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Barzolvolimab Improves Urticaria Control and Quality of Life in Patients with Chronic Spontaneous Urticaria: 52-Week Data

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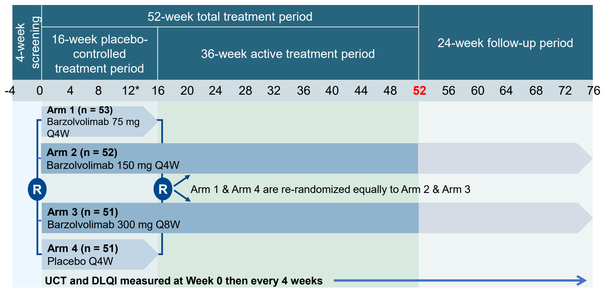
Background

- Mast cells are key effector cells of chronic spontaneous urticaria (CSU).
- New therapies are urgently needed for CSU. Most patients remain symptomatic despite standard or high dose second generation antihistamines, and one-third of these nonresponders or partial responders have no response or inadequate response to omalizumab.
- CSU significantly impacts every aspect of life, with varying severity and persistence in symptoms.
- Barzolvolimab is an anti-KIT monoclonal antibody that inhibits activation of and depletes mast cells.
- In this Phase 2 study (NCT05368285), barzolvolimab demonstrated rapid and durable improvement in urticaria activity (as measured by Urticaria Activity Score over 7 days [UAS7]); up to 71% of patients achieved complete response (UAS7 = 0) at Week 52.
- Here we describe the impact of barzolvolimab treatment on disease control (Urticaria Control Test [UCT]) and quality of life (Dermatology Life Quality Index [DLQI]) over 52 weeks of treatment.

Study Design

A Randomized, Double-blind, Placebo-controlled, Dose-finding Study



*Primary endpoint was assessed at Week 12

- Biologic-naïve and -experienced patients refractory to antihistamines.
- **Primary endpoint:** mean change from baseline to Week 12 of UAS7
- **Exploratory endpoints:**
  - **UCT:** total score of 0 to 16 over 4 weeks. Scores ≥ 12 indicate well-controlled urticaria, and a score of 16 indicates complete response. Minimum clinically important difference is 3 points.
  - **DLQI:** scores of 0 to 30, with higher scores indicating greater impact of disease on QoL. The minimal clinically important difference is a 4-point reduction. A score of 0 or 1 indicates no impact on the patient's QoL.

Results

Demographics and Baseline Characteristics

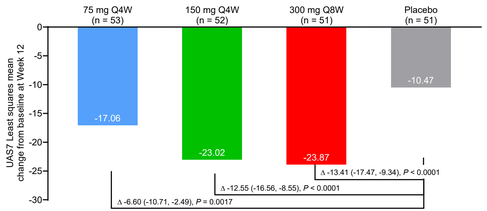
- Well balanced across groups; patients with severe urticaria symptoms

	Barzolvolimab 75 mg Q4W (n = 53)	Barzolvolimab 150 mg Q4W (n = 52)	Barzolvolimab 300 mg Q8W (n = 51)	Placebo (n = 51)
Age, years	42.2 (18-69)	46.0 (21-81)	47.2 (20-80)	44.4 (20-76)
Female, n (%)	40 (76)	39 (75)	41 (80)	36 (71)
Weight, kg	77.5 (50-129)	80.9 (55-169)	85.7 (47-163)	83.8 (51-143)
Prior omalizumab therapy, n (%)	11 (21)	11 (21)	11 (22)	8 (16)
UAS7 score	30.3 (14-42)	30.8 (12-42)	31.3 (17-42)	30.1 (13-42)
UAS7, severe disease, n (%)	34 (64)	36 (69)	39 (76)	33 (65)
UCT score	3.7 (0-8)	3.7 (0-9)	3.0 (0-9)	3.4 (0-11)
DLQI score	15.9 (3-30)	15.7 (3-29)	17.4 (1-30)	17.0 (3-30)

Severe disease = UAS7 ≥ 28
Data shown are mean (range) unless otherwise specified

Barzolvolimab Drives Rapid and Durable Improvement in Clinical Symptoms, Urticaria Control, and Quality of Life in Patients with Antihistamine-Refractory CSU

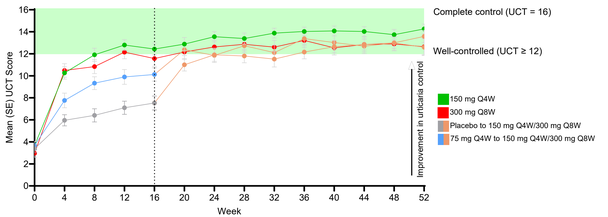
Primary Endpoint Achieved: Statistically Significant and Profound Improvement in UAS7 Compared to Placebo at Week 12



Data were analyzed using an ANCOVA model and multiple imputation. The Benjamini-Hochberg procedure was used for multiplicity adjustments.
Δ: treatment difference least squares mean (95% confidence interval)

Rapid and Sustained Improvement in Urticaria Control With Barzolvolimab Over 52 Weeks

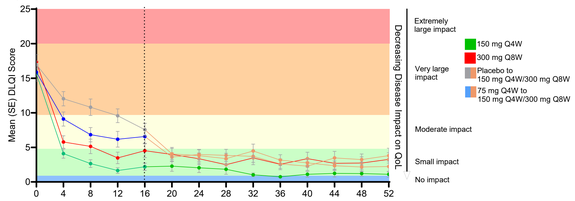
- Patients had poorly-controlled urticaria at baseline, which improved markedly over 52 weeks



The dotted line at Week 16 marks the start of the Active Treatment Phase, during which patients who had received placebo or barzolvolimab 75 mg Q4W during the Placebo-controlled Phase were re-randomized to receive barzolvolimab 150 mg Q4W or 300 mg Q8W.

