Barzolvolimab shows profound efficacy and favorable safety over 52 weeks in patients with Chronic Spontaneous Urticaria

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European Academy of Dermatology and Venereology (EADV 2024)

Disclosures

Martin Metz has received honoraria as a speaker and/or advisor for: AbbVie, ALK-Abello, Almirall, Amgen, Argenx, AstraZeneca, Astria, Attovia, Celldex, Celltrion, Escient, Ga2len, Galderma, gsk, Incyte, Jasper, Lilly, Novartis, Pfizer, Pharvaris, Regeneron, Sanofi, Teva, ThirdHarmonicBio, Vifor

Introduction

- New therapies are urgently needed for chronic spontaneous urticaria (CSU), a mast cell-driven disease
  - Many patients remain symptomatic despite standard or up-dosed antihistamines and omalizumab therapy
- Barzolvolimab is an anti-kit monoclonal antibody, which inhibits activation of and depletes mast cells
- In this ongoing Phase 2 study, barzolvolimab demonstrated statistically significant improvement in UAS7, ISS7 and HSS7 at week 12 vs placebo in patients with CSU remaining symptomatic with second generation H1–AHs[1]

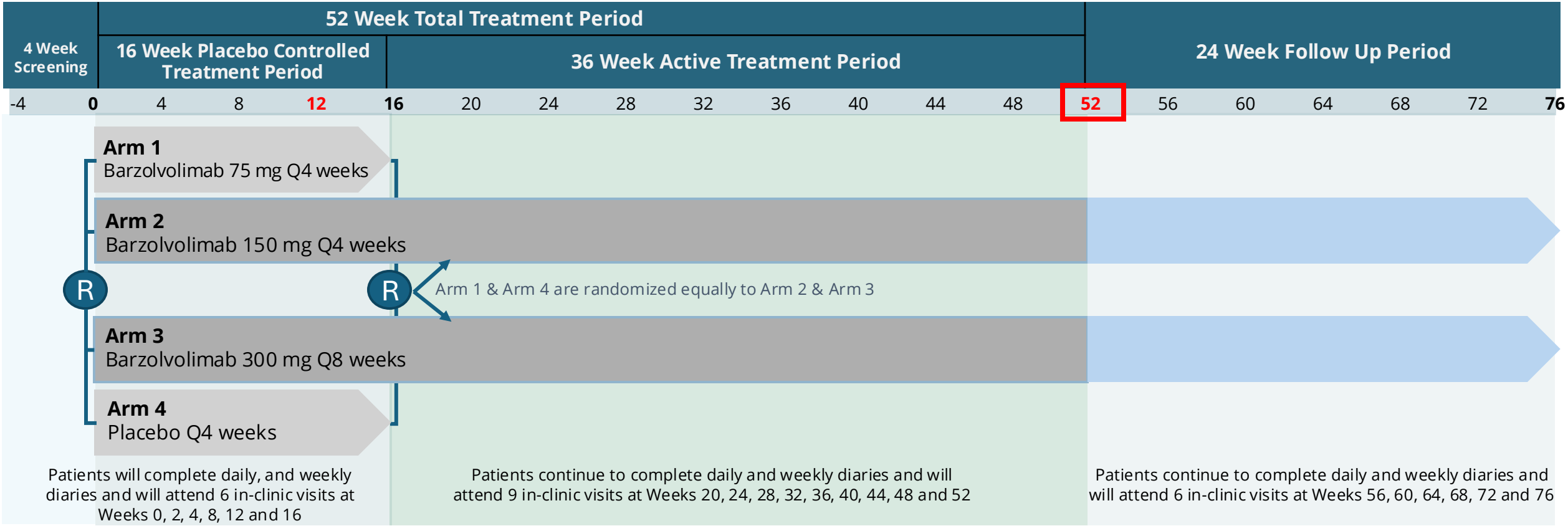
Here we present the long-term (week 52) analysis of this Phase 2 study

AH, antihistamine; H1, histamine-1; UAS7, weekly Urticaria Activity Score, ISS7, weekly Itch Severity Score, HSS7, weekly Hives Severity Score.

