Complete symptom control in patients with chronic spontaneous urticaria is associated with an improvement in health-related quality of life: Data from the Phase 2b ligelizumab study

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Disclosure

Bernstein J.A. reports grants and personal fees from Novartis, Astra Zeneca, Allakos, Genentech, Sanofi Regeneron, Celldex, and Amgen outside the submitted work. Giménez-Arnau 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. 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, GllInnovation, Kyowa Kirin, Leo Pharma, Menarini, Novartis, Moxie, MSD, Roche, Sanofi, Third Harmonic, UCB, and Uriach. Staubach P. has received research funding and/or fees for consulting and/or lectures from Novartis, CSL Behring, Shire, MSD, Schering-Plough, Abbvie, Viropharma, Leo Pharma, Leti Pharma, Pohl-Boskamp GmbH, Astella, Allergika, Karrer, Allmirall, Sanofi, Octapharma, Pfleger GmbH, Beiersdorf, L’Oreal, Lilly, Janssen, Celgene, Hermal, UCB, Allmirall, Astelas, Sobi, and Pfizer. Barbier N., Severin T., Joubert Y. and Balp M-M. are full time employees of Novartis Pharma AG, Basel, Switzerland. Hua E. is an employee of China Novartis Institutes for Biomedical Research Co. Ltd.
Introduction

- Chronic spontaneous urticaria (CSU) reduces patients’ health-related quality of life (HRQoL), impacting daily activities, sleep and work\textsuperscript{1–5}

- Many patients with CSU do not achieve complete control of signs and symptoms despite using standard of care treatments (H\textsubscript{1}-antihistamines and omalizumab)\textsuperscript{6,7}

- Ligelizumab, a next generation high-affinity humanised monoclonal anti-IgE antibody, has been shown to be effective in patients with CSU inadequately controlled by H\textsubscript{1}-antihistamines alone or in combination with H\textsubscript{2}-antihistamine and/or leukotriene receptor antagonist during a 20-week core Phase 2b study (NCT02477332)\textsuperscript{8}

- Here, the relationship between complete urticaria control (UAS7=0) and PROs using the Phase 2b study data were analysed

CSU, Chronic Spontaneous Urticaria; IgE, Immunoglobulin E; PROs, Patient Reported Outcomes; UAS7, weekly Urticaria Activity Score.


Bernstein JA, et al. EADV 29\textsuperscript{th} September–2\textsuperscript{nd} October, 2021, Virtual Meeting Experience.
Methods

- A dose-finding, multicentre, randomised, double-blind, active- and placebo-controlled phase 2b study was previously reported. The present analysis includes all patients in the study who were randomised to receive ligelizumab 24 mg, 72 mg, 120 mg (single-dose arm) or 240 mg, or omalizumab 300 mg, or placebo.

- Patients received treatment q4w with a total of 5 injections over 20 weeks and a treatment-free follow-up for 24 weeks.

- The percentage of evaluations achieving DLQI 0-1 response, SIS7=0, AIS7=0, and overall work impairment=0 per UAS7 band (urticaria free=0, well-controlled=1–6, mild=7–15, moderate=16–27 and severe=28–42) were reported.

- Observed data were considered up to Week 32 (after which the majority of patients switched to an extension study upon relapse) for all patients in the full analysis set.

- The percentage of evaluations of each response among consecutive UAS7 bands was compared using ORs.

- Pooled phase 2b trial data from patients treated with ligelizumab 72 mg, 240 mg, omalizumab 300 mg, or placebo q4w for 20 weeks are used for the analysis.

- Generalised Estimating Equations were used to obtain ORs, 95% CI and nominal p-values.

AIS7, weekly Activity Interference Score (daily scores summed over 7-days); CI, Confidence Interval; DLQI, Dermatology Life Quality Index; OR, Odds Ratio; q4w, every 4 weeks; SIS7, weekly Sleep Interference Score (daily scores summed over 7-days); UAS7, weekly Urticaria Activity Score. 1. Maurer M et al. *N Engl J Med*, 2019;381:1321–32. Bernstein JA, et al. *EADV 29th September–2nd October, 2021, Virtual Meeting Experience.*
Baseline characteristics were well-balanced across the groups

Data from 382 patients who were randomized in this study were used in the current analysis

