Ligelizumab Achieves Sustained Control of Angioedema in Patients With Chronic Spontaneous Urticaria

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Disclosures

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Introduction

- Ligelizumab, a next generation, high affinity humanized monoclonal anti-IgE antibody, was studied in a Phase 2b trial (NCT02477332) and its extension study (NCT02649218) in patients with chronic spontaneous urticaria (CSU) inadequately controlled by standard of care including H<sub>1</sub>-antihistamines

- The primary objective of the core Phase 2b trial, to demonstrate a dose response relationship with ligelizumab with respect to the achievement of compete hives response (7-day hives severity score of 0) at Week 12, was achieved with 30.2%, 51.2% and 42.4% of patients treated with ligelizumab 24, 72 and 240 mg, respectively, versus 25.9% of patients with 300 mg omalizumab and 0% with placebo<sup>1</sup>

- Here, we report the impact of ligelizumab treatment compared with omalizumab and placebo on angioedema occurrence and severity during the core Phase 2b trial and extension study

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Study design of the core Phase 2b trial and follow-up period leading to the extension study

- Eligible patients enter the open-label, single arm (ligelizumab 240 mg q4w) 52 week extension study at Week 32 onwards if they remained in the core study follow-up period for at least 12 weeks and UAS7 ≥12

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The ligelizumab 24 mg and 120 mg s.d. arms are not presented further as they were not relevant on any outcome. Patients who remained in the follow-up period for at least 12 weeks and had active disease (UAS7 ≥12), could enter the extension study from Week 32 onwards. Following the 52-week open label period, patients entered a 52-week treatment free follow up period to assess durability of treatment effect.

n, number of patients; q4w, every 4 weeks; SD, single dose; UAS7, weekly Urticaria Activity Score

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Patient disposition during the core Phase 2b trial and the open-label, single-arm extension study

**Core Study**
- 382 patients randomised
- 349 patients\(^a\) entered post-treatment follow-up

**Extension Study**
- 226 patients with UAS\(_7>12\) entered the extension
- 201 patients completed open-label treatment

- **44 patients discontinued the double-blind treatment period:**
  - Protocol deviation (n=10)
  - Lack of efficacy (n=8)
  - Adverse event (n=7)
  - Subject/guardian decision (n=7)
  - Physician decision (n=5)
  - Non-compliance with med. (n=3)
  - Lost to follow-up (n=2)
  - Pregnancy (n=1)
  - Technical problems (n=1)

- **29 patients discontinued the post-treatment follow-up period:**
  - Subject/guardian decision (n=15)
  - Pregnancy (n=3)
  - Lost to follow-up (n=3)
  - Physician decision (n=3)
  - Lack of efficacy (n=1)
  - No longer needs treatment (n=1)
  - New therapy for CSU (n=1)
  - Non-compliance with med. (n=2)

- **25 patients discontinued the open-label treatment period:**
  - Adverse event (n=8)
  - Lack of efficacy (n=8)
  - Pregnancy (n=3)
  - Protocol deviation (n=3)
  - Subject/guardian decision (n=2)
  - Physician decision (n=1)

\(^a\)Patients who discontinued treatment during the double-blind period of the core study were encouraged to enter the post-treatment follow-up period and remain in the study for the safety analysis.

CSU, chronic spontaneous urticaria; n, number of patients; UAS\(_7\), weekly Urticaria Activity Score; Wk, Week

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Patient demographics and baseline disease characteristics were mostly balanced across treatment groups

<table>
<thead>
<tr>
<th>Core Phase 2b trial&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ligelizumab 72 mg (N=84)</th>
<th>Ligelizumab 240 mg (N=85)</th>
<th>Omalizumab 300 mg (N=85)</th>
<th>Placebo (N=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>44.3±12.4</td>
<td>42.9±10.5</td>
<td>41.8±13.1</td>
<td>45.4±11.2</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>61 (72.6)</td>
<td>67 (78.8)</td>
<td>66 (77.6)</td>
<td>31 (72.1)</td>
</tr>
<tr>
<td>Duration of CSU (years)</td>
<td>3.9±5.4</td>
<td>4.1±5.6</td>
<td>5.1±7.5</td>
<td>3.6±3.5</td>
</tr>
<tr>
<td>Angioedema, n (%)</td>
<td>40 (47.6)</td>
<td>39 (45.9)</td>
<td>45 (52.9)</td>
<td>25 (58.1)</td>
</tr>
<tr>
<td>AAS7&lt;sup&gt;c&lt;/sup&gt;</td>
<td>42.2 ± 25.0</td>
<td>32.8 ± 28.1</td>
<td>31.2 ± 22.7</td>
<td>39.6 ± 24.9</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data are mean ± standard deviation unless otherwise stated; <sup>b</sup>Treatment were administered every 4 weeks; <sup>c</sup>AAS7 measures angioedema activity over 7 days on a scale ranging 0–105

AAS7, weekly Angioedema Activity Score; n, number of evaluable patients; N, number of total patients; CSU, chronic spontaneous urticaria

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6 Business Use Only
Ligelizumab 240 mg achieved similar proportion of angioedema-free patients in both core and the extension study

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7 Business Use Only
Ligelizumab 240 mg achieved greater reductions in AAS7 compared to other treatment arms and this effect was sustained throughout the treatment period and follow-up period*.

*Patients were eligible to enter the extension study from Week 32 onwards. Red arrows indicate treatment visits. The dashed red vertical line indicates the end of treatment phase in the core study.

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Ligelizumab 240 mg achieved similar mean percentage changes from baseline for patients with AAS7>0 in the extension study compared with the core Phase 2b study.

AAS7, weekly Angioedema Activity Score; BL, baseline
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Conclusions

- Ligelizumab 240 mg achieved the highest percentage of angioedema-free patients in the core Phase 2b study, followed by ligelizumab 72 mg, omalizumab 300 mg, and placebo, at Week 12
- Treatment with ligelizumab 240 mg in the extension study achieved a similar high percentage of angioedema-free patients at Week 12 compared to the core Phase 2 study
- Ligelizumab 240 and 72 mg achieved greater percentage reductions in AAS7 compared with omalizumab and placebo at Week 12 in patients reporting angioedema in the core study
- Treatment with ligelizumab 240 mg achieved greater percentage reductions in AAS7 compared with omalizumab and placebo from baseline to the end of the core Phase 2b study and similar reductions in AAS7 were maintained throughout the extension study

AAS7, weekly Angioedema Activity Score
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