1. Maurer M, et al. Oral presentation at: AAAAI 2024 Annual Scientific Meeting; February 23-26, 2024; Washington DC. Abstract 366. Study ID: NCT05368285

Results based on interim data cut: July 31, 2024

Study Design and Key Eligibility



Randomized, double-blind, placebo-controlled, dose-finding study

208 patients enrolled at ~75 sites/10 countries

Biologic naive & experienced patients refractory to antihistamines

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

Secondary Endpoints:
ISS7 (Itch Severity Score)
HSS7 (Hives Severity Score)
AAS7 (Angioedema Activity Score)
Safety

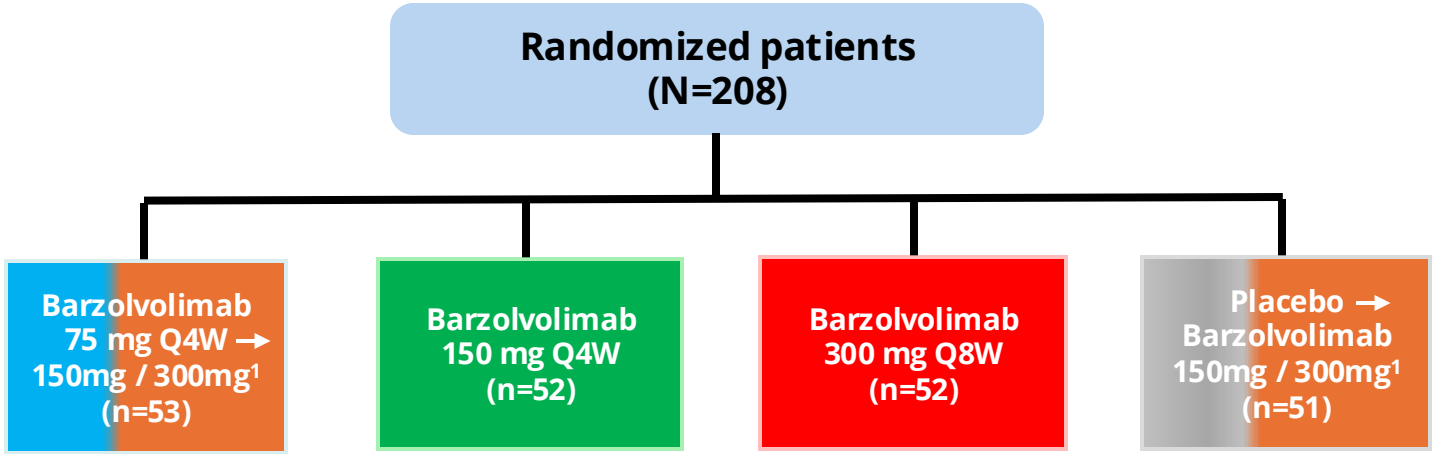
Demographics and Baseline Characteristics

- Well balanced across groups; majority 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)	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)
UAS7 score	30.3 (14-42)	30.8 (12-42)	31.3 (17-42)	30.0 (13-42)
UAS7, severe disease n (%)	34 (64%)	36 (69%)	39 (76%)	33 (65%)
ISS7 score	15.4 (7-21)	15.7 (7-21)	16.4 (8-21)	15.6 (6-21)
HSS7 score	14.9 (7-21)	15.1 (3.5-21)	14.9 (7-21)	14.5 (1-21)
Angioedema at baseline, n (%)	40 (75%)	35 (67%)	42 (82%)	32 (63%)
Previous experience to omalizumab, Yes n(%)	11 (21%)	11 (21%)	11 (22%)	8 (16%)

