Barzolvolimab Significantly Decreases Chronic Spontaneous Urticaria Disease Activity and is Well Tolerated: Top Line Results from a Phase 2 Trial

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Conflict Of Interest Statement

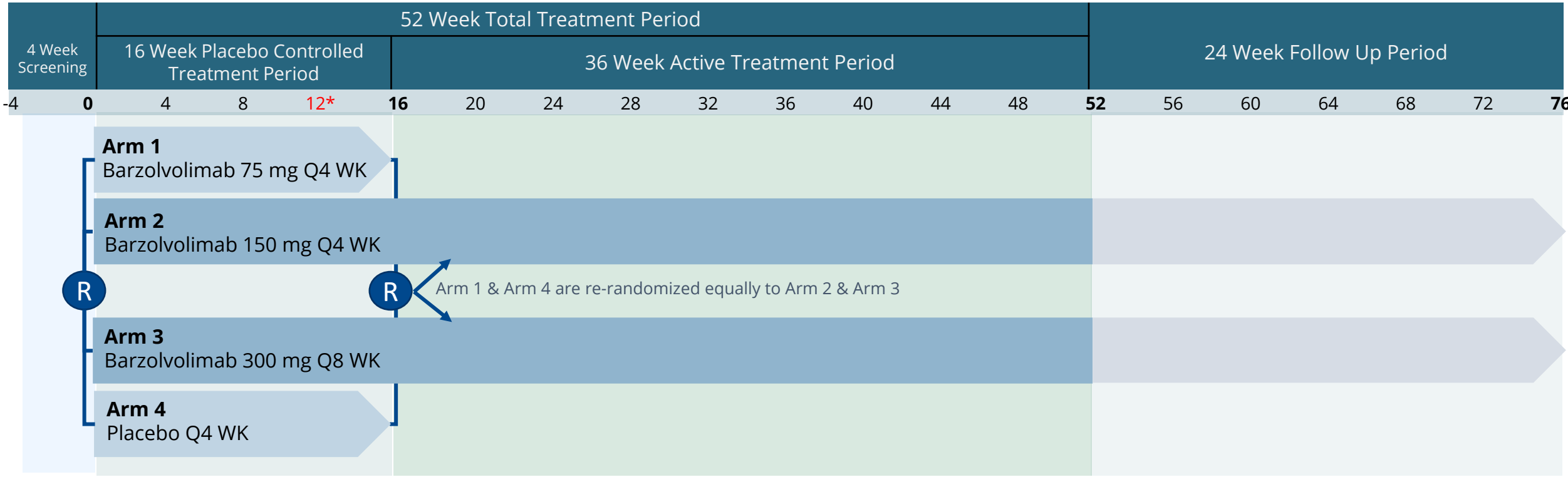
Marcus Maurer is or recently was a speaker and/or advisor for and/or has received research funding from Allakos, Alvotech, Amgen, Aquestive, Aralez, AstraZeneca, Bayer, Celldex, Celltrion, Evommune, GSK, Ipsen, Kashiv, Kyowa Kirin, Leo Pharma, Lilly, Menarini, Mitsubishi Tanabe Pharma, Moxie, Noucor, Novartis, Orion Biotechnology, Resoncance Medicine, Sanofi/Regeneron, Septerna, Trial Form Support International AB, Third HarmonicBio, ValenzaBio, Yuhan Corporation, Zurabio

Background

- Chronic spontaneous urticaria (CSU) is a mast cell driven disease characterized by itchy wheals, angioedema, or both
- Mast cells require engagement of their KIT receptors by stem cell factor (SCF) for activation, tissue recruitment and survival
- Barzolvolimab (CDX-0159), a first-in-class anti-KIT monoclonal antibody, has demonstrated improvement in itch and urticarial lesions accompanied by depletion of skin mast cells in chronic urticarias
- Here we report the primary analysis (Week 12) of a Phase 2 study evaluating the efficacy and safety of barzolvolimab compared with placebo in CSU patients whose disease is inadequately controlled by antihistamines

Study Design

A randomized, double-blind, placebo-controlled, dose-finding Phase 2 study



- Patients maintained a stable dose of a second generation H1 antihistamine at 1-4 times the approved dose throughout the study
- Rescue therapy: increase H1antihistamine dose or short course of corticosteroids

***Primary analysis at Week 12** (all patients who completed Week 12 or discontinued prior to Week 12)

Patient Eligibility

Key Inclusion Criteria

- Age ≥18 years
- Diagnosis of CSU ≥ 6 months
- Itch and hives for ≥ 6 consecutive weeks despite the use of 2nd generation antihistamine
- Biologic naïve/experienced patients
- Refractory to a stable 2nd generation antihistamine regimen at 1 to 4 times the approved dose
- Baseline UAS7 ≥16
- Baseline ISS7 ≥8

