Ligelizumab Achieves Rapid Onset of Action, Improved and Sustained Efficacy Compared with Omalizumab in Patients with Chronic Spontaneous Urticaria Not Adequately Controlled by H1-antihistamines

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Introduction

- Ligelizumab is a humanised monovalent anti-IgE antibody that binds with higher affinity to IgE than omalizumab, which is currently the only licensed therapy available for patients with chronic spontaneous urticaria (CSU) that is inadequately controlled by H1-antihistamines (H1-AHS).
- This phase 2b dose-finding study examined the efficacy and safety of ligelizumab in patients with CSU, whose symptoms remain uncontrolled with H1-AHS alone or in combination with H1-AH and leukotriene receptor antagonists.

Methods

- This Phase 2b dose-finding, multicentre, randomised, double-blind, active and placebo-controlled study was designed to establish a dose-response relationship of QGE031 and evaluate its efficacy and safety compared to placebo and omalizumab.
- Adult patients with moderate to severe CSU (Urticaria Activity Score [UAS7] ≥ 16) were enrolled.
- Patients were randomised to receive subcutaneous ligelizumab 24, 72 or 240 mg, omalizumab 300 mg, or placebo every 4 weeks (q4w) over 20 weeks (5 administrations in each arm), or a single dose of ligelizumab 120 mg.
- The primary endpoint was complete hives response (Hives Severity Score [HSS7] = 0) at Week 12.
- Patients completed a daily diary Urticaria Activity score, which assessed itch and hives scores (ISS and HSS) and allowed calculation of weekly scores UAS7, ISS7 and HSS7.
- Safety was analysed during 20 weeks of treatment and 24 weeks of follow-up.

Results

Patients

- In total, 382 patients were included in this study.
- Baseline demographics and disease characteristics are presented in e-poster P2279.

Dose Response of Ligelizumab

- The primary objective of the study was achieved, with ligelizumab demonstrating a dose-response relationship with respect to complete hives response rates (HSS7 = 0) at Week 12 (p<0.001) (Figure 1).

Figure 1. Dose-response curve based on the proportion of patients achieving HSS7=0 at Week 12 (primary endpoint)

Urticaria Activity & Complete Response to Treatment

- Improved changes from baseline in HSS7, ISS7 and UAS7 were observed with ligelizumab 72 and 240 mg vs. omalizumab and ligelizumab 24 mg (Figure 2); the benefit in favour of ligelizumab 72 and 240 mg was sustained up to Week 32.
- At the end of the treatment period (Week 20), mean changes from BL in UAS7 were -15.2, -23.1 and -22.5 for ligelizumab 24, 72 and 240 mg, respectively, -18.2 for omalizumab 300 mg and -13.6 for placebo.
- High complete response rates (UAS7 = 0) were observed as early as Week 4; more patients were symptom-free with ligelizumab 72 and 240 mg vs. omalizumab throughout the 20-week treatment period.

Time to Loss of Complete Response

- Following the end of the treatment period, the median time to loss of complete response (i.e., time to re-presentation with active disease) was 10.5 weeks for ligelizumab 240 mg, 4 weeks each for ligelizumab 72 mg and omalizumab 300 mg, and 3 weeks for ligelizumab 24 mg.

Safety

- Similar incidences of adverse events were observed across all treatment groups (Table 1).
- No deaths or anaphylaxis were reported.

Table 1. Safety

<table>
<thead>
<tr>
<th>Category</th>
<th>Ligelizumab 72 mg</th>
<th>Omalizumab 300 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>105 (74.0)</td>
<td>100 (75.0)</td>
<td>56 (67.5)</td>
</tr>
<tr>
<td>Any SAE</td>
<td>14 (10.0)</td>
<td>12 (9.3)</td>
<td>5 (6.0)</td>
</tr>
<tr>
<td>AEs leading to discontinuation</td>
<td>4 (2.9)</td>
<td>4 (3.0)</td>
<td>3 (3.6)</td>
</tr>
<tr>
<td>Injection site reactions possibly related to treatment</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Most frequent AEs (% in any group)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomitus</td>
<td>3 (2.2)</td>
<td>2 (1.5)</td>
<td>2 (2.4)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>2 (1.5)</td>
<td>1 (0.8)</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Headache</td>
<td>4 (2.9)</td>
<td>4 (3.0)</td>
<td>4 (4.8)</td>
</tr>
</tbody>
</table>

Data are reported as observed. The dashed vertical line indicates the end of treatment period.

Figure 2. Mean change from baseline and the percentage of complete responders for (A) HSS7, (B) ISS7, and (C) UAS7 up to Week 32.

Conclusion

- In patients with moderate to severe CSU, ligelizumab exhibited a clear dose-response in the achievement of HSS7 = 0 at Week 12.
- Both ligelizumab 72 mg and 240 mg exhibited earlier and greater improvements in clinical responses (complete responses and change from BL in HSS7, ISS7 and UAS7) throughout Week 20 compared with ligelizumab 24 mg, omalizumab 300 mg and placebo.
- Ligelizumab 240 mg demonstrated a more durable treatment effect than omalizumab.
- Ligelizumab was well-tolerated and the safety profile was comparable with that of omalizumab.

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AE, adverse event; q4w, every 4 weeks; N, number of patients in the corresponding category; SAE, serious adverse event; SD, single dose; AE, adverse event; q4w, every 4 weeks; N, number of patients in the corresponding category; SAE, serious adverse event; SD, single dose;