Re-treatment with ligelizumab achieves high rates of completely- and well-controlled symptoms in chronic spontaneous urticaria

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Chronic spontaneous urticaria (CSU) is a skin disorder characterized by the occurrence of itchy wheals (hives), angioedema, or both for 6 weeks or more in the absence of specific external stimuli, and has a significant negative impact on the quality of life. Ligelizumab is a next generation, high affinity humanized monoclonal anti-IgE antibody, which has shown greater control of symptoms compared with omalizumab in this Phase 2b trial (NCT02477332).

Here, we report the time to response and cumulative response rates in the ligelizumab core Phase 2b trial compared to the 52-week treatment period of the extension study.

Phase 2b trial and open-label extension study of ligelizumab in patients with CSU inadequately controlled with H₁-antihistamines

The 120 mg single-dose (SD) arm was chosen to characterise the pharmacokinetics/pharmacodynamics. Data from this arm assesses the duration of the response and correlates this with the concentration of drug in the serum at the time when symptoms reappear. 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, including potential for disease modification.
Patient disposition during the core Phase 2b trial and the open-label, single-arm extension study

**Core Study**

- 382 patients randomised
- 349 patients entered post-treatment follow-up
- 226 patients with UAS7 ≥ 12 entered the extension
- 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)

**Extension Study**

- 201 patients completed open-label treatment
- 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)

**Timeline**

- Wk -2: Screening
- Wk 0: End of Core Study
- Wk 20: Double-blind treatment
- Wk 32: Follow-up
- Wk 44: End of Extension Study
- Wk 52: Open-label treatment
- Wk 104: Follow-up

* 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

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*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.*
All ligelizumab doses achieved higher cumulative UAS7=0 response rates in the core Phase 2b trial than omalizumab and placebo.

### Study phase | Cumulative UAS7=0 response rates
--- | ---
Core study | Ligelizumab 24 mg, 72 mg, and 240 mg treatments achieved higher cumulative UAS7=0 response rates compared with omalizumab and placebo at Week 20
Re-treatment with ligelizumab 240 mg resulted in similar cumulative UAS7=0 response rates compared to core study.
Re-treatment with ligelizumab 240 mg resulted in similar cumulative UAS7=0 response rates compared to core study.
Re-treatment with ligelizumab 240 mg beyond Week 20 further increased the cumulative UAS7=0 and UAS7≤6 response rates up to 75.8% and 84.2%.

<table>
<thead>
<tr>
<th>Response rate</th>
<th>Extension study</th>
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<tbody>
<tr>
<td>UAS7=0</td>
<td>Ligelizumab 240 mg achieved cumulative UAS7=0 response rates of 36.9% at Week 4, 62.4% at Week 20, and 75.8% at Week 52</td>
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<tr>
<td>UAS7≤6</td>
<td>Ligelizumab 240 mg achieved cumulative UAS7≤6 response rates of 58.7% at Week 4, 76.8% at Week 20, and 84.2% at Week 52</td>
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</tbody>
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Re-treatment with ligelizumab resulted in similar efficacy to core study regardless of the initial treatment dose.

- **UAS7 = 0**
  - Core study Week 12: 47.1% (72 mg), 52.9% (240 mg), 45.7% (240 mg → 240 mg), 52.2% (240 mg → 240 mg)
  - Extension study Week 12: 60.8% (72 mg), 60.8% (240 mg), 47.8% (240 mg), 60.9% (240 mg → 240 mg)

- **UAS7 ≤ 6**
  - Core study Week 12: 60.8% (72 mg), 52.9% (240 mg), 45.7% (240 mg → 240 mg), 52.2% (240 mg → 240 mg)
  - Extension study Week 12: 60.8% (72 mg), 60.8% (240 mg), 47.8% (240 mg), 60.9% (240 mg → 240 mg)

q4w, every 4 weeks; UAS7, 7-day urticaria activity score

Patients were on 72 mg and 240 mg q4w dose in the Phase 2b core study. All patients received ligelizumab 240 mg q4w in the extension study.
More patients achieved UAS7=0 responses with ligelizumab treatment compared to omalizumab 300 mg treatment or placebo.

In patients who were treated with ligelizumab in the initial phase 2b trial, re-treatment with ligelizumab 240 mg resulted in similar response rates.

Phase 3 studies are ongoing to evaluate the efficacy and safety of ligelizumab treatment up to 1 year in patients with CSU inadequately controlled with H1-antihistamines at approved doses.
Thank you