Key Exclusion Criteria

- Other skin conditions with symptoms of hives or angioedema
- Skin conditions associated with chronic itching that could confound the trial results
- Chronic urticaria with a clearly defined predominant or sole trigger

CSU, Chronic Spontaneous Urticaria; UAS7, weekly Urticaria Activity Score; ISS7, weekly Itch Severity Score

Study Outcomes

- Primary endpoint
  - Mean change from baseline to Week 12 in UAS7

    The UAS7 is the composite of the weekly itch severity score (ISS7) and hives severity score (HSS7) and is a widely accepted tool to measure the signs and symptoms of CSU with a score range of 0-42 (higher score indicates higher disease activity)

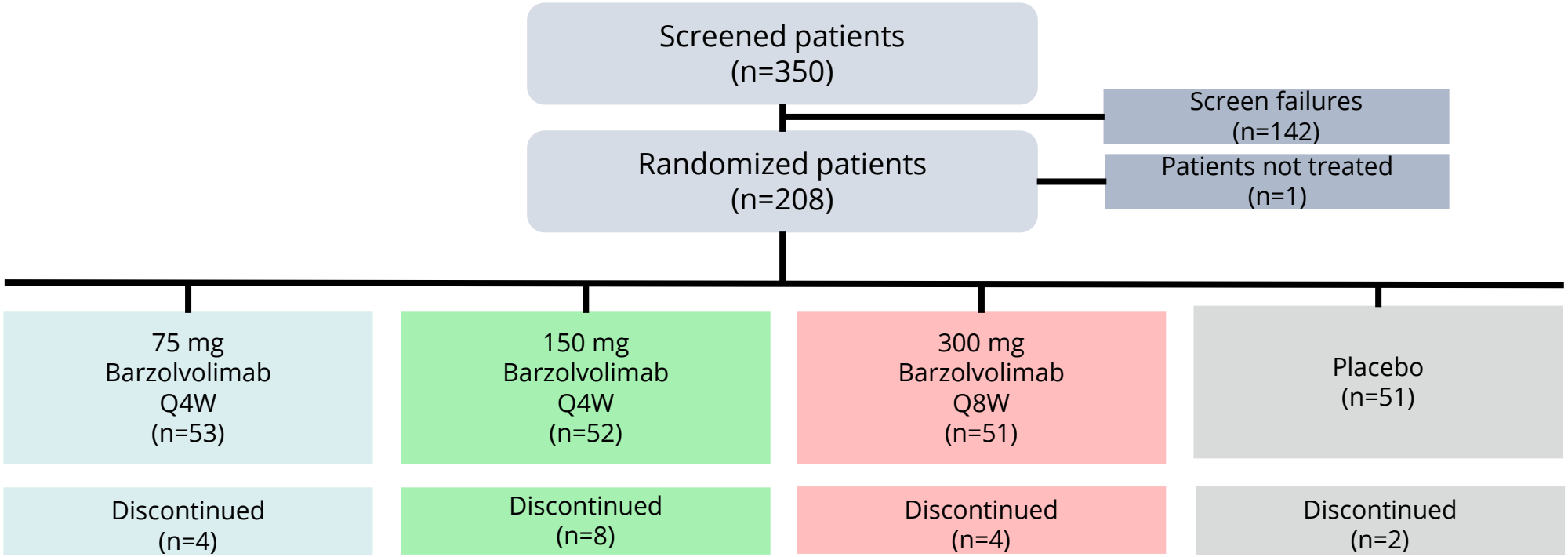
- Secondary endpoints
  - Mean change from baseline to Week 12 in ISS7
  - Mean change from baseline to Week 12 in HSS7
  - Safety and tolerability of barzolvolimab

- Exploratory analyses
  - Percentage of patients achieving UAS7≤6, UAS7=0 by Week 12
  - UAS7 response in omalizumab experienced and refractory patients

UAS7, weekly Urticaria Activity Score; ISS7, weekly Itch Severity Score; HSS7, weekly Hives Severity Score

Disposition

- In total, 350 patients screened, 208 patients randomized, 207 included in the mITT* and safety set**
- Overall, 189 (91%) completed the 12-week treatment period



*mITT population is all randomized patients who received at least 1 dose of study treatment and analyzed based on the treatment group to which they were randomized
**Safety population is all patients who received at least 1 dose of study treatment

Demographics and Baseline Characteristics

Well balanced across groups; majority of patients had severe CSU (UAS7≥28)

