Ligelizumab Achieves Fast Control Of Symptoms In Numerically More Patients With Chronic Spontaneous Urticaria Versus Omalizumab

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In relation to this presentation, I declare the following, real or perceived conflicts of interest:

<table>
<thead>
<tr>
<th>Type</th>
<th>Company</th>
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<tbody>
<tr>
<td>Employment full time / part time</td>
<td>Novartis Pharma AG, Basel, Switzerland</td>
</tr>
<tr>
<td>Research Grant (P.I., collaborator or consultant; pending and received grants)</td>
<td>NA</td>
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<tr>
<td>Other research support</td>
<td>NA</td>
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<td>Speakers Bureau / Honoraria</td>
<td>NA</td>
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<tr>
<td>Ownership interest (stock, stock-options, patent or intellectual property)</td>
<td>Novartis shareholder</td>
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<td>Consultant / advisory board</td>
<td>NA</td>
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Introduction

- Chronic spontaneous urticaria (CSU) is characterized by the occurrence of itchy wheals (hives), angioedema, or both for 6 weeks or more in the absence of specific external stimuli\(^1\) and has a significant negative impact on the quality of life\(^2\)

- Ligelizumab is a next generation high-affinity humanized monoclonal anti-IgE antibody developed for the treatment of CSU patients inadequately controlled by an H\(_1\)-AH

- In a Phase 2b clinical trial, ligelizumab, demonstrated improved symptom control in patients with moderate to severe CSU inadequately controlled with H\(_1\)-AH\(^3\)

- Here, we analyzed the early response after the first dose (the first 4 weeks) and the sustainability over the first 12 weeks with ligelizumab 72 mg and 240 mg vs. omalizumab 300 mg

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H1-AH, H1-antihistamines; CSU, chronic spontaneous urticaria; IgE, immunoglobulin E
Phase 2b study of ligelizumab in patients with CSU inadequately controlled with H₁-AH

- The ligelizumab 24 and 120 mg SD arms are not presented further as they were not relevant to outcomes presented here.

- 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 onward; H₁-AH, H₁-antihistamines; CSU, chronic spontaneous urticaria; n, number of patients; q4w, every 4 weeks; R, randomized; SD, single dose; UAS7, weekly Urticaria Activity Score

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R = Randomization

= Treatment visit in the core study

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a The ligelizumab 24 and 120 mg SD arms are not presented further as they were not relevant to outcomes presented here.

b 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 onward; H₁-AH, H₁-antihistamines; CSU, chronic spontaneous urticaria; n, number of patients; q4w, every 4 weeks; R, randomized; SD, single dose; UAS7, weekly Urticaria Activity Score
Methods

- Adult patients with moderate to severe CSU (UAS7≥16 at baseline) were included in the study and were provided with an electronic diary to capture their daily urticaria symptoms (Urticaria Activity Score [UAS])

- The UAS7 is a 7 day cumulative score of daily itch severity (scored 0[itch free]–3[severe itch]) and daily number of hives (scored 0–3: 0=no hives, 1=1–6 hives, 2=7–12 hives, and 3=13 hives or more) with a total score ranging between 0 and 42

- The weekly proportion of patients with either complete control of urticaria symptoms (UAS7=0) or well controlled urticaria (UAS7≤6), and the mean percentage of weeks that patients were urticaria free or well controlled up to Week 12 was analyzed
Patients treated with ligelizumab 72 mg and 240 mg achieved UAS7=0 as early as Week 2 and at a numerically higher rate than with omalizumab*.

*Analysis performed on as observed data
N, total number of number of patients in each arm at that time point; q4w, every 4 weeks; UAS7, weekly Urticaria Activity Score
Patients treated with ligelizumab 72 mg and 240 mg achieved UAS7≤6 as early as Week 1, with numerically higher rates than with omalizumab as early as Week 2*

*Analysis performed on as observed data
N, total number of number of patients in each arm at that time point; q4w, every 4 weeks; UAS7, weekly Urticaria Activity Score
For patients with well-controlled urticaria at Week 12, the rate of urticaria free weeks was numerically higher for ligelizumab vs. omalizumab.

For cumulative % of weeks with response, patients with UAS7≤6 at week 12 were analyzed. Error bars represent standard deviation.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Weeks 1-4</th>
<th>Weeks 1-12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ligelizumab 72 mg q4w</td>
<td>34.4</td>
<td>56.0</td>
</tr>
<tr>
<td>Ligelizumab 240 mg q4w</td>
<td>37.2</td>
<td>60.6</td>
</tr>
<tr>
<td>Omalizumab 300 mg q4w</td>
<td>22.5</td>
<td>38.1</td>
</tr>
</tbody>
</table>

For cumulative % of weeks with response, patients with UAS7≤6 at week 12 were analyzed. Error bars represent standard deviation. n, number of patients (who achieved UAS7≤6 at Week 12) analyzed; N, total number of patients in the arm; q4w, every 4 weeks; UAS7, weekly urticaria activity score.
For patients with well-controlled urticaria at Week 12, the rate of well-controlled urticaria weeks was numerically higher for ligelizumab vs. omalizumab.

For cumulative % of weeks with response, patients with UAS7≤6 at week 12 were analyzed. Error bars represent standard deviation.

**Table: UAS7≤6**

<table>
<thead>
<tr>
<th>Group</th>
<th>UAS7≤6 Weeks 1-12</th>
</tr>
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<tbody>
<tr>
<td>Ligelizumab 72 mg q4w n/N=49/84</td>
<td>77.8</td>
</tr>
<tr>
<td>Ligelizumab 240 mg q4w n/N=41/85</td>
<td>77.9</td>
</tr>
<tr>
<td>Omalizumab 300 mg q4w n/N=40/85</td>
<td>71.9</td>
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</tbody>
</table>

For cumulative % of weeks with response, patients with UAS7≤6 at week 12 were analyzed. Error bars represent standard deviation. n, number of patients (who achieved UAS7≤6 at Week 12) analyzed; N, total number of patients in the arm; q4w, every 4 weeks; UAS7, weekly urticaria activity score.
Complete urticaria control (UAS7=0) was achieved numerically faster with ligelizumab than with omalizumab.
Well-controlled urticaria (UAS7≤6) was achieved numerically faster with ligelizumab than with omalizumab.

### Graph

- **Ligelizumab 72 mg q4w**
  - N=84
  - Kaplan-Meier median 3 weeks
  - 5 weeks
  - 6 weeks

- **Ligelizumab 240 mg q4w**
  - N=85

- **Omalizumab 300 mg q4w**
  - N=85

**Legend**
- UAS7≤6
- Cumulative proportion of patients with UAS7≤6 response (%)
- Weeks

q4w, every 4 weeks; UAS7, weekly Urticaria Activity Score
Conclusion

- In the Phase 2b study, a numerically larger proportion of CSU patients treated with ligelizumab showed complete symptom control after the first dose (within 2 weeks) vs. omalizumab.

- For patients who were well-controlled at Week 12, ligelizumab provided a numerically more pronounced and stable response in terms of complete control of urticaria symptoms vs. omalizumab throughout the first 12 weeks of treatment.

- Time to first response for patients who achieved complete control of urticaria and well-controlled urticaria was numerically faster with ligelizumab than with omalizumab.

- The ongoing Phase III studies (PEARL 1 and PEARL 2) will provide additional insights into the clinical use of ligelizumab for patients with CSU.