R080

Barzolvolimab Improves Urticaria Control On and Off Treatment in Chronic Spontaneous Urticaria

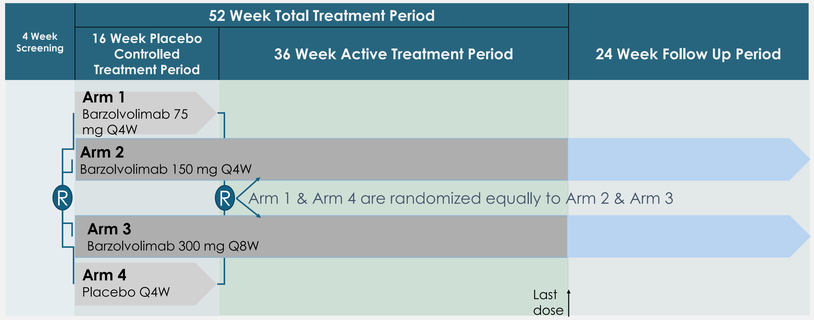
M. Metz[1,2], J. Anderson[3], J. Leflein[4], M. Gotua[5], N. Talreja[6], D. Maurer[7], S. Greenberg[7], U. Chaudhry[7], E. Paradise[7], L. Duan[7], J. A. Bernstein[8]

[1]Institute of Allergology, Charité-Universitätsmedizin Berlin, corporate member of Freie Universitäts Berlin and Humboldt-Universitäts zu Berlin, Berlin, Germany; [2]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany; [3]University of Alabama, Birmingham and VA Medical Center, Clinical Research Center of Alabama, AllerVie Health, Birmingham, AL; [4]Respiratory Medicine Research Institute of Michigan, Ypsilanti, MI; [5]Center of Allergy and Immunology, Tbilisi, Georgia; [6]The Allergy Group and Treasure Valley Medical Research, Boise, ID; [7]Celldex Therapeutics, Hampton, New Jersey, USA; [8]University of Cincinnati College of Medicine and Bernstein Allergy Group/Clinical Research Center, Cincinnati, Ohio, USA

Background

- Mast cells (MCs) are key effector cells in chronic spontaneous urticaria (CSU).
- Barzolvolimab, a humanized monoclonal antibody that inhibits KIT activation by SCF, demonstrated rapid and durable depletion of skin MCs[1].
- We previously reported that barzolvolimab treatment resulted in statistically significant and clinically meaningful improvement in weekly Urticaria Activity Score (UAS7) at 12 weeks, with deepening of response over 52 weeks in antihistamine-refractory CSU patients (NCT05368285), including patients who received prior omalizumab.
- Here, we describe the impact of barzolvolimab treatment on Urticaria Control Test over 7-days (UCT7) through 76 weeks.

Study Design and Key Eligibility



- Randomized, double-blind, placebo-controlled, dose-finding study.
- Patients with moderate to severe CSU who remain symptomatic despite treatment with up to 4X labeled dose of antihistamines; including patients with prior biologics.
- 208 patients enrolled and 207 patients treated
  - A single patient was randomized but did not receive study treatment
- 189 patients entered the follow-up period.

Primary Endpoint:
Mean change from baseline to Week 12 of UAS7 (Urticaria Activity Score)

Exploratory Endpoint:
Urticaria Control Test 7 (UCT7)

Demographics and Baseline Characteristics

- Well balanced across groups; majority (~70%) of patients had 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 (range)		42.20 (18.0-69.0)	46.0 (21.0-81.0)	47.2 (20.0-80.0)	44.4 (20.0-76.0)
Female, n (%)		40.0 (76.0)	39.0 (75.0)	41.0 (80.0)	36.0 (71.0)
Weight, kg (range)		77.5 (50.0-129.0)	80.9 (55.0-169.0)	85.7 (47.0-163.0)	83.8 (51.0-143.0)
UAS7 score (range)		30.3 (14.0-42.0)	30.8 (12.0-42.0)	31.3 (17.0-42)	30.0 (13.0-42.0)
UAS7, severe disease n (%)		34.0 (64.0)	36.0 (69.0)	39.0 (76.0)	33.0 (65.0)
UCT7 score (range)		4.1 (0.0 – 11.0)	4.4 (0.0 – 10.0)	3.9 (0.0-9.0)	5.0 (0.0 – 11.0)
DLQI score (range)		15.9 (3.0-30.0)	15.7 (3.0-30)	17.4 (1.0-30.0)	17.0 (3.0-30.0)
Angioedema at baseline, n (%)		40.0 (75.0)	35.0 (67.0)	42.0 (82.0)	32.0 (63.0)
Prior omalizumab status, n (%)	**Omalizumab refractory[1]**	6 (11.3)	7 (13.5)	7 (13.7)	3 (5.9)
	Omalizumab non-refractory[2]	47 (88.7)	45 (86.5)	44 (86.3)	48 (94.1)

