High proportion of patients with moderate to severe chronic spontaneous urticaria achieved complete response with ligelizumab: data from the phase 2b study

Bernstein J. A.¹, Maurer M.², Giménez-Arnau A.³, Soong W.⁴, Sussman G.⁵, Metz M.², Sitz K.⁶, Hide M.⁷, Hua E.⁸, Barve A.⁹, Severin T.¹⁰, Janocha R.¹⁰

¹University of Cincinnati College of Medicine and Bernstein Clinical Research Center, Cincinnati, United States; ²Department of Dermatology and Allergy, Charité Universitätsmedizin, Berlin, Germany; ³Dermatology Department, Hospital del Mar-Parc de Salut Mar, Universitat Autònoma, Barcelona, Spain; ⁴Alabama Allergy and Asthma Center, Clinical Research Center of Alabama, Alabama, United States; ⁵Division of Allergy and Clinical Immunology, University of Toronto, Toronto, Canada; ⁶Clinical Research Center, Little Rock Allergy and Asthma Clinic, Little Rock, Arkansas, United States; ⁷Hiroshima University, Hiroshima, Japan; ⁸Shanghai Novartis Trading Ltd, Shanghai, China; ⁹Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, United States; ¹⁰Novartis Pharma AG, Basel, Switzerland.

Disclosures

Bernstein JA reports grants and personal fees from Novartis, Astra Zeneca, Allakos, and Genentech outside the submitted work. Maurer M. is or recently was a speaker and/or advisor for and/or has received research funding from Amgen, Allakos, Aralez, AstraZeneca, Celldex, FAES, Genentech, GIIInnovation, Kyowa Kirin, Leo Pharma, Menarini, Novartis, Moxie, MSD, Roche, Sanofi, Third Harmonic, UCB, and Uriach. Giménez-Arnaú A. reports roles as a Medical Advisor for Uriach Pharma, Sanofi and Genentech, Novartis, FAES, GSK and has research grants supported by Uriach Pharma, Novartis and Instituto Carlos III- FEDER; she also participates in educational activities for Uriach Pharma, Novartis, Genentech, Menarini, LEO- PHARMA, GSK, MSD, Almirall and Sanofi. Soong W has been an advisor and/or clinical investigator and/or received speaker’s honoraria and/or received consulting fee and/or grants and/or participated as a clinical investigator for/from AbbVie, Aimmune Therapeutics, Inc., AstraZeneca, Galderma, Genentech, GlaxoSmithKline, Greer, Novartis, Pfizer, Regeneron, Sanofi and Teva. Sussman G. has received research support from Aimmune, Amgen, Astra-Zeneca, DBV technologies, Genentech, Kedrion S.p.A, Leo Pharma Inc., Novartis, Nuvo Pharmaceuticals Inc., Sanofi, Stallergenes, Merck and Schering-Plough; is a medical advisor and/ or has received payment for lectures from Merck, Novartis, CSL Behring, Pfizer, Anaphylaxis Canada, the Allergy Asthma and Immunology Society of Ontario and the Canadian Hereditary Angioedema Network. Metz M reports personal fees from Aralez, moxie, Novartis, Roche, Sanofi and from Uriach. Hide M. has received lecture and/or consultation fees from TAIHO Pharmaceutical, Novartis, MSD, Teikoku Seiyaku, Mitsubishi Tanabe Pharma Uriach and Kyowahakko-Kirin. Hua E. is an employee of Shanghai Novartis Trading Ltd., Shanghai, China. Barve A. is an employee of Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, United States. Severin T., and Janocha R. are employees of Novartis Pharma AG, Basel Switzerland.
Introduction

- **Ligelizumab** is a **next generation high-affinity** humanized monoclonal **anti-IgE antibody** that has demonstrated **good efficacy and safety** in patients with chronic spontaneous urticaria (CSU) inadequately controlled by H1-antihistamine

- In the core Phase 2b study, ligelizumab exhibited a dose dependent response in terms of complete control of hives (HSS7=0) at Week 12 (primary endpoint) and achieved **improved control of symptoms** compared with omalizumab and placebo

- Here, we present an exploratory **analysis of the efficacy of ligelizumab** 72 mg and 240 mg vs. omalizumab at Weeks 4 and 12 in patients with moderate or severe CSU

CSU, chronic spontaneous urticaria; HSS7, weekly Hives Severity Score
Phase 2b study of ligelizumab in patients with CSU inadequately controlled with an H1-antihistamine

- **Screening**
- **Randomization**
- **Treatment**
- **Follow-up**

<table>
<thead>
<tr>
<th>Week 0</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ligelizumab 240 mg q4w (n=85)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ligelizumab 72 mg q4w (n=84)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ligelizumab 24 mg q4w (n=43)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omalizumab 300 mg q4w (n=85)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ligelizumab 120 mg SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo q4w (n=42)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n=43)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Eligible to enrol in the extension study**

---

*a* The ligelizumab 24 and 120 mg SD arms are not presented further as they were not relevant to outcomes presented in this oral presentation.

