P0133

# Barzolvolimab Treatment Leads to Achievement of Both Complete Response as Well as No Impact of Disease on Quality of Life in Chronic Spontaneous Urticaria

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## INTRODUCTION

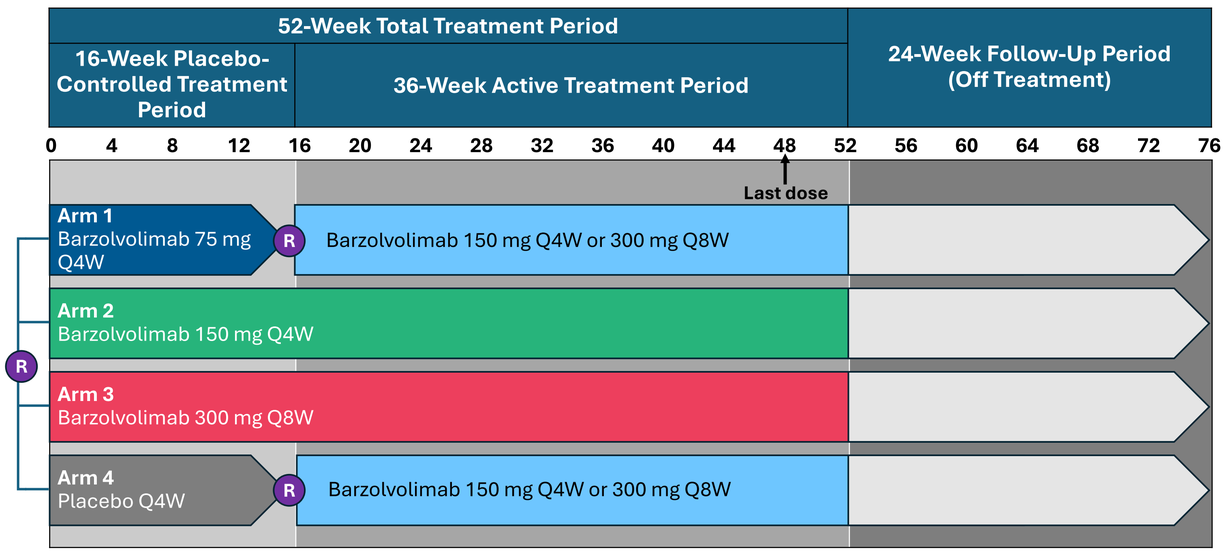
- Activated mast cells (MCs) drive the pathogenesis of inflammatory diseases, including chronic spontaneous urticaria (CSU)[1]
- Symptoms of CSU include itch, hives, and angioedema place a substantial burden on patients' quality of life (QoL)[1]
- Stem cell factor (SCF)/KIT signaling regulates MC biology and factors such as their differentiation, maturation, and survival. Barzolvolimab, a humanized monoclonal antibody (mAb), inhibits SCF-mediated KIT activation, resulting in rapid and profound depletion of MCs[2]
- In a Phase 2 study in patients with antihistamine (H1AH)-refractory CSU (NCT05368285), barzolvolimab demonstrated significant improvement in Urticaria Activity Score over 7 days (UAS7), with 71% of participants receiving barzolvolimab 150 mg every 4 weeks (Q4W) and 52% of those receiving 300 mg every 8 weeks (Q8W) achieving a Complete Response (UAS7 = 0), representing the absence of itch and hives after 52 weeks of treatment; these benefits were sustained to Week 76, 7 months after the last dose of barzolvolimab[3,4]
- Treatment with barzolvolimab had a significant impact on QoL, as measured by the Dermatology Life Quality Index (DLQI), with up to 82% of participants achieving a DLQI score of 0 or 1, indicating no impact of disease on QoL, at Week 52
- **Objective**: To determine the relationship between barzolvolimab treatment (150 mg Q4W and 300 mg Q8W) and itch severity, hives severity, and QoL over 76 weeks