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

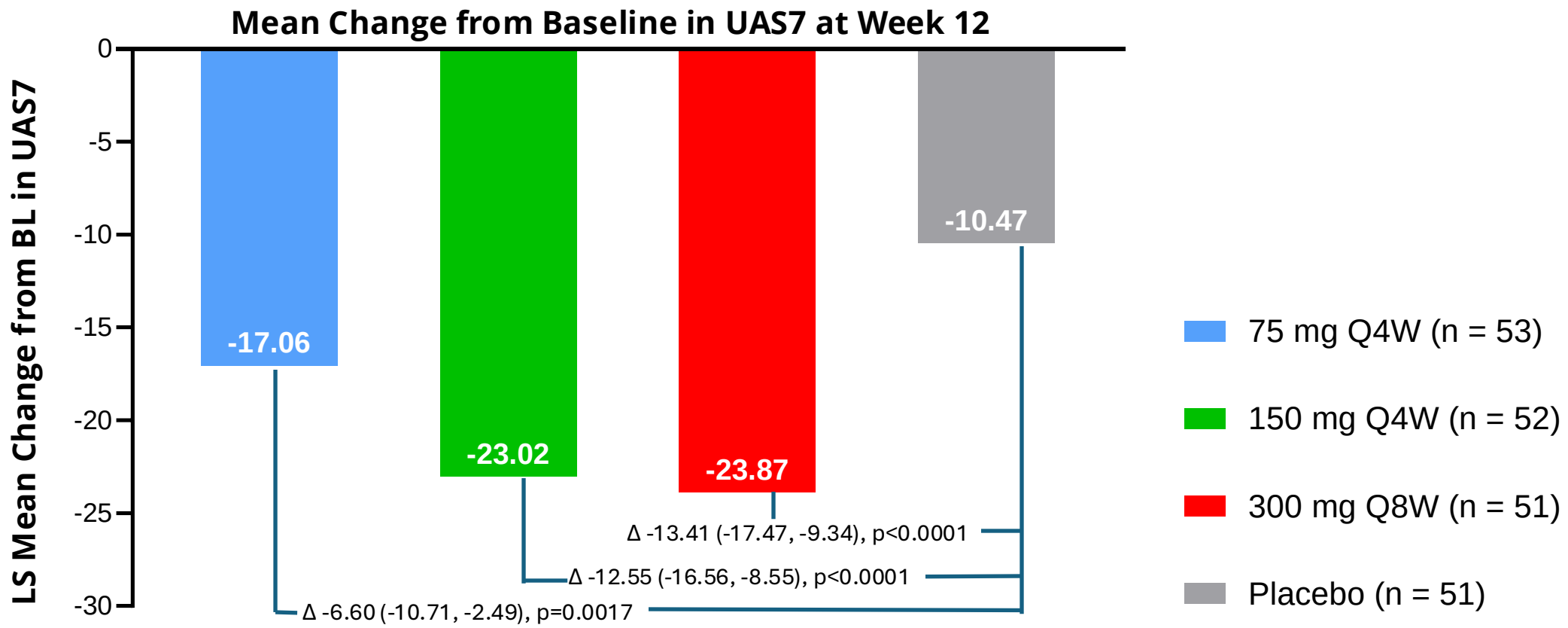
Patient Disposition Through 52 Weeks



Discontinued Treatment, n (%)	13 (25%)	13 (25%)	13 (25%)	8 (16%)[2]
Adverse Event[3]	7 (13%)	4 (8%)	7 (13%)	2 (4%)
Patient Decision	1 (2%)	3 (6%)	1 (2%)	3 (6%)
Non-Compliance of the Patient	2 (4%)	1 (2%)	1 (2%)	2 (4%)
Lack of Clinical Response	1 (2%)	0	2 (4%)	1 (2%)
Other	2 (4%)	5 (10%)	2 (4%)	0

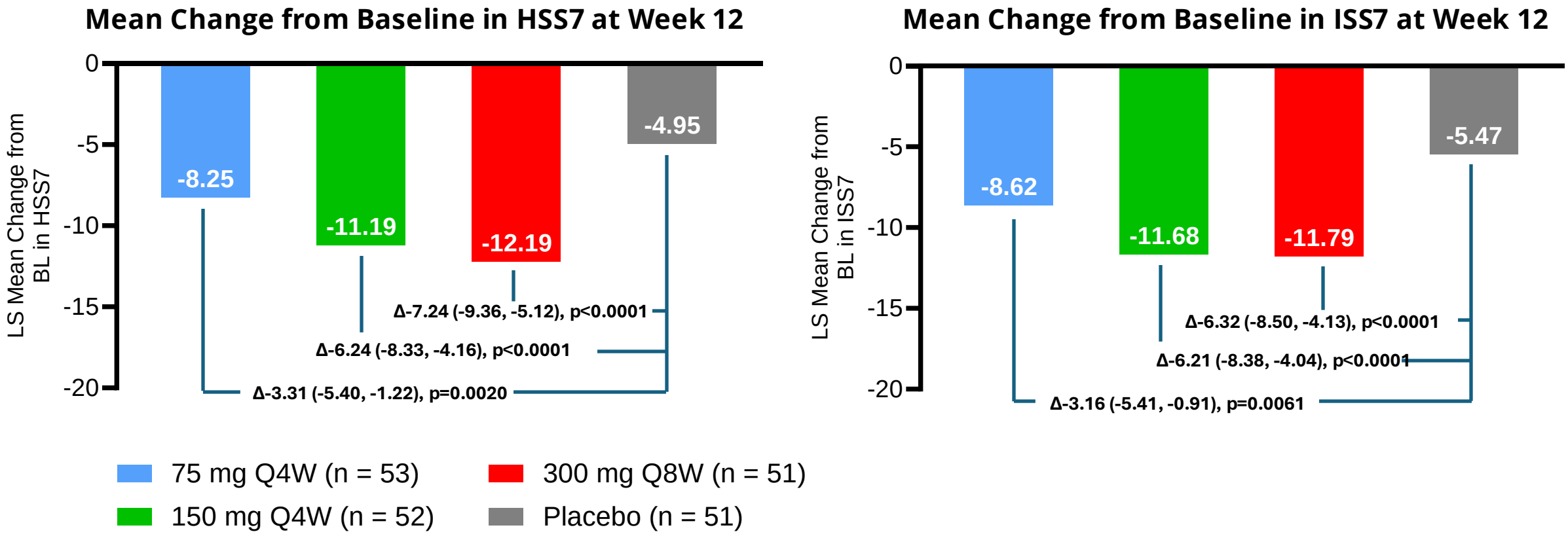
[1] Placebo and 75mg Q4W re-randomized to 150mg Q4W or 300mg Q8W at Week 16
[2] Three patients discontinued placebo during the 16 week placebo-controlled period due to patient decision (2), non compliance (1)
[3] Adverse event discontinuations in more than one patient: hair color changes (6), urticaria (5), macrocytic anemia (2)