*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.

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


4 Business Use Only
Patients were categorised into five groups based on their CSU activity (UAS7 scores):

- **UAS7=28–42**, severe activity CSU
- **UAS7=16–27**, moderate activity CSU
- **UAS7=7–15**, mild activity CSU
- **UAS7=1–6**, well-controlled CSU
- **UAS7=0**, urticaria-free

Patients with moderate or severe disease activity were included in this exploratory analysis.

**Response to ligelizumab (72 and 240 mg) and omalizumab 300 mg** at Week 4 and Week 12 was analysed in each group of patients separately*

*Data of Phase 2b trial (NCT02477332), a randomised, double-blind study of ligelizumab (24, 72 or 240 mg q4w or 120 mg single dose) vs. omalizumab 300 mg q4w or placebo in adult patients with moderate to severe CSU (UAS7≥16) was analysed.

BL, baseline; CSU, chronic spontaneous urticaria; q4w, every 4 weeks; UAS7, weekly Urticaria Activity Score

Balanced distribution of patients across treatment arms: Majority of patients were of severe CSU activity at BL

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ligelizumab 72 mg q4w (N=84)</td>
<td>75.0</td>
</tr>
<tr>
<td>Ligelizumab 240 mg q4w (N=85)</td>
<td>65.9</td>
</tr>
<tr>
<td>Omalizumab 300 mg q4w (N=85)</td>
<td>58.8</td>
</tr>
</tbody>
</table>

Protocol deviations have been captured for subjects who did not qualify based on UAS7 score.
BL, baseline; CSU, chronic spontaneous urticaria; N, number of patients; q4w, every 4 weeks; UAS7, weekly Urticaria Activity Score
In patients with moderate CSU activity, complete response was achieved by a markedly higher percentage of patients with ligelizumab vs omalizumab

- At Week 4, 35.0% and 25.9% of patients achieved UAS7=0 with ligelizumab 72 and 240 mg, respectively, vs. 12.5% with omalizumab 300 mg

- At Week 12, 60.0% and 40.7% of patients achieved UAS7=0 with ligelizumab 72 and 240 mg, respectively, vs. 34.4% with omalizumab 300 mg

*The percentages do not add up to 100% since some subjects discontinued the study early or due to missing data at the visit.

BL, baseline; CSU, chronic spontaneous urticaria; N, number of patients; q4w, every 4 weeks; UAS7, weekly Urticaria Activity Score

In patients with severe CSU activity, complete response was achieved by a markedly higher percentage of patients with ligelizumab vs omalizumab

- At Week 4, 28.6% and 32.1% of patients achieved UAS7=0 with ligelizumab 72 and 240 mg, respectively, vs. 22.0% with omalizumab 300 mg

- At Week 12, 38.1% and 41.1% of patients achieved UAS7=0 with ligelizumab 72 and 240 mg, respectively, vs. 20.0% with omalizumab 300 mg

*The percentages do not add up to 100% since some subjects discontinued the study early or due to missing data at the visit

BL, baseline; CSU, chronic spontaneous urticaria; N, number of patients; q4w, every 4 weeks; UAS7, weekly Urticaria Activity Score

Conclusions

- In the Phase 2b core study, **ligelizumab** achieved **numerically higher response rates** in patients with moderate or severe CSU compared with omalizumab, and a **numerically higher rate of complete response** compared with omalizumab
  - As early as Week 4, in moderate CSU at baseline, up to 90% of patients decreased by at least 1 activity band, after ligelizumab treatment
  - As early as Week 4, in severe CSU at baseline, up to ~70% of patients decreased by 1 activity band or more, after ligelizumab treatment
- These results will be **explored further in the ongoing Phase 3 pivotal trials** of ligelizumab in CSU