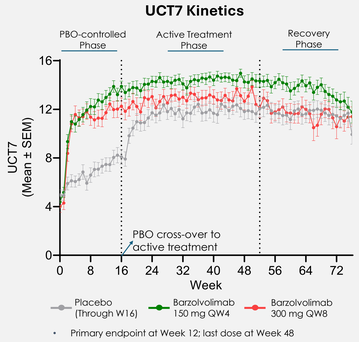
[1] Denotes patients with inadequate response or intolerance to omalizumab; [2] Includes patients who never received omalizumab, received prior omalizumab but are not refractory, or with unknown status. All data shown are mean (range) unless otherwise specified. Severe disease=UAS7 ≥ 28

Methodology

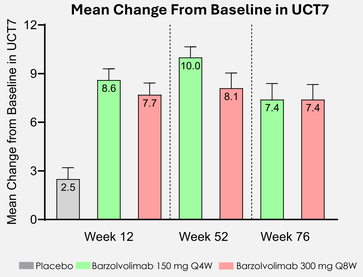
Data analysis was done using observed data. Analyses shown reflect mean ± SE values.

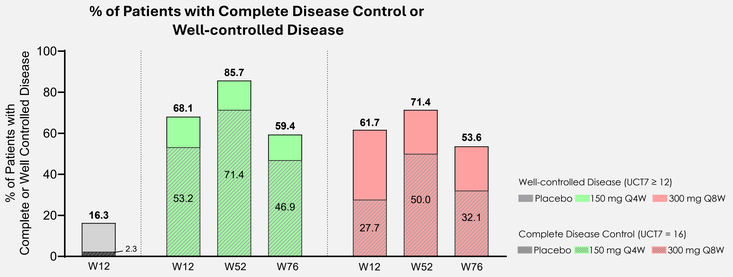
Results

Barzolvolimab leads to rapid and profound improvement in UCT7 scores, with sustained disease control off treatment

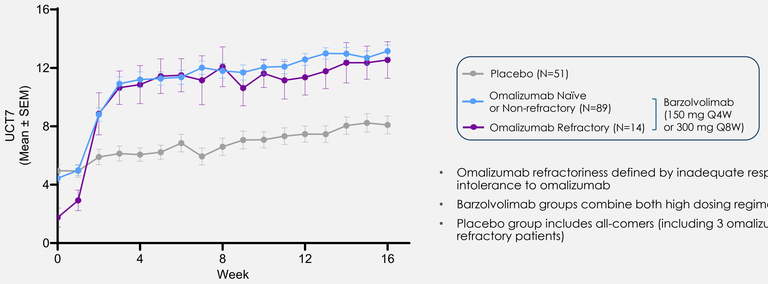


- Primary endpoint at Week 12; last dose at Week 48





Similar activity in patients with omalizumab refractory vs. naïve or non-refractory disease



- Omalizumab refractoriness defined by inadequate response or intolerance to omalizumab
- Barzolvolimab groups combine both high dosing regimens
- Placebo group includes all-comers (including 3 omalizumab refractory patients)

Safety

- Barzolvolimab was well tolerated with no new safety findings identified during follow up period
- Most adverse events were mild (grade 1), KIT-mediated effects and reversible[1,2]
- Neutropenia events resolved while on treatment
- No association between infections and neutropenia
- Resolution of hair color changes and skin hypopigmentation observed following discontinuation of treatment

1. Maurer M, et al. Barzolvolimab Significantly Decreases Chronic Spontaneous Urticaria Disease Activity and is Well Tolerated: Top Line Results from a Phase 2 Trial. AAAAI February 23-26, 2024; Washington DC.

2. 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.

Discussion

- Long-term barzolvolimab treatment demonstrated rapid and profound improvement in urticaria control with sustained off-treatment efficacy in patients with CSU refractory to antihistamines
- Significant improvements in urticaria control test (UCT7) scores relative to placebo were observed by Week 12, which deepened with prolonged treatment through 52 weeks.
- At Week 52 86% of patients achieved well-controlled disease and 71% of patients achieved complete disease control at the 150 mg Q4W dose
- Sustained urticaria control observed for 28 weeks following the last dose
- Most patients had well controlled disease at Week 76 suggestive of disease modification
- Barzolvolimab was well tolerated with no new safety findings identified during the follow up period
- Barzolvolimab is being evaluated in ongoing parallel Phase 3 studies in patients with CSU