Barzolvolimab Demonstrated Significant Improvement in UAS7 vs Placebo at Week 12 (Primary Endpoint)



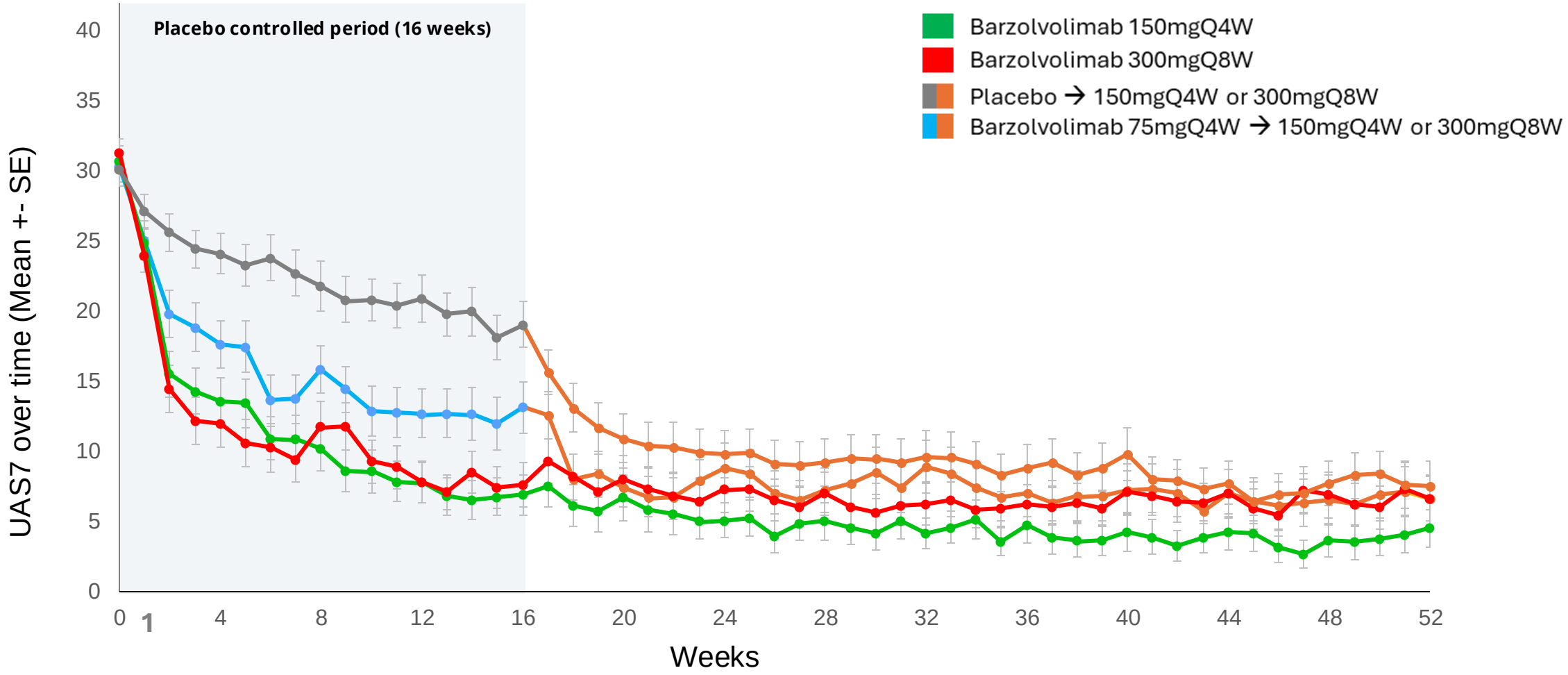
Data were analyzed using ANCOVA model and multiple imputation. Benjamini-Hochberg were used for multiplicity adjustment
Δ treatment difference LS mean (95% CI)
CI, confidence interval; LS, least squares; n, number of patients who received at least one dose of study drug, UAS7-weekly Urticaria Activity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

