Sebetralstat Effectiveness in the Treatment of Hereditary Angioedema Attacks Rated Mild or Moderate at Baseline in the Phase 2 Trial

Hilary J. Longhurst,1* Michael D. Smith,2 Christopher Yea,2 Paul Audhya2

1 Auckland District Health Board and University of Auckland, Auckland, New Zealand; 2KalVista Pharmaceuticals, Salisbury, UK, and Cambridge, MA, US

*Presenting author

Introduction

- Hereditary angioedema (HAE) is a rare and potentially life-threatening genetic disease characterized by unpredictable recurrent episodes of swelling: abdominal and periorbital attacks are painful and can have a significant impact on patients’ quality of life.1
- Treatment guidelines for HAE recommend that all patients have access to medications for on-demand treatment and attacks as early as possible, aiming to decrease the intensity of symptoms, reduce attack duration, and achieve a more rapid resolution.2
- Currently, all approved on-demand treatments require parenteral administration, which presents significant challenges with time needed for medication preparation, finding a private area to administer medication, and injection-site associated pain and discomfort.3

Results

Baseline Attack Severity

- The medium time from recognition of attack onset to oral administration of study drug was 30 minutes.
- Baseline attack severity was categorized using PGI-S:
  - 20 (43%) of sebetralstat-treated attacks were categorized as mild and
  - 31 (57%) of placebo-treated attacks were categorized as mild.
- 23 (43%) were categorized as moderate.
- Paired comparisons for each patient who treated two attacks (n=53) showed a nearly even distribution of mild/moderate/mild, mixed severity (mild/mild/mixed moderate and mixed severity), and mixed severity.

<table>
<thead>
<tr>
<th>Attack Severity</th>
<th>Sebetralstat (n=57)</th>
<th>Placebo (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>41.5% (19/23)</td>
<td>60.9% (34/56)</td>
</tr>
<tr>
<td>Moderate</td>
<td>58.5% (28/48)</td>
<td>39.1% (21/54)</td>
</tr>
</tbody>
</table>

Symptom Relief by PGI-C

- Attacks of both mild and moderate severity that were treated with sebetralstat were more likely to achieve symptom relief by PGI-S within 12 hours compared to those treated with placebo.
- Improvement by PGI-S
  - Attacks of both mild and moderate severity that were treated with sebetralstat were more likely to achieve symptom relief by PGI-S compared to those treated with placebo (Table 2, Figure 4).
- Placebo-adjusted improvement by PGI-S was similar for mild and moderate attacks

<table>
<thead>
<tr>
<th>Severity of 2 Attacks by PGI-S</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild/Mild</td>
<td>18</td>
</tr>
<tr>
<td>Mild/Moderate/Mild</td>
<td>11</td>
</tr>
<tr>
<td>Moderate/Mild/Mild</td>
<td>6</td>
</tr>
<tr>
<td>Moderate/Moderate/Moderate</td>
<td>18</td>
</tr>
</tbody>
</table>

Figure 4. Achievement of Improvement by PGI-S Within 12 Hours of Study Drug by Baseline Attack Severity

Symptom Relief by VAS

- Attacks of both mild and moderate severity that were treated with sebetralstat were more likely to achieve symptom relief by VAS compared to those treated with placebo.
- Placebo-adjusted symptom relief by VAS was higher for mild compared with moderate attacks

Figure 6. Achievement of Symptom Relief by VAS Within 12 Hours of Study Drug by Baseline Attack Severity

Discussion

- Sebetralstat treatment provided relief of mild and moderate HAE attacks, showing meaningful treatment effect regardless of baseline attack severity, as shown by PGI-C, PGI-S, and VAS

Acknowledgments

The study was sponsored by KalVista Pharmaceuticals. Medical writing services were provided under the direction of the author by Courtyard Communications, a Healthcare writing company, and were supported by KalVista Pharmaceuticals.

Presented during the 2022 ANCA Workshop, October 31, 2022, Melbourne, Australia.

References