## METHODS

- Itch- and hive-free status was determined as a score of 0 on the Itch Severity Score over 7 days (ISS7) and the Hive Severity Score over 7 days (HSS7), respectively.
- Complete Response was assessed using the Urticaria Activity Score over 7 days (UAS7) score of 0, and no impact of disease on QoL was assessed by the DLQI questionnaire (DLQI = 0/1)
- The relationships between attainment of Complete Response (UAS7 = 0) and no impact of CSU on QoL (DLQI = 0/1) over time using Chi-square tests were determined for the pooled barzolvolimab 150 mg Q4W and 300 mg Q8W populations
- In a post hoc analysis, the relationships between the mean change from baseline (CfB) in UAS7, ISS7, HSS7, and DLQI at Week 4 through Week 76 by Pearson correlation coefficients (*r*) were investigated among patients treated with barzolvolimab 150 mg Q4W or 300 mg Q8W

## STUDY DESIGN

### A Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study




Q4W, every 4 weeks; Q8W, every 8 weeks; R, randomization.

### Treatment Groups

- This double-blind trial randomized patients to receive placebo or barzolvolimab subcutaneously at 75 mg Q4W, 150 mg Q4W, or 300 mg Q8W for 16 weeks followed by 36 weeks of active treatment and 24 weeks of follow-up
- During active treatment, the placebo and 75 mg Q4W groups were re-randomized to either 150 mg Q4W or 300 mg Q8W

### Key Eligibility Criteria

- Patients with moderate to severe CSU who remain symptomatic despite treatment with up to 4x approved doses of H1AH and includes patients with prior biologics

### Primary Endpoint

- The primary endpoint was mean CfB in UAS7 at Week 12

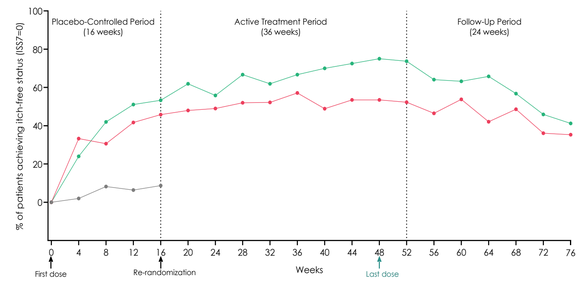
## Baseline demographics & disease characteristics

| | Barzolvolimab 150 mg Q4W (N=52) | Barzolvolimab 300 mg Q8W (N=51) |
|---|---|---|
| **Age (years), median (range)** | 47.2 (20-80) | 44.4 (20-76) |
| **Female, n (%)** | 41 (80) | 36 (71) |
| **Weight (kg), mean (range)** | 85.7 (47-163) | 83.8 (51-143) |
| **UAS7 score, median (range)** | 31.3 (17-42) | 30.0 (13-42) |
| **UAS7, severe disease, n (%)** | 39 (76) | 33 (65) |
| **ISS7, median (range)** | 16.4 (8-21) | 15.6 (6-21) |
| **HSS7, median (range)** | 14.9 (7-21) | 14.5 (1-21) |
| **Angioedema at baseline, n (%)** | 42 (82) | 32 (63) |
| **Previous experience with omalizumab, n (%)** | 11 (22) | 8 (16) |
| **DLQI, mean (SD)** | 17.4 (7.5) | 17.0 (6.6) |

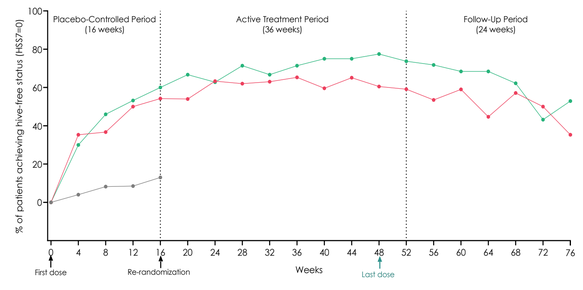
DLQI, Dermatology Life Quality Index; HSS7, Hive Severity Score over 7 days; ISS7, Itch Severity Score over 7 days; QxW, every x weeks; SD, standard deviation; UAS7, Urticaria Activity Score over 7 days.

