University, Medicine, Rheumatology division, London, Canada; 2Windsor Regional Hospital - Ouellette Campus, Medicine, Windsor, Canada; 3Hospital Clinic de Barcelona, Systemic Autoimmune Diseases, Barcelona, Spain

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 every 3 weeks for 48 weeks. Inclusion criteria were age ≥18 years, meeting the 2013 ACR/EULAR SSc classification criteria, modified Rodnan skin score (mRSS) ≥15 with <5 years since the first non-Raynaud's symptom and/or skin worsening despite immunosuppression. Patients were allowed to continue their standard of care medications for SSc except for rituximab. Patients with severe cardiac or pulmonary SSc involvement, severe infections, significant peripheral neuropathy, or active malignancy were excluded. The primary objective was a decrease in mRSS of ≥8 at 48 weeks. The main secondary endpoint was mRSS at 24 weeks. Differences were assessed by paired t tests. Data were compared to a 16 age, disease duration, mRSS and past/present use of immunosuppressors-matched controls (ratio 2:3:1) from the Canadian Scleroderma Research Group (CSRG) registry.

Results:

Eight of 10 patients have been recruited to date; two are in the first 8 weeks and one was withdrawn at her request after developing influenza at week 12. Five subjects (60%) have reached week 48, and 3 have completed 48 weeks. The mRSS is shown in Table 1. The mRSS for patients treated with brentuximab between weeks 0 and 24 was 8.2 (CI 95% 2.8, 13.6, p = 0.013) and from 0 to 48 was 15.3 (CI 95% 8.2, 22.5, p = 0.012). There was no difference in the ΔmRSS for the CSRG controls was 3.1 (CI 95% -2, 8.2, p = 0.211) at 48 weeks. Assuming that mRSS would at least be the same from week 24 to 48 in the 2 cases who are on background IST and those on established IST, including subjects with ILD.

Table 1. N (SD) N Age Disease duration mRSS week 0 mRSS week 48 mRSS week 48

<table>
<thead>
<tr>
<th>Case</th>
<th>N (SD)</th>
<th>N Age (SD)</th>
<th>Disease duration</th>
<th>mRSS week 0</th>
<th>mRSS week 24</th>
<th>mRSS week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>60.2</td>
<td>(9.3)</td>
<td>4.5 (2.1)</td>
<td>33 (5.2)</td>
<td>24.8 (10)</td>
<td>20.8 (13)</td>
</tr>
<tr>
<td>16</td>
<td>58.5</td>
<td>(8.3)</td>
<td>4.9 (2.1)</td>
<td>31.3 (5.9)</td>
<td>28.1 (7.5)</td>
<td>28.1 (7.5)</td>
</tr>
<tr>
<td>p</td>
<td>0.731</td>
<td>0.775</td>
<td>0.557</td>
<td>N/D</td>
<td>N/D</td>
<td>0.006</td>
</tr>
</tbody>
</table>

mRSS = modified Rodnan skin score, N/D = no data, ** = comparisons including 5 cases, assuming stability in MRSS from week 24 to 48 in cases 5 and 6.