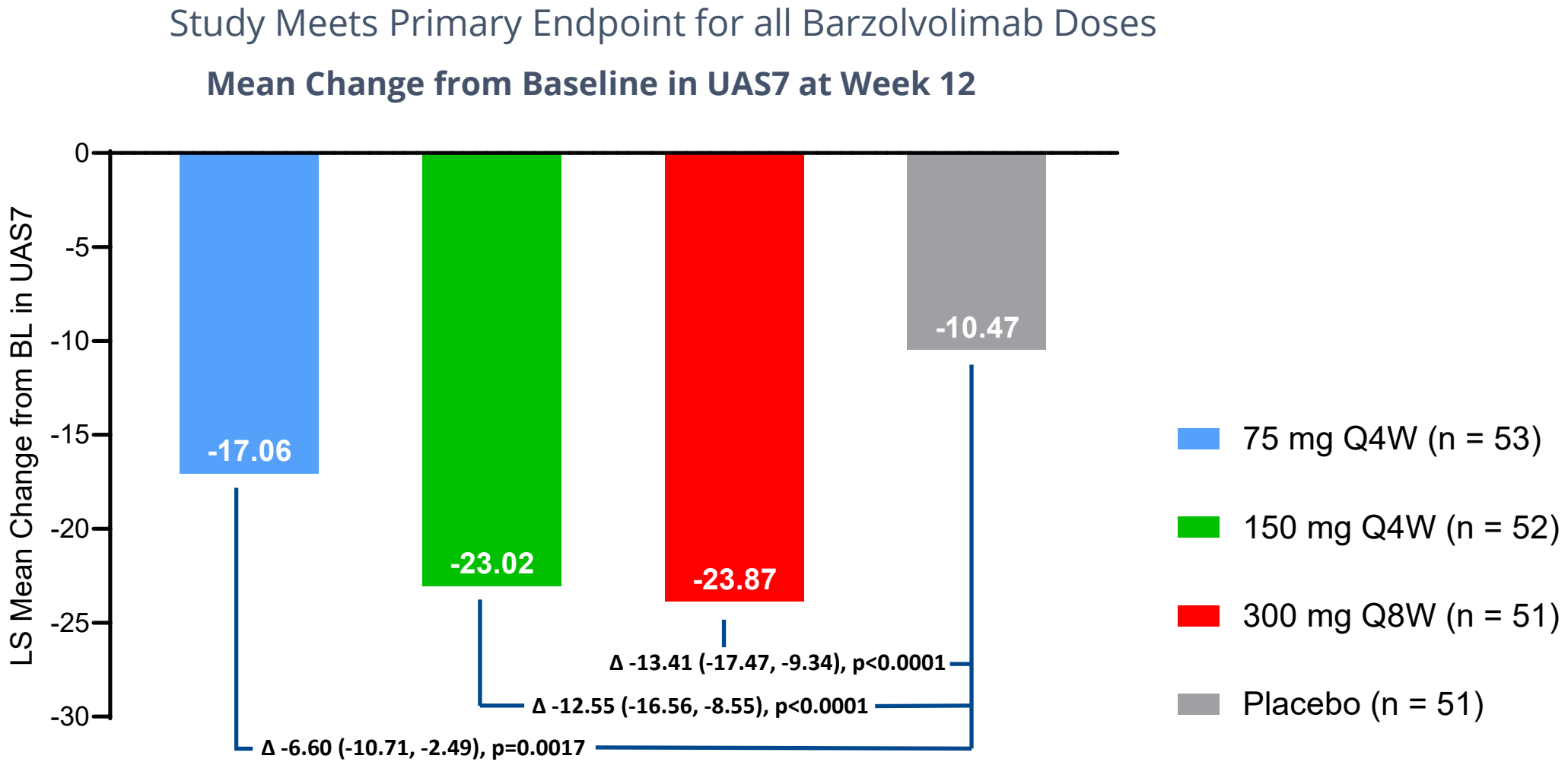
	Barzolvolimab 75 mg Q4W (N= 53)	Barzolvolimab 150 mg Q4W (N= 52)	Barzolvolimab 300 mg Q8W (N= 51)	Placebo (N= 51)
Age (years)	42.2 (15.4)	46.0 (12.8)	47.2 (13.1)	44.4 (15.4)
Gender, Female, n (%)	40 (76%)	39 (75%)	41 (80%)	36 (71%)
Race*				
White, n (%)	40 (76%)	42 (81%)	40 (78%)	40 (78%)
Black, n (%)	9 (17%)	6 (12%)	7 (14%)	7 (14%)
Asian, n (%)	7 (13%)	6 (12%)	4 (8%)	3 (6%)
Weight (kg)	77.5 (20.4)	80.9 (21.4)	85.7 (24.9)	83.8 (19.9)
UAS7 score	30.3 (8.1)	30.8 (7.7)	31.3 (6.9)	30.1 (8.1)
UAS7, severe disease, n (%)	34 (64%)	36 (69%)	39 (76%)	33 (65%)
UCT score	3.74 (2.8)	3.67 (2.5)	2.96 (2.6)	3.38 (2.5)
Angioedema at baseline, n (%)	40 (75%)	35 (67%)	42 (82%)	32 (63%)
Duration of CSU (years)	5.5 (5.4)	5.5 (6.5)	6.3 (6.6)	5.3 (6.6)
Previous experience with omalizumab, n (%)	11 (21%)	11 (21%)	11 (22%)	8 (16%)
Baseline tryptase (ng/ml) (range)	5.9 (<1-36.2)	6.6 (2.8-21.1)	5.7 (<1-15.1)	5.1 (<1-13.9)