<table>
<thead>
<tr>
<th>Characteristics</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>
<th>Study Total (N=382)</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>
<td>43.3±12.5</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>61 (73.0)</td>
<td>67 (79.0)</td>
<td>66 (78.0)</td>
<td>31 (72.0)</td>
<td>286 (75.0)</td>
</tr>
<tr>
<td>BMI†</td>
<td>28.5±7.1</td>
<td>27.9±6.1</td>
<td>28.1±6.4</td>
<td>27.4±6.5</td>
<td>27.9±6.5</td>
</tr>
<tr>
<td>Race no. (%)+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>20 (23.8)</td>
<td>19 (22.4)</td>
<td>12 (14.1)</td>
<td>9 (20.9)</td>
<td>76 (20)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>57 (67.9)</td>
<td>65 (76.5)</td>
<td>67 (78.8)</td>
<td>31 (72.1)</td>
<td>283 (74.1)</td>
</tr>
<tr>
<td>Time since diagnosis 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>
<td>4.3±6.0</td>
</tr>
<tr>
<td>IgE level (IU/mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>101.0</td>
<td>74.1</td>
<td>86.2</td>
<td>111.5</td>
<td>87.2</td>
</tr>
<tr>
<td>Range</td>
<td>0–942.0</td>
<td>0–3480.0</td>
<td>0–14,100.0</td>
<td>2.2–870.0</td>
<td>0–14,100.0</td>
</tr>
</tbody>
</table>

*Plus-minus values are mean ± SD; †BMI is the weight in kilograms divided by the square of the height in meters; ‡Race was reported by the patient or determined by the investigator. The 120 mg single-dose arm was chosen to characterize the pharmacokinetics/pharmacodynamics; the ligelizumab 24 mg and 120 mg arms are not included in the table but are included in the total column. BMI, Body Mass Index; CSU, Chronic Spontaneous Urticaria; IgE, Immunoglobulin E; n, Number of Patients; N, Number of Associated Evaluations.

Disease demographics were well-balanced across the groups

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<th>Study Total (N=382)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekly itch-severity score* §</td>
<td>13.6 ± 4.1</td>
<td>13.0 ± 4.3</td>
<td>12.7 ± 4.4</td>
<td>13.6 ± 4.1</td>
<td>13.1 ± 4.1</td>
</tr>
<tr>
<td>Weekly hives-severity score* §</td>
<td>18.1 ± 4.3</td>
<td>17.3 ± 4.3</td>
<td>16.6 ± 4.7</td>
<td>17.6 ± 4.1</td>
<td>17.3 ± 4.4</td>
</tr>
<tr>
<td>Weekly urticaria-activity score* ¶</td>
<td>31.7 ± 7.3</td>
<td>30.3 ± 7.3</td>
<td>29.3 ± 7.9</td>
<td>31.1 ± 6.8</td>
<td>30.4 ± 7.4</td>
</tr>
<tr>
<td>Positive chronic urticaria index, n (%)**</td>
<td>32 (38.1)</td>
<td>35 (41.2)</td>
<td>33 (38.8)</td>
<td>14 (32.6)</td>
<td>145 (38.0)</td>
</tr>
</tbody>
</table>

**Background medication**

| Locally approved dose of H₄AH          | 35 (41.7)                | 36 (42.4)               | 37 (44.0)               | 19 (44.2)      | 164 (42.9)        |
| Escalated dose of locally approved H₄AH | 49 (58.3)                | 49 (57.6)               | 48 (56.5)               | 24 (57.1)      | 218 (57.1)        |

*Plus-minus values are means ± SD. § The weekly itch-severity and hives-severity scores measure the severity of itch and hives, respectively, over a period of 7 days on scales ranging from 0 to 21, with higher scores indicating greater severity. ¶ The weekly urticaria activity score is a composite of the weekly itch-severity and hives-severity scores. Scores range from 0 to 42, with higher scores indicating greater severity. **A positive CU Index (scores range from 1 to 50, with scores ≥ 10 representing a positive result) indicates that the patient has either an autoimmune basis for the urticaria or an alternative histamine-releasing factor that has been associated with greater disease severity than that in patients with a negative CU Index. The 120 mg single-dose arm was chosen to characterize the pharmacokinetics/pharmacodynamics; the ligelizumab 24 mg and 120 mg arms are not included in the table but are included in the total column. AH, Antihistamines; n, Number of Patients; N, Number of Associated Evaluations.