Barzolvolimab Demonstrated Significant Improvement in Both Itch and Hives vs Placebo at Week 12

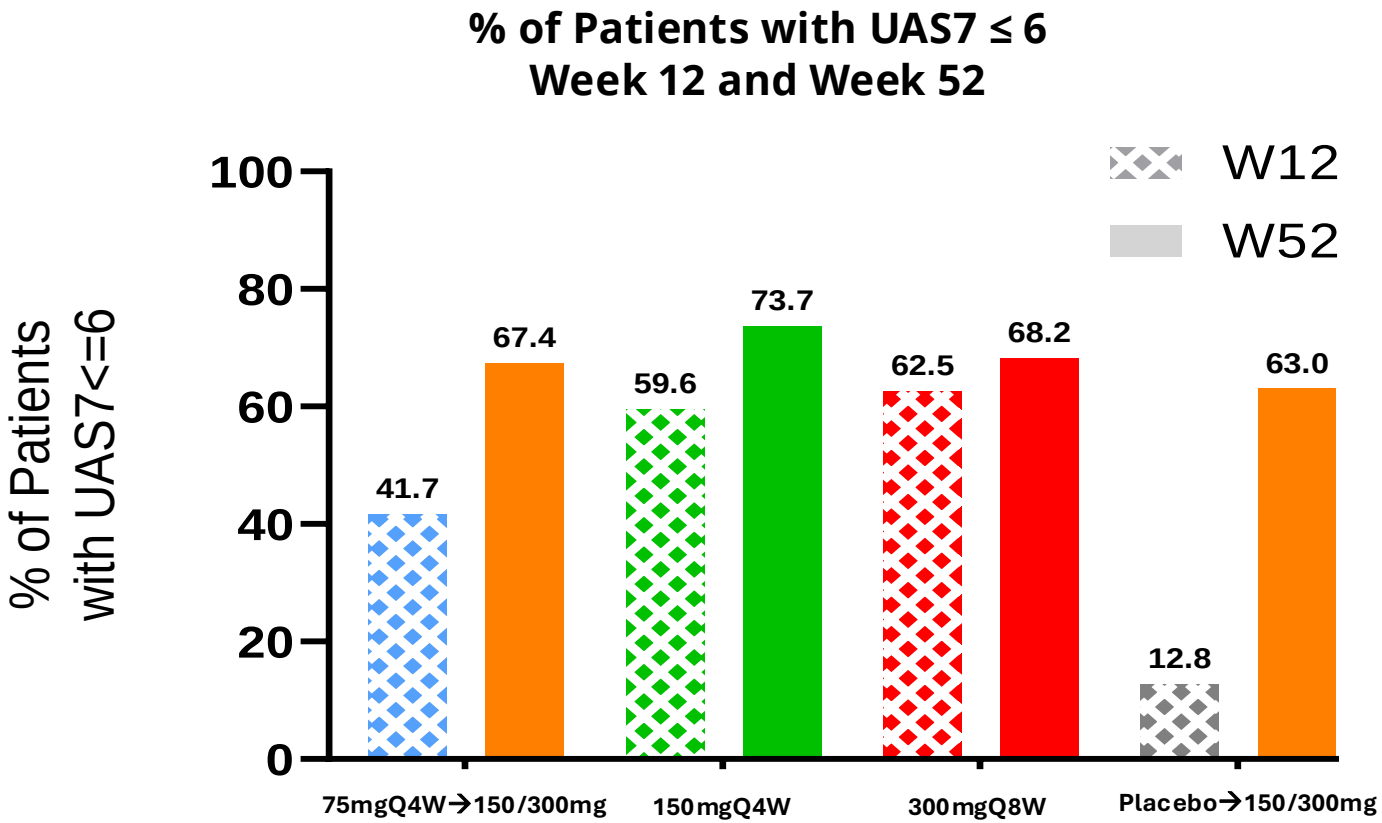


Data were analyzed using ANCOVA model and multiple imputation
Δ treatment difference LS mean (95% CI)
CI, confidence interval; LS, least squares; n, number of patients who received at least one dose of study drug
HSS7, weekly Hives Severity Score; ISS7, weekly Itch Severity Score

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