Data are mean and standard deviation unless otherwise indicated

*Subjects may be counted in more than one category in the case of multiple races; however, a subject is counted at most once per category

CSU, Chronic Spontaneous Urticaria; UAS7, weekly Urticaria Activity Score; UCT, Urticaria Control Test

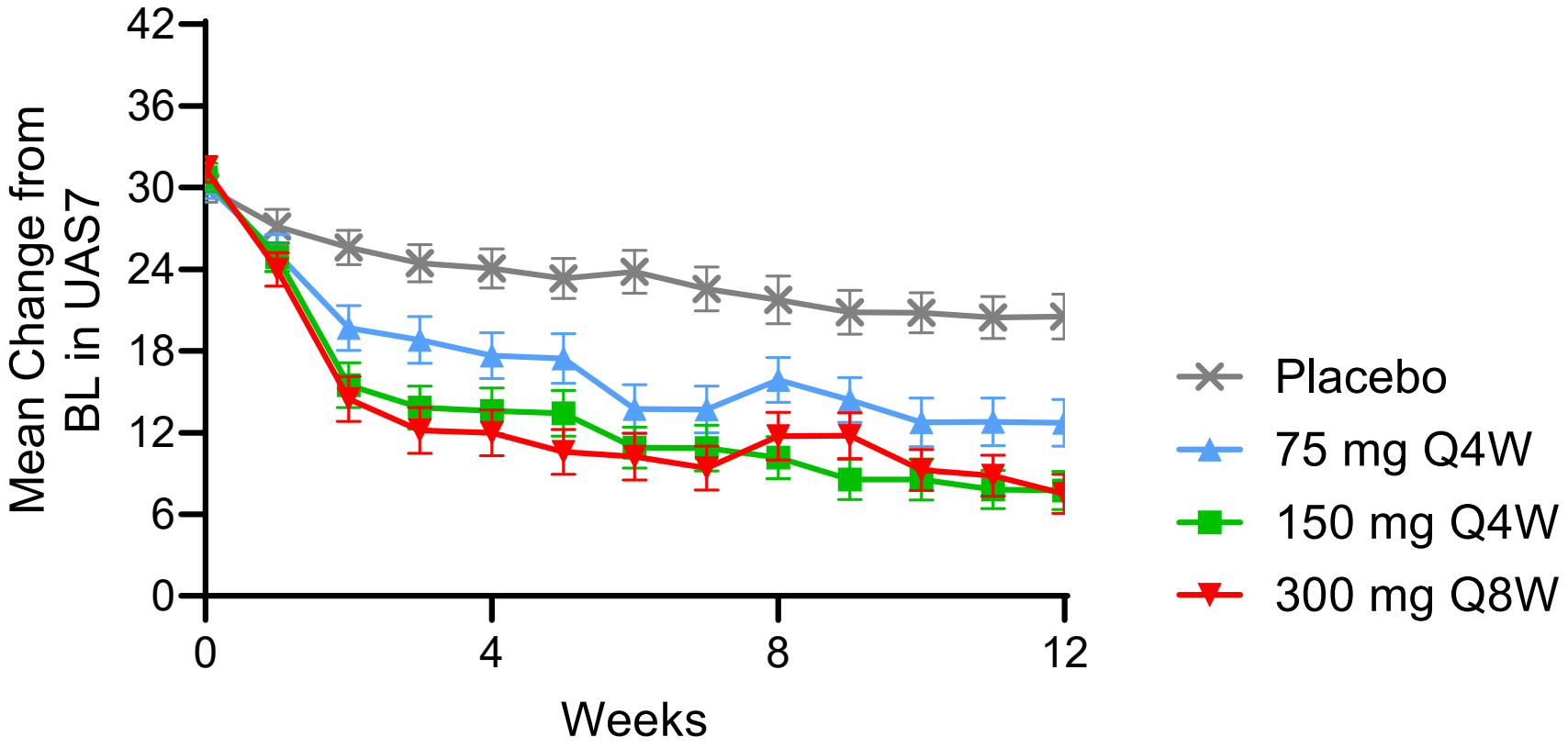
Significant Improvement in UAS7 in Patients with Moderate to Severe CSU at all Barzolvolimab Doses



