BACKGROUND

- Sickle cell disease (SCD) is an autosomal recessive disorder caused by a mutation in the $\alpha$-chain of hemoglobin that leads to the production of sickle hemoglobin (HbS).
- When deoxygenated, HbS polymerizes and deforms red blood cells into a sickle shape and damages cell membranes.
- These damaged red blood cells block capillaries and undo harm, which triggers downstream effects of anemia, fatigue, tissue ischemia, vaso-occlusive crisis, vascular injury, and organ damage, leading to a decreased quality of life.
- A patient-reported outcome (PRO) instrument that penetrates the core elements of SCD would greatly aid drug development by giving insight into treatment impact.
- The Sickle Cell Disease Record of Daily Symptom Burden (SSCRDSB), formerly known as the Sickle Cell Disease Severity Measure, is a novel 9-item electronic PRO instrument developed to evaluate changes in SCD symptom burden—the first instrument in accord with US Food and Drug Administration (FDA) guidance for clinical trial endpoints.
- Subjective language use around pain and fatigue, the core symptoms of SCD, made the proper translation and cultural adaptation of the instrument paramount for the global phase 3 Hemoglobin Oxygen Afflux Modulation to Inhibit HbS Polymerization (HOPE) trial.

METHODS AND RESULTS

- **Development, translation, and patient cultural sensitivity validation**
- **SCRIBE SICKLE CELL RECORD OF DAILY SYMPTOM BURDEN™:**
  - To develop, test, translate, and culturally adapt the SSCRDSB for use in the HOPE trial
  - Subjective language use around pain and fatigue, the core symptoms of SCD, made the proper translation and cultural adaptation of the instrument paramount for the global phase 3 Hemoglobin Oxygen Afflux Modulation to Inhibit HbS Polymerization (HOPE) trial.
- Cognitive debriefing (10-item version) in adults (n=8) and adolescents (n=10) showed ambiguity around 1 question between US and UK English speakers that leads to the production of sickle hemoglobin (HbS).1
- **Hypothetical conceptual framework**
- **Hypothesized conceptual framework**
- **Concept elicitation interviews in 4 groups of adult (n=56) and adolescent patients (n=10)**
- **Draft item set developed after group 1 and 2 interviews**
- **Final 9-item SSCRDSB (version 1.1)**

<table>
<thead>
<tr>
<th>Grouping Variable</th>
<th>Group</th>
<th>APOVA (F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Considering your SCD symptoms in general, today was a good or bad day?</td>
<td>Good day</td>
<td>0.0 (1.0)</td>
</tr>
<tr>
<td>SSCRDSB location, mean (SD) (range)</td>
<td>40.7 (13.2)</td>
<td>20.4–64.5</td>
</tr>
<tr>
<td>Considering all your symptoms combined, how severe was your SCD today?</td>
<td>Severe</td>
<td>0.0 (1.0)</td>
</tr>
<tr>
<td>SSCRDSB location, mean (SD) (range)</td>
<td>54.2 (14.5)</td>
<td>20.4–78.7</td>
</tr>
</tbody>
</table>
| All items with threshold value were translated for each of the target languages: Chinese (Simplified, Traditional), Dutch, French, German, Italian, Portuguese, Russian, Spanish, and Turkish.

**Table 2: SSCRDSB Exploratory Anchor Questions**

- **Table 3: SSCRDSB Discriminates Daily Symptom Severity and Correlates With Self-Reported Crisis Rate**
- **Conclusions**

**References**


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