Effects of Nintedanib in Patients with Diffuse and Limited Cutaneous Systemic Lupus Erythematosus: Subgroup Analysis of the SENSICS® Trial

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Introduction

Systemic sarcoidosis (SSc) is classified into two types according to the extent of skin involvement:

- Limited cutaneous SSc (lcSSc), with skin involvement limited to the hands, face and feet;

- Diffuse cutaneous SSc (dcSSc), with skin involvement present on the extremities.

Patients with SSc are at greater risk of developing interstitial lung disease (ILD) due to their SSc status, but the presence of ILD is associated with a poorer rate of mortality in patients with lcSSc and dcSSc.1

In the SENSICS trial, patients with SSc-ILD were randomized to receive nintedanib or placebo. In the overall population, nintedanib was associated with a significant reduction versus placebo in the annual rate of decline in forced vital capacity (FVC) in patients with lcSSc and dcSSc.

Patients

Patients with SSc with onset of first non-Raynaud symptom ≤7 years before screening, extent of fibrotic ILD on high-resolution computed tomography ≥15%, and treatment-naïve or treated with corticosteroids for ≤6 months prior to randomization were allowed to participate.

Patients were randomized 1:1 to receive 150 mg or 150 mg placebo. Patients were classified as having lcSSc or dcSSc by the investigators.

Analysis

We assessed the following in the lcSSc and dcSSc subgroups of subgroups with lcSSc or dcSSc respectively:

- Annual rate of decline in FVC (in mL/year) over 52 weeks
- Proportions of patients with minimal clinically important differences for improvement in FVC, stable FVC, and worsening of FVC at week 52
- Rates of adverse events

Results

Annual rate of decline in FVC

- The annual rate of FVC decline in patients who received placebo was numerically greater in patients with lcSSc than dcSSc (Figure 3). The effect of nintedanib versus placebo on reducing the annual rate of decline in FVC was numerically lower in patients with lcSSc (Figure 4), our previous finding did not indicate heterogeneity in the treatment effect of nintedanib between these subgroups (Figure 2).

Categorical changes in FVC % predicted

- The proportion of patients with worsening of FVC (absolute decrease in FVC of ≥3.3% predicted) was lower, and the proportion of patients with improvement in FVC (absolute increase in FVC of ≥3.0% predicted) was higher, with nintedanib than placebo in both subgroups (Figure 3 and 4).

Adverse events

- The adverse event profile of nintedanib was similar between patients with lcSSc and dcSSc (Table). The adverse event profile of nintedanib was similar between patients with lcSSc and dcSSc.

CONCLUSIONS

- The annual rate of FVC decline in patients who received placebo was numerically greater in patients with lcSSc than dcSSc.

- Nintedanib reduced the progression of ILD both in patients with lcSSc and dcSSc.

- No effect of nintedanib on skin fibrosis assessed using the mRSS was observed in patients with lcSSc or dcSSc.

- The adverse event profile of nintedanib was consistent between patients with lcSSc and dcSSc.

References


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Table. Adverse events reported irrespective of causality in patients with lcSSc and dcSSc.

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Patients with lcSSc</th>
<th>Patients with dcSSc</th>
<th>Patients with lcSSc</th>
<th>Patients with dcSSc</th>
</tr>
</thead>
<tbody>
<tr>
<td>All adverse events</td>
<td>105 (32.3)</td>
<td>107 (33.4)</td>
<td>105 (32.3)</td>
<td>107 (33.4)</td>
</tr>
<tr>
<td>Most frequent adverse events</td>
<td>Nasopharyngitis 56 (17.1)</td>
<td>37 (11.6)</td>
<td>Diarrhea 10 (3.0)</td>
<td>9 (2.8)</td>
</tr>
<tr>
<td>Fatal adverse event</td>
<td>2 (0.6)</td>
<td>1 (0.3)</td>
<td>2 (0.6)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Serious adverse event(s)</td>
<td>49 (15.3)</td>
<td>43 (13.2)</td>
<td>49 (15.3)</td>
<td>43 (13.2)</td>
</tr>
<tr>
<td>Severe adverse event(s)</td>
<td>33 (10.2)</td>
<td>24 (7.5)</td>
<td>33 (10.2)</td>
<td>24 (7.5)</td>
</tr>
<tr>
<td>Any adverse event(s)</td>
<td>107 (33.4)</td>
<td>107 (33.4)</td>
<td>107 (33.4)</td>
<td>107 (33.4)</td>
</tr>
</tbody>
</table>