Data were analyzed using ANCOVA model and multiple imputation. Benjamini-Hochberg were used for multiplicity adjustment.
Δ treatment difference LS mean (95% CI)
CI, confidence interval; LS, least squares; n, number of patients who received at least one dose of study drug
UAS7, weekly Urticaria Activity Score

Barzolvolimab Demonstrated Rapid, Significant, and Durable Improvement in UAS7 Score

UAS7 Change from Baseline Through Week 12

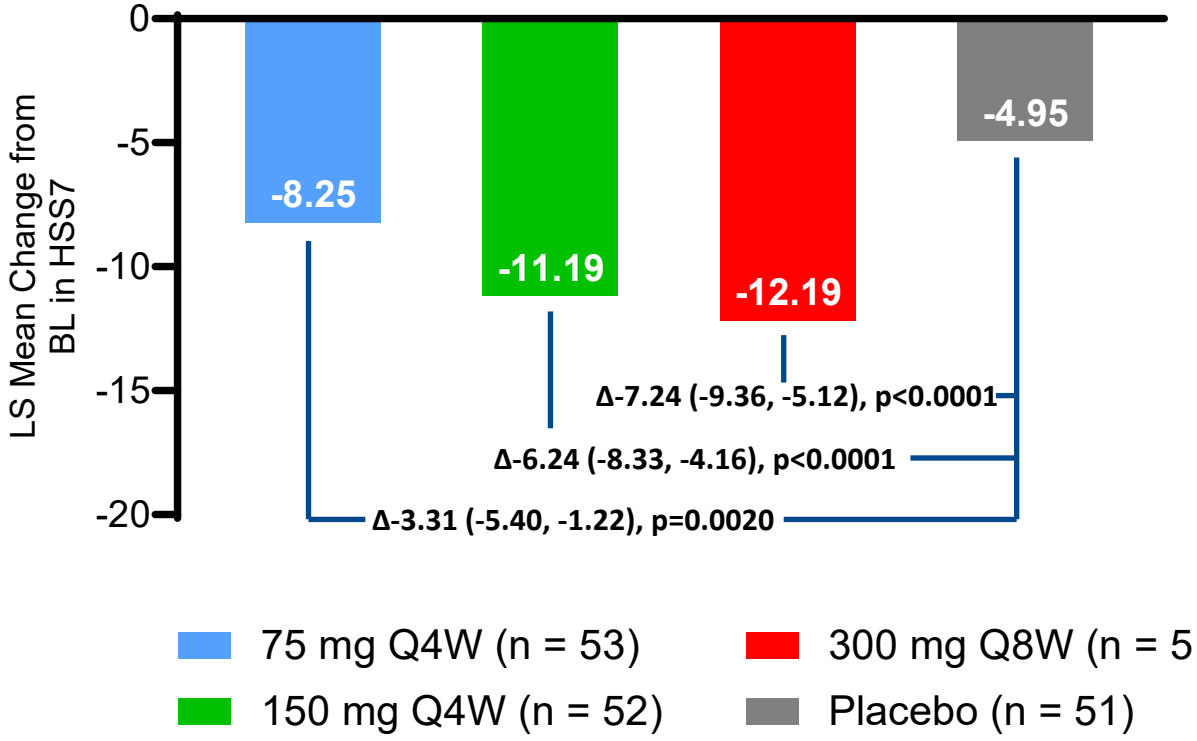


Data are LS mean +/- SE

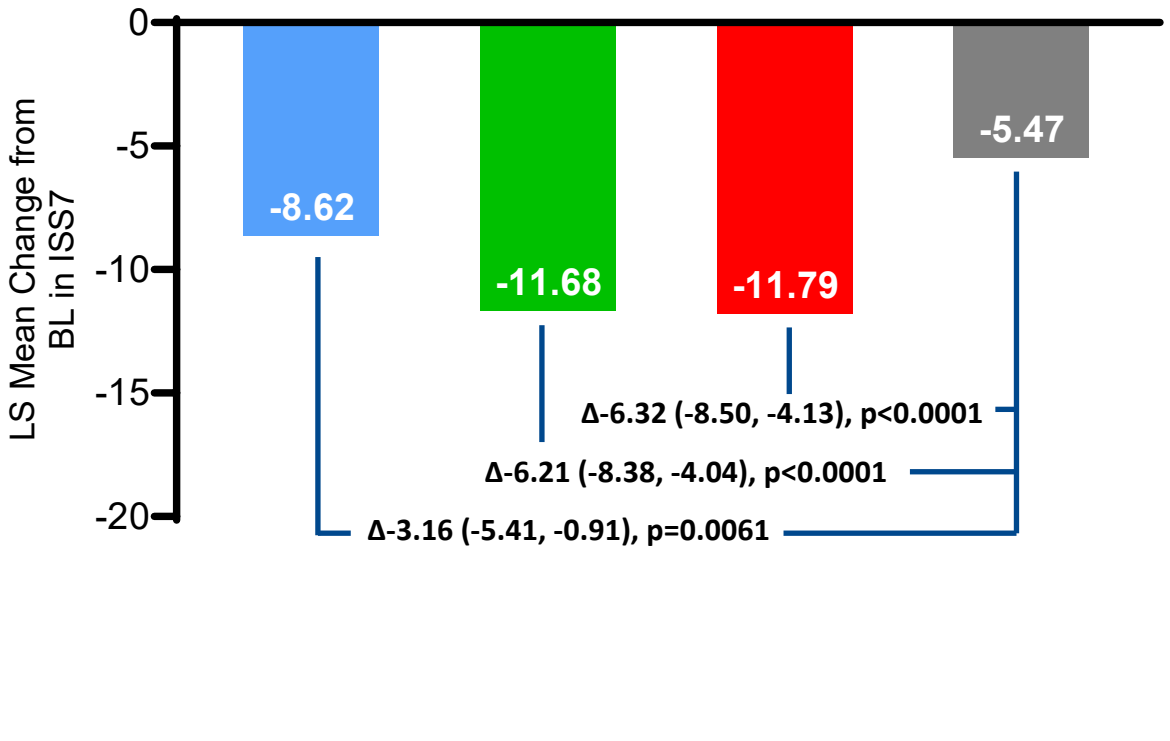
UAS7, weekly Urticaria Severity Score