## Barzolvolimab treatment increased attainment of itch-free and hive-free status, disease control, and no impact of disease on QoL vs placebo over 76 weeks*

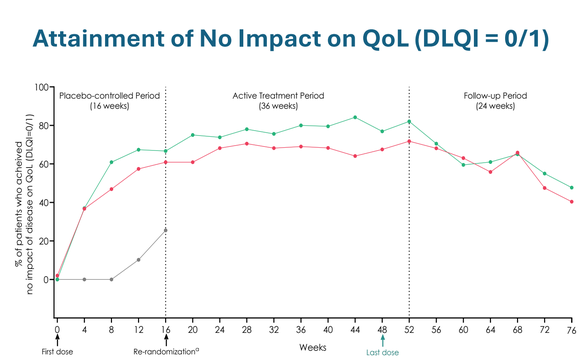
### Attainment of Itch-Free Status (ISS7 = 0)



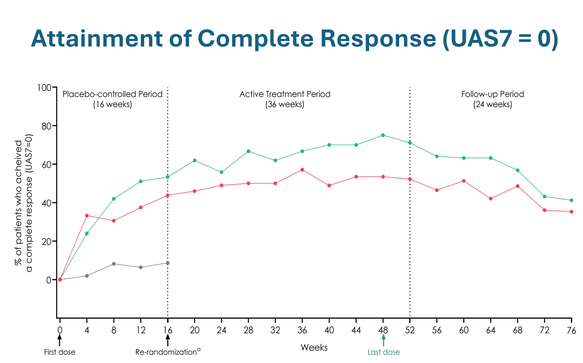

### Attainment of Hive-Free Status (HSS7 = 0)




### Attainment of No Impact on QoL (DLQI = 0/1)




### Attainment of Complete Response (UAS7 = 0)





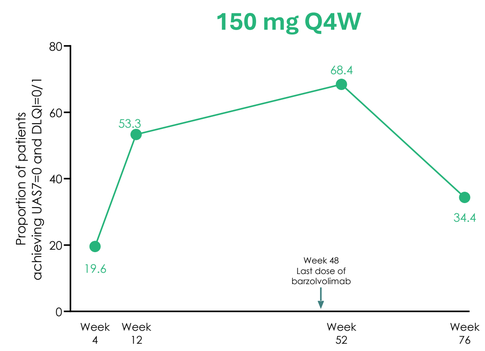


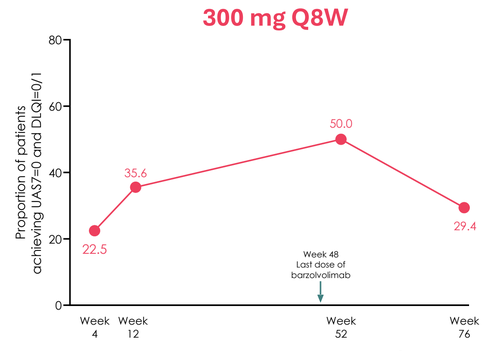
*The 76-week study included a 52-week treatment period and a 24-week off-treatment follow-up period.
DLQI, Dermatology Life Quality Index; HSS7, Hive Severity Score over 7 days; ISS7, Itch Severity Score over 7 days; Q4W, every 4 weeks; Q8W, every 8 weeks; QoL, Quality of Life; UAS7, Urticaria Activity Score over 7 days.

- Attainment of ISS7 = 0 increased from 24.0% and 33.3% at Week 4 to 73.7% and 52.3% at Week 52 for barzolvolimab 150 mg Q4W and 300 mg Q8W, respectively; 41.2% and 35.3% maintained ISS7 = 0 at Week 76, 28 weeks after the final dose of barzolvolimab
- Similarly, attainment of HSS7 = 0 increased from 30.0% and 35.3% at Week 4 to 73.7% and 59.1% at Week 52 for barzolvolimab 150 mg Q4W and 300 mg Q8W, respectively; at Week 76, 52.9% and 35.3% maintained HSS7 = 0
- At Week 4, 37.0% and 36.7% had achieved DLQI = 0/1 for barzolvolimab 150 mg Q4W and 300 mg Q8W, respectively; this increased to 82.1% and 71.8% at Week 52. At Week 76, 47.7% and 40.4% maintained DLQI = 0/1
- UAS7 = 0 was attained by 24.0% and 33.3% at Week 4, and 71.1% and 52.3% at Week 52, for patients receiving barzolvolimab 150 mg Q4W and 300 mg Q8W, respectively; 41.2% and 35.3% maintained UAS7 = 0 at Week 76

