Quality of life improvements are correlated with improved disease control: Results from ligelizumab treatment in chronic spontaneous urticaria patients with angioedema

Giménez-Arnau A\textsuperscript{1}, Maurer M\textsuperscript{2}, Soong W\textsuperscript{3}, Bernstein JA\textsuperscript{4}, Sussman G\textsuperscript{5}, Metz M\textsuperscript{2}, Lanier B\textsuperscript{6}, Hide M\textsuperscript{7}, Sitz K\textsuperscript{8}, Hua E\textsuperscript{9}, Gupta P\textsuperscript{10}, Barve A\textsuperscript{11}, Severin T\textsuperscript{12}, Janocha R\textsuperscript{12}, Balp M\textsuperscript{12}

\textsuperscript{1}Dermatology Department, Hospital del Mar-Parc de Salut Mar, Universitat Autònoma, Barcelona, Spain; \textsuperscript{2}Department of Dermatology and Allergy, Charité - Universitätsmedizin Berlin, Germany; \textsuperscript{3}Alabama Allergy and Asthma Center, Clinical Research Center of Alabama, Birmingham, Alabama, United States; \textsuperscript{4}University of Cincinnati College of Medicine and Bernstein Clinical Research Center, Cincinnati, Ohio, United States; \textsuperscript{5}Division of Allergy and Clinical Immunology, University of Toronto, Ontario, Canada; \textsuperscript{6}Department of Dermatology, Hiroshima University, Hiroshima, Japan; \textsuperscript{7}Little Rock Allergy and Asthma Clinic, Little Rock, Arkansas, United States; \textsuperscript{8}Shanghai Novartis Trading Ltd., Shanghai, China; \textsuperscript{9}Novartis Healthcare Pvt. Ltd, Hyderabad, India; \textsuperscript{10}Novartis Pharmaceuticals, East Hanover, New Jersey, United States; \textsuperscript{11}Novartis Pharma AG, Basel, Switzerland

Poster presentation at 29\textsuperscript{th} European Academy of Dermatology and Venereology Virtual Congress, 29–31 October, 2020.
Disclosures

Giménez-Arnaud A. has served as medical advisor for Uriach Pharma, Genentech, Novartis, FAES, GSK, Sanofi, and received research grants supported by Uriach Pharma, Novartis, Grants from Instituto Carlos III- FEDER and has been involved in educational activities for Uriach Pharma, Novartis, Genentech, Menarini, LEO Pharma, GSK, MSD, Almirall and Sanofi. Maurer M. has received grant/ research support and/or honoraria for consulting or lectures from Aralez, Allakos, FAES, Genentech, Merckle Recordati, Moxie, Novartis, Roche, Sanofi, MSD, UCB, Uriach. 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 the following companies: AbbVie, Aimmune Therapeutics, AstraZeneca, Cara, Galderma, Genentech, GlaxoSmithKline, Stallergesens/ Greer, Optinose, Glenmark, Gossamer Bio, Vanda, Relaxar, Avillion, Menlo, Novartis, Pfizer, Regeneron, Sanofi and Teva. Bernstein J. A. reports grants and personal fees from Novartis, AstraZeneca, Allakos, and Genentech outside the submitted work. 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. Sitz K. has provided consultancy to BioCryst Pharmaceuticals Inc. Hua E. is an employee of Shanghai Novartis Trading Ltd., Shanghai, China. Gupta P. was an employee of Novartis Healthcare Pvt. Ltd, Hyderabad, India. Barve A. is an employee of Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, United States. Severin T., Janocha R. and Balp M-M. are employees of Novartis Pharma AG, Basel Switzerland.
Introduction

- Ligelizumab is a next generation, high affinity humanized monoclonal anti-IgE antibody, which has shown control of symptoms in a higher percentage of patients compared with omalizumab in a phase 2b trial (NCT02477332)

- Chronic spontaneous urticaria (CSU) disease activity and quality of life (QoL) impairment can be assessed by the use of the Urticaria Activity Score (UAS) / Angioedema Activity Score (AAS) and of the Dermatology Life Quality Index (DLQI), respectively

- Here, we analyzed changes of the UAS7, AAS7, and the DLQI, and assessed correlation of UAS7 and AAS7 with DLQI in a subgroup of CSU patients with angioedema at baseline

AAS7, weekly Angioedema Activity Score; CSU, chronic spontaneous urticaria; DLQI, Dermatology Life Quality Index; QoL, quality of life; UAS7, weekly Urticaria Activity Score
3 Business Use Only
Methods

- Adult patients with CSU inadequately controlled by an H\textsubscript{1}-antihistamine and with moderate to severe disease activity (UAS7≥16) were randomised to receive subcutaneous ligelizumab 72 or 240 mg, omalizumab 300 mg, or placebo q4w for 20 weeks.