Statistically Significant and Clinically Meaningful Change From Baseline in HSS7 and ISS7 at Week 12

Mean Change from Baseline in HSS7 at Week 12



Mean Change from Baseline in ISS7 at Week 12



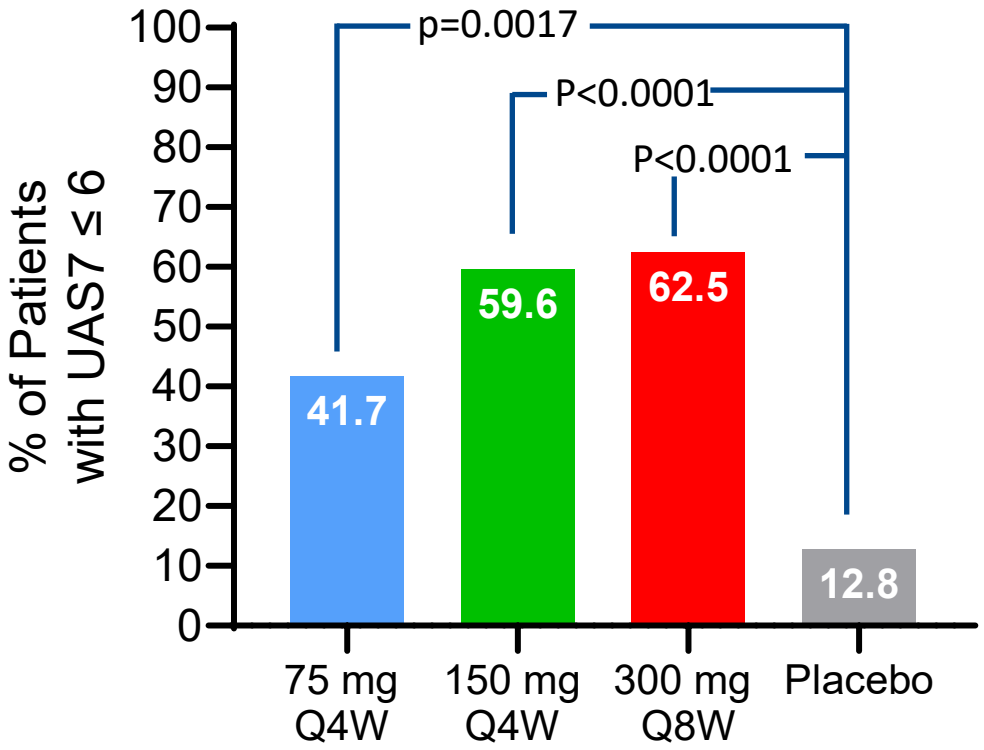
75 mg Q4W (n = 53)
150 mg Q4W (n = 52)
300 mg Q8W (n = 51)
Placebo (n = 51)

Data were analyzed using ANCOVA model and multiple imputation
Δ treatment difference LS mean (95% CI)
CI, confidence interval; LS, least squares; n, number of patients who received at least one dose of study drug
HSS7, weekly Hives Severity Score; ISS7, weekly Itch Severity Score