## Barzolvolimab treatment led to concurrent attainment of Complete Response and no impact of disease on QoL

### Achievement of both of UAS7 = 0 and DLQI = 0/1 from Week 4 to Week 76*,†




*The 76-week study includes a 52-week treatment period and a 24-week off-treatment follow-up period. †Chi-square statistics at Weeks 4, 12, 52, and 76 were $\chi^2(1)=12.5$ ($P=0.0004$), $\chi^2(1)=25.7$ ($P<0.0001$), $\chi^2(1)=13.4$ ($P=0.0002$), and $\chi^2(1)=10.5$ ($P=0.0012$), respectively, for patients receiving barzolvolimab 150 mg Q4W; corresponding values for patients receiving barzolvolimab 300 mg Q8W were $\chi^2(1)=12.5$ ($P=0.0004$), $\chi^2(1)=13.2$ ($P=0.0003$), $\chi^2(1)=8.6$ ($P=0.0033$), and $\chi^2(1)=11.6$ ($P=0.0007$). Sample sizes were 9, 24, 26, and 11 patients, respectively, at Weeks 4, 12, 52, and 76 for the 150 mg Q4W group, and 11, 16, 19, and 10 patients, respectively, for the 300 mg Q8W group.
DLQI, Dermatology Life Quality Index; Q4W, every 4 weeks; Q8W, every 8 weeks; UAS7, Urticaria Activity Score over 7 days.

- The proportion of patients achieving UAS7 = 0 and DLQI = 0/1 concurrently in the 150 mg Q4W treatment group was 19.6% at Week 4, 53.3% at Week 12, and 68.4% at Week 52; 34.4% achieved UAS7 = 0 and DLQI = 0/1 concurrently at Week 76, 28 weeks after the final dose of barzolvolimab
- A similar pattern was noted for the 300 mg Q8W treatment group with attainment of UAS7 = 0 and DLQI = 0/1 concurrently in 22.5% at Week 4, 35.6% at Week 12, and 50.0% at Week 52 of patients; at Week 76, 29.4% achieved UAS7 = 0 and DLQI = 0/1 concurrently

## Disease severity/activity was positively correlated with QoL improvements

| | Pooled Population (Barzolvolimab 150 mg Q4W and 300 mg Q8W) | | | |
|---|---|---|---|---|
| | Week 4 (N=93) | Week 12 (N=87) | Week 52 (N=75) | Week 76 (N=65) |
| ISS7, *r* | +0.50*** | +0.39*** | +0.43*** | +0.48*** |
| HSS7, *r* | +0.51*** | +0.47*** | +0.50*** | +0.45*** |
| UAS7, *r* | +0.52*** | +0.46*** | +0.50*** | +0.50*** |

***$P<0.001$
HSS7, Hive Severity Score over 7 days; ISS7, Itch Severity Score over 7 days; QoL, quality of life; UAS7, Urticaria Activity Score over 7 days.

- Positive correlations (*r*) between changes from baseline in DLQI and changes from baseline in UAS7, ISS7, and HSS7 over time for the 150 mg Q4W and 300 mg Q8W treatment groups were between 0.39 and 0.52 (all $P<0.001$)

## CONCLUSIONS

- **Barzolvolimab treatment resulted in rapid, deepening, and sustained itch-free and hive-free status and marked improvement in QoL, consistent with previously reported Complete Response rates**
- **The proportion of patients that achieved both Complete Response (UAS7 = 0) and no effect of disease on QoL (DLQI = 0/1) increased over time during treatment; over a quarter of patients maintained UAS7 = 0 and DLQI = 0/1 for 7 months after the last dose of barzolvolimab (i.e., to Week 76)**
- **Benefits of barzolvolimab treatment in itch, hives, and urticaria activity positively correlated with improvements in QoL**
- **Barzolvolimab represents a promising treatment for CSU, offering the possibility of Complete Response and improved QoL in patients with H1AH-refractory CSU**


### References

1. Kolkhir P, et al. *JAMA*. 2024;332(17):1464-1477. 2. Alvarado D, et al. *Allergy*. 2022;77(8):2393-2403. 3. Metz M, et al. Presentation at: EAACI 2025; June 13-16, 2025; Glasgow, United Kingdom. 4. Metz M, et al. Poster presented at: AAAAI 2026; February 26-March 2, 2026; Philadelphia, PA, USA.