- Changes from baseline (CFB) to week 4, 12 and 20 in UAS7, AAS7 and DLQI in each arm (ligelizumab 72 mg, 240 mg, omalizumab 300 mg and placebo) were analyzed.

- Additionally, Pearson correlation coefficients (R-Value) of UAS7 / AAS7 with DLQI on pooled data over time (baseline to week 20 were pooled) for each treatment were calculated.

AAS7, weekly Angioedema Activity Score; CFB, changes from baseline; CSU, chronic spontaneous urticaria; DLQI, Dermatology Life Quality Index; q4w, every 4 weeks; UAS7, weekly Urticaria Activity Score; Giménez-Arnau A et al. EADV October 29–31, 2020, Virtual congress.
Study design of the Phase 2b trial of ligelizumab in patients with CSU inadequately controlled with H₁-antihistamines

- **Screening**
  - Week -2

- **Treatment**
  - Week 0
  - Week 12
  - Week 20

- **Groups**
  1. **Ligelizumab 240 mg q4w (n=85)**
  2. **Ligelizumab 72 mg q4w (n=84)**
  3. **Omalizumab 300 mg q4w (n=85)**
  4. **Placebo (n=43)**

- **Randomisation**
  - Week 12 = Primary endpoint
  - Treatment visit in the core study

- **q4w, every 4 weeks**

Giménez-Arna A et al. *EADV* October 29–31, 2020, Virtual congress

5 Business Use Only
Patient disposition during the core Phase 2b trial: Data were available from 165 patients with CSU and angioedema at baseline.

CSU, chronic spontaneous urticaria; R, randomization; Wk, week
Giménez-Arnau A et al. EADV October 29–31, 2020, Virtual congress
6 Business Use Only
Reduction in UAS7 and AAS7 score in each treatment arm were accompanied by improvement in DLQI

- The mean (SD) UAS7 baseline scores for patients treated with ligelizumab 72 mg, 240 mg, omalizumab and placebo were: 33.1 (6.66), 29.8 (7.46), 30.2 (8.51) and 32.0 (6.49), respectively
- The mean (SD) AAS7 baseline scores for patients treated with ligelizumab 72 mg, 240 mg, omalizumab and placebo were: 42.2 (25.04), 32.8 (28.11), 30.6 (22.82) and 39.5 (24.91), respectively

Post hoc exploratory analysis of a sub group of CSU patients with angioedema at baseline are presented

AAS7, weekly Angioedema Activity Score; DLQI, Dermatology Life Quality Index; UAS7, weekly Urticaria Activity Score; Wk, week


7 Business Use Only
DLQI improvements correlates well with the UAS7 and AAS7 scores improvement

- Correlations between UAS7 and DLQI were observed in each treatment arm and achieved R-values of 0.85 (p≤0.001), 0.81 (p≤0.001), 0.78 (p≤0.001) and 0.69 (p≤0.001) for ligelizumab 72 mg, 240 mg, omalizumab and placebo, respectively.

- Correlations between AAS7 and DLQI were observed in each treatment arm and achieved R-values of 0.72 (p≤0.001), 0.66 (p≤0.001), 0.59 (p≤0.001) and 0.52 (p≤0.001) for ligelizumab 72 mg, 240 mg, omalizumab and placebo, respectively.

<table>
<thead>
<tr>
<th>UAS7, AAS7 and DLQI changes over time in patients with angioedema per treatment group*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ligelizumab 72 mg N=43</td>
</tr>
<tr>
<td>UAS7 / DLQI</td>
</tr>
<tr>
<td>AAS7 / DLQI R-Value**</td>
</tr>
</tbody>
</table>

*CSU patients with angioedema at baseline are presented.
**Pearson’s correlation coefficient R-values are based on pooled data from baseline, Week 4, Week 12 and Week 20.
AAS7, weekly Angioedema Activity Score; DLQI, Dermatology Life Quality Index; UAS7, weekly Urticaria Activity Score
Conclusions

- This exploratory analysis shows that CSU patients with angioedema treated with ligelizumab 72 and 240 mg show a similar improvement trend on UAS7, AAS7 and DLQI in comparison to omalizumab and placebo over time.

- DLQI improvements correlates well with the UAS7 and AAS7 score improvement, which reflects the reduction of disease symptoms.

- Results of this Phase 2b trial support the two ongoing Phase 3 trials examining the efficacy and safety of ligelizumab 72 and 120 mg q4w treatment up to 1 year in patients with CSU inadequately controlled with H₁-antihistamines at approved doses.

AAS7, weekly Angioedema Activity Score; CSU, chronic spontaneous urticaria;
DLQI, Dermatology Life Quality Index; q4w, every 4 weeks; UAS7, weekly Urticaria Activity Score

9 Business Use Only