In patients with UAS7=0, 91.1% (n=317) reached DLQI 0–1, simultaneously

- In patients with UAS7=0 vs those with UAS7=1–6, there was a 5 times higher (OR 95% CI 3.2 to 9.1) likelihood of having DLQI 0-1
- The least square (LS) mean total score of DLQI in patients with completely controlled disease vs patients with well-controlled disease was 0.8 vs 2.3 (P=0.0003), making this clinically relevant

OR 5.37, P<0.0001

Data up to Week 32 of the Phase 2b core study, including baseline results, were included in this analysis. DLQI= 0-1 score of 0-1 equates to no effect on patient's quality of life.

UAS7 disease activity categories; complete control (UAS7=0); well-controlled (UAS7=1–6); mild (UAS7=7–15); moderate (UAS7=16–27); severe (UAS7=28–42). CI, Confidence Interval; DLQI, Dermatology Life Quality Index; n, Number of Associated Evaluations; OR, Odds Ratio; UAS7, weekly Urticaria Activity Score.

In patients with UAS7=0, 99.7% (n=2,895) reached SIS7=0, simultaneously

- In patients with UAS7=0 vs those with UAS7=1–6, there was a 137 times higher (OR 95% CI 37.2 to 502.8) likelihood of having SIS7=0
- The least square (LS) mean total score of SIS7 in completely controlled patients vs well-controlled disease was 0.2 vs 1.0 (P<0.0001)

Data up to Week 32 of the Phase 2b core study, including baseline results, were included in this analysis. SIS7 of 0 equates to no effect on patient’s sleep. UAS7 disease activity categories: complete control (UAS7=0); well-controlled (UAS7=1–6); mild (UAS7=7–15); moderate (UAS7=16–27); severe (UAS7=28–42). CI, Confidence Interval; n, Number of Associated Evaluations; OR, Odds Ratio; SIS7, weekly Sleep Interference Score; UAS7, weekly Urticaria Activity Score.

In patients with UAS7=0, 99.7% (n=2,898) reached simultaneously an AIS7=0

- In patients with UAS7=0 vs those with UAS7=1–6, there was a 178 times higher (OR 95% CI 29.2 to 1085.8) likelihood of having AIS7=0

Data up to Week 32 of the Phase 2b core study, including baseline results, were included in this analysis. AIS7 score of 0 equates to no effect on patient’s activity. UAS7 disease activity categories; complete control (UAS7=0); well-controlled (UAS7=1–6); mild (UAS7=7–15); moderate (UAS7=16–27); severe (UAS7=28–42). AIS7, weekly Activity Interference Score; n, Number of Associated Evaluations; OR, Odds Ratio; UAS7, weekly Urticaria Activity Score.

In patients with UAS7=0, 85.3% (n=209) reached an Overall Work Impairment =0

- In patients with UAS7=0 vs those with UAS7=1–6, there was a 3 times (OR 95% CI 1.8 to 5.1) higher likelihood of having Overall Work Impairment=0

Data up to Week 32 of the Phase 2b core study, including baseline results, were included in this analysis. Overall Work Impairment score of 0 equates to no effect on patients’ work. UAS7 disease activity categories; complete control (UAS7=0); well-controlled (UAS7=1–6); mild (UAS7=7–15); moderate (UAS7=16–27); severe (UAS7=28–42). n, Number of Associated Evaluations; OR, Odds Ratio; UAS7, weekly Urticaria Activity Score.


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Conclusions

- Control of the signs and symptoms of CSU improves overall HRQoL
- Higher SIS7 and DLQI scores were associated with disease activity and were reduced with decreased disease activity, showing clinically relevant differences in the percentage of patients achieving SIS7 — 0 and DLQI 0—1 between adjacent UAS7 disease bands
- Patients who were urticaria free (according to the UAS7 bands) were those most likely to have no impact on QoL (DLQI score 0—1), emphasising the importance of complete disease control
- Urticaria free patients (UAS7=0) also have a high likelihood of achieving no impact on sleep, work productivity and activity interference, highlighting the importance of achieving complete urticaria control

CSU, Chronic Spontaneous Urticaria; DLQI, Dermatology Life Quality Index; HRQoL, Health-Related Quality of Life; QoL, Quality of Life; SIS7, weekly Sleep Interference Score (daily scores summed over 7-days); UAS7, weekly Urticaria Activity Score.