### Disclosures

**MM:** advisory board (honoraria): Novartis, Regeneron Pharmaceuticals Inc., Sanofi, Galderma, Amgen, AstraZeneca, Celldex Therapeutics, Inc., Argenx, GlaxoSmithKline Immunology, Incyte Corporation, Jasper Therapeutics, Escient Pharmaceuticals, Inc., Arcutis Biotherapeutics, Astria Therapeutics, Blueprint Medicines, Deep Apple Therapeutics, Evommune, Inc., Granular Therapeutics, Johnson & Johnson; Research & Development: Eli Lilly, RAPT Therapeutics, Santa Ana Bio, Septerna, Allegria Therapeutics; speaker (honoraria): Pfizer Inc., Sanofi, Almirall, Celltrion, Galderma, Novartis, AbbVie, Berlin Chemie; speaker/faculty education (honoraria): Almirall; paid consultant: Argenx, Attovia Therapeutics, Lycia Therapeutics, Enanta Pharmaceuticals, Bayer, Candid, Excellergy, FatiAbGen, Generate Biomedicines, InflaRx, Japan Tobacco Inc., Ono, Tupos Therapeutics; investigator (no compensation. received): Bayer. **JA:** speaker bureau member for Astra Zeneca, Sanofi/Blueprint, CSL Behring, Ionis, GSK, KalVista, Pharming, Takeda; received consulting fees from Astria, BioCryst, Sanofi/Blueprint, CSL Behring, Ionis, GSK, Kalvista, Novartis, Pharming, Santa Ana Bio, Takeda; and is a clinical trial investigator for Astria, Sanofi/Blueprint, Biocyrst, Celldex Therapeutics, Inc., CSL Behring, Kalvista, Novartis, and Pharming. **JL, MG, AL:** Have no disclosures to report. **NT:** received grant research funding for clinical trials with the following sponsors: AbbVie, Aclaris, Allakos, Amgen, AnaptysBio Inc, Arcutis, Ardelyx, Arena, ARS, AstraZeneca, BioHaven, Blueprint, Braintree, Castle, Celldex Therapeutics, Inc., CinDome Pharma, Dr. Falk Pharma GmbH, Eli Lilly, Escient, Evommune, Gossamer, GSK, Incyte, Janssen, Jasper, Knopp, NeRRe Therapeutics, Novartis, Optinose, Pearl Therapeutics, Pfizer, Phathom, Q32, Regeneron, Sanofi, Seres, Teva, Uniquity, Upstream Bio, and 9 Meters. **SG, AH, LD, JV:** employees of Celldex Therapeutics, Inc. with stock, stock options, and salary. **JAB:** investigator (paid to institution) and consultant (honoraria): ADARx, Ajou University, Allergy Therapeutics, Amgen, Apogee, Areteia, ARS, Astra Zeneca, Astria, Biocryst, Blueprint Medicines, Celldex Therapeutics, Inc., Cogent, CSL Behring, Eli Lilly, Escient, Evommune, Fresenius Kabi, Genentech, GSK, Incyte, Intellia, Ionis, Japan Tobacco Inc., Jasper, Johnson & Johnson, Kalvista, Kenvue, Kymera Therapeutics, Kyowa, Kirin, Lycia, Medscape, Merck, Nasus, Neffy, Nektar, Neopharma, Novartis, Opella, Pharming, Pharvaris, Proctor & Gamble, Regeneron, Sanofi, Takeda/Shire, Telios, Teledoc, TEVA, Yuhan, WebMD, Peer Review; consultant (honoraria): Enanta, Pfizer, RAPT); speaker (honoraria): Pharming, Kalvista, CSL Behring – honoraria; chairman (salaried): American Academy of Allergy, Asthma, and Immunology Foundation; organizational (no compensation): President of Global Asthma Association - Interasma, WE CU Board of Directors, US Hereditary Angioedema Association Medical Advisory Board, Cincinnati Urticaria Center of Reference and Excellence/Angioedema Center of Reference and Excellence, World Allergy Organization Centers of Excellence, Cincinnati American Initiative in Mast Cell Diseases Center of Excellence.