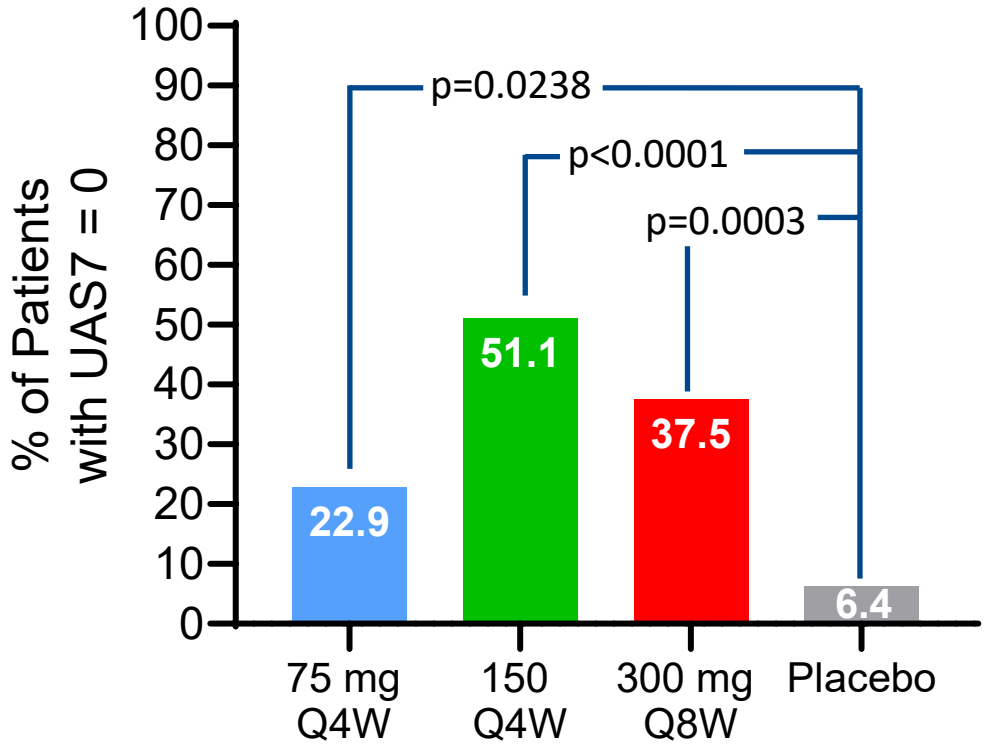
Enhanced Disease Control with Barzolvolimab at Week 12

Significantly more patients treated with barzolvolimab compared to placebo had well controlled disease (UAS7≤ 6) or achieved a complete response (UAS7=0)