Barzolvolimab Drives Rapid and Sustained Improvement in Quality of Life Over 52 Weeks

- At baseline, patients reported a "very large" impact of CSU disease on their QoL; the impact of CSU on QoL rapidly decreased over 52 weeks with barzolvolimab treatment.



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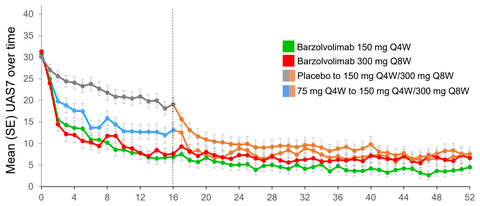
Improvements in UAS7 With Barzolvolimab Were Observed as Early as Week 1 and Were Sustained to Week 52



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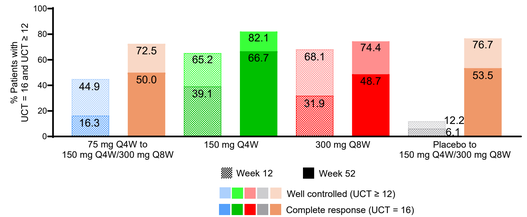
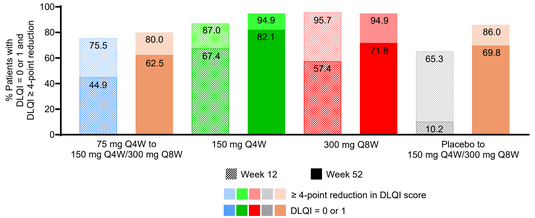
Up to 82% of Patients Reported Well-controlled or Completely Controlled Urticaria as Measured by UCT at Week 52



At Week 16, patients who had received placebo or barzolvolimab 75 mg Q4W were re-randomized to receive barzolvolimab 150 mg Q4W or 300 mg Q8W.

Up to 95% of Patients Reported Meaningful Improvement in Quality of Life at Week 52



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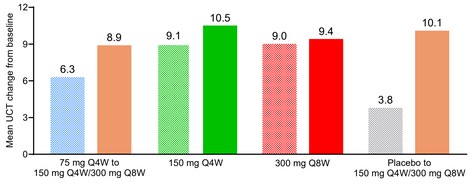
Treatment With Barzolvolimab Demonstrated Marked Improvement in Urticaria Control Sustained Through Week 52



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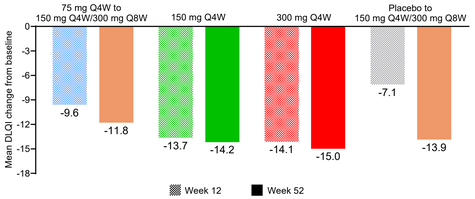

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Barzolvolimab Was Well Tolerated Through 52 Weeks of Treatment

- Most adverse events were mild. Adverse events reported by ≥ 10% of patients in any group over 52 weeks were hair color changes (26%), neutropenia/neutrophil count decrease (17%), urticaria (15%), skin hypopigmentation (13%), and nasopharyngitis (10%).[1]
- Most common events were mechanism related (KIT) and expected to be reversible.
- Adverse events were not dose dependent.
- No association between infections and neutropenia/decreased neutrophil counts. Neutropenia was transient.

Summary

- Treatment with barzolvolimab resulted in rapid and sustained improvement in urticaria control (UCT) and quality of life (DLQI) in patients with CSU refractory to antihistamines.
  - Up to 82% of patients reported well-controlled urticaria based on UCT, and approximately half of patients reported complete control at Week 52.
  - Up to 95% of patients reported meaningful improvement in quality of life based on DLQI; 82% of patients reported that CSU symptoms no longer had an impact on their quality of life at Week 52.
- Barzolvolimab was well tolerated through 52 weeks of treatment.
- Given the previously reported efficacy against hives and itch, and the profound resultant impact on quality of life described herein, barzolvolimab has the potential to be an important new treatment option. Global Phase 3 studies are actively enrolling (EMBARQ-CSU1 [NCT06445023] and EMBARQ-CSU2 [NCT06455202]).

Reference: 1. Maurer et al. Barzolvolimab shows profound efficacy and favorable safety over 52 weeks in patients with Chronic Spontaneous Urticaria. Presented at the European Academy of Dermatology and Venereology Congress September 25-28, 2024, Amsterdam, Netherlands. **Funding and acknowledgements:** This study was funded by Celldex Therapeutics, Inc. We wish to thank all the Investigators and their patients who contributed to this trial. **Disclosures:** M. Metz is or recently was a speaker and/or advisor for Amgen, AstraZeneca, argenx, Celldex, Celltrion, Escient, Jasper Therapeutics, Novartis, Pharvaris, Regeneron, Sanofi, and ThirdHarmonic Bio. I. Kobielusz-Gembala, E. Mitha, J. Leflein, and M. Gotua do not have any declarations at this time. E. Paradise, S. Greenberg, and D. Young are employees of Celldex Therapeutics. J. Fuentes-Duculan and R. Ma were employees of Celldex at the time of this study. J.A. Bernstein is a PI, consultant and speaker for Novartis, Genentech, Astra Zeneca, Sanofi Regeneron, Biocryst, CSL Behring, Takeda/Shire, Pharming, GSK; PI and consultant for Celldex, Cogent, Escient, Jasper Amgen, Roche, Ionis, Kalvista, Allakos, Biomarin, Blueprint Medicine; PI for Teva; Consultant for Incyte, Astria, ONO, Cycle, Escient, Pharvaris, and TLL.