Results from the phase 2b study demonstrate that ligelizumab achieves sustained control of CSU symptoms during treatment-free follow-up

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Introduction

- Ligelizumab is a next generation high affinity humanized monoclonal anti-IgE antibody which results in rapid, strong and sustained symptom control for patients with CSU.
- Ligelizumab was well tolerated and achieved greater control of symptoms of hives, itch and angioedema versus omalizumab and placebo in patients with CSU up to Week 20 in the Phase 2b study.

Objective

To examine the maintenance of CSU symptom control following treatment withdrawal for ligelizumab 24, 72 and 240 mg compared with omalizumab 300 mg and placebo in the core phase 2b trial.

AEs, Adverse events; CSU, Chronic spontaneous urticaria; IgE, Immunoglobulin E; SAEs, Serious adverse events

1Maurer M. et al., Poster presented at EADV 2018 (12-16 September, Paris, France)
Phase 2b trial of ligelizumab in patients with CSU inadequately controlled with standard of care including H₁-antihistamines

The ligelizumab 120 mg s.d. arm is not presented further.

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.

q4w, every 4 weeks; sc, subcutaneous; s.d., single dose

*The ligelizumab 120 mg s.d. arm is not presented further

4 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
Patient disposition during the core phase 2b trial

382 patients randomised

Week -2

Screening

Double-blind treatment

338 patients (88.5%) completed the treatment phase

Week 20

349 patients a (91.4%) entered the follow-up

Follow-up

320 patients (83.8%) completed the follow-up

Week 44

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)

a Patients who discontinued treatment during the double-blind period were encouraged to remain in the study for the safety analysis and enter the post-treatment follow-up
Ligelizumab exhibited a clear dose-response in the achievement of complete hives response at Week 12\textsuperscript{a} during the core study.

Dose-response curve based on HSS7=0 response at Week 12\textsuperscript{b}

Proportion of patients achieving HSS7=0 at Week 12

HSS7, weekly hives severity score (measures the severity of hives over a period of 7 days on a scale ranging from 0 to 21, with higher scores indicating greater severity)

\textsuperscript{a}The proportion of patients achieving HSS7=0 at Week12 was the primary endpoint of the core study; \textsuperscript{b}The dose-response curve shows the median, 20 and 80 percentile, from 1000 bootstrap samples. Dots with error bars represent point estimates and asymptotic 60% confidence interval for each dose in observed data.
Ligelizumab 240 mg demonstrated longer sustained complete hives response vs ligelizumab 24 and 72 mg, omalizumab and placebo.

Time to loss of HSS7=0 for patients achieving the response at Week 20

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Median time to loss of HSS7=0 (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ligelizumab 240 mg</td>
<td>9.5</td>
</tr>
<tr>
<td>Ligelizumab 72 mg</td>
<td>4.0</td>
</tr>
<tr>
<td>Ligelizumab 24 mg</td>
<td>3.0</td>
</tr>
<tr>
<td>Omalizumab 300 mg</td>
<td>4.0</td>
</tr>
<tr>
<td>Placebo</td>
<td>1.0</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Study week</th>
<th>Cumulative proportion of patients, %</th>
</tr>
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<tbody>
<tr>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>28</td>
<td>20</td>
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<tr>
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<td>44</td>
<td>60</td>
</tr>
<tr>
<td>48</td>
<td>70</td>
</tr>
</tbody>
</table>

HSS7, weekly hives severity score (measures the severity of hives over a period of 7 days on a scale ranging from 0 to 21, with higher scores indicating greater severity)
Ligelizumab 240 mg demonstrated longer complete control of symptoms vs ligelizumab 24 and 72 mg, omalizumab and placebo.

Time to loss of UAS7=0 for patients achieving the response at Week 20

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</table>

\textsuperscript{a}For patients achieving the response at Week 20.
\textsuperscript{b}The median time to loss of UAS7 is based on a small sample size of 2 patients who achieved complete symptom control at Week 20.

UAS7, weekly urticaria activity score (composite of the weekly itch severity and hives severity scores; the scale ranges from 0 to 42, with higher scores indicating greater severity)
Conclusions

• Ligelizumab 240 mg demonstrated more sustained control of symptoms compared with ligelizumab 24 and 72 mg, omalizumab 300 mg and placebo during treatment-free follow-up

• Ligelizumab 240 mg demonstrated the slowest return of uncontrolled symptoms during the treatment-free follow-up for patients having achieved a well-controlled disease state

• Time to loss of response in the ligelizumab 72 mg and omalizumab 300 mg arms were similar

• Data from phase 3 studies, examining the efficacy and safety of ligelizumab (72 and 120 mg) versus omalizumab 300 mg and placebo, will be used to determine the optimal dose to achieve sustained control of CSU symptoms in patients who are inadequately controlled with H₁-antihistmines
Thank you