% of Patients with UAS7≤ 6 Well Controlled

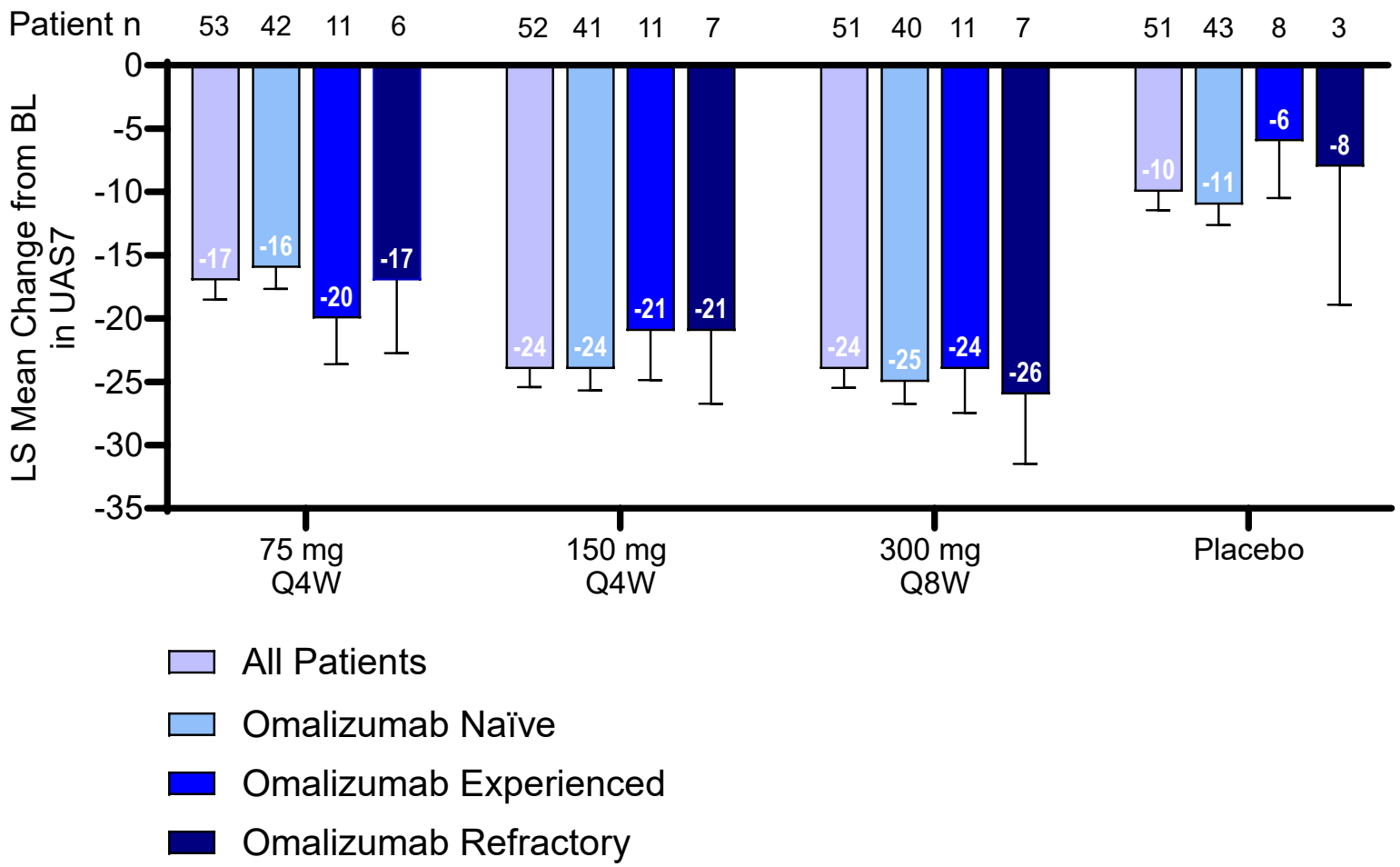


% of Patients with UAS7=0 Complete Control



Data were analyzed under mITT population with Cochran-Mantel-Haenszel tests for comparison between each active dosing regimen versus placebo.
UAS7, weekly Urticaria Activity Score

Comparable Improvement in UAS7 in Omalizumab Naïve and Experienced/Refractory* Patients at Week 12



Data are LS mean +/- SE

*Omalizumab refractory is a subset of omalizumab experienced patients who have had an inadequate clinical response or were intolerant to omalizumab

Barzolvolimab Demonstrated a Favorable Safety Profile at all Doses

Patients, n (%)	Barzolvolimab 75 mg Q4W (N= 53)	Barzolvolimab 150 mg Q4W (N= 52)	Barzolvolimab 300 mg Q8W (N= 51)	Any barzolvolimab dose (N= 156)	Placebo (N= 51)
Patients with ≥1 AE	28 (53)	29 (56)	31 (61)	88 (56)	14 (28)
Patients with SAE(s)	0	0	1 (2)	1 (1)	0
Discontinued study treatment due to AE(s)	2 (4)	1 (2)	4 (8)	7 (4)	0
Most frequent AEs by primary system organ class (≥10% of all patients receiving any barzolvolimab dose)					
Skin and subcutaneous tissue disorders	10 (19)	11 (21)	14 (28)	35 (22)	5 (10)
Infections and Infestations	9 (17)	9 (17)	12 (24)	30 (19)	9 (18)
Nervous System Disorders	5 (9)	6 (12)	7 (14)	18 (12)	0
Most frequent AEs by Preferred Term (≥10% of patients in any treatment group)					
Urticaria/CSU	8 (15)	5 (10)	3 (6)	16 (10)	5 (10)
Hair color changes	0	5 (10)	9 (18)	14 (9)	0
Neutropenia	4 (8)	3 (6)	5 (10)	12 (8)	0

Most AEs were mild to moderate in severity; infections were not accompanied by neutropenia
SAE of external ear canal cholesteatoma considered unrelated to treatment
Discontinuations due to AE: neutropenia, abdominal pain, hair color change, hair color change/dizziness, urticaria, neutropenia/thrombocytopenia

Conclusions

- In this ongoing Phase 2 study, barzolvolimab, an anti-KIT mAb, demonstrated a statistically significant and clinically meaningful decrease in UAS7 vs placebo at Week 12 in patients with CSU who are symptomatic on antihistamines
  - The majority of patients had well controlled urticaria at Week 12 (UAS7≤6)
  - UAS7=0 was observed in 51% of patients in the 150 mg Q4W and in 37.5% of patients in the 300 mg Q8W groups compared to 6.4% in the placebo group
  - Sustained activity with rapid onset within 2 weeks
  - Statistically significant and clinically meaningful decrease in both ISS7 and HSS7 at Week 12
  - Similar pattern of improvement observed in patients with omalizumab-experienced/refractory and omalizumab-naïve CSU consistent with mechanism of action
- Barzolvolimab demonstrated a favorable safety profile across the dose ranges studied
- Phase 3 studies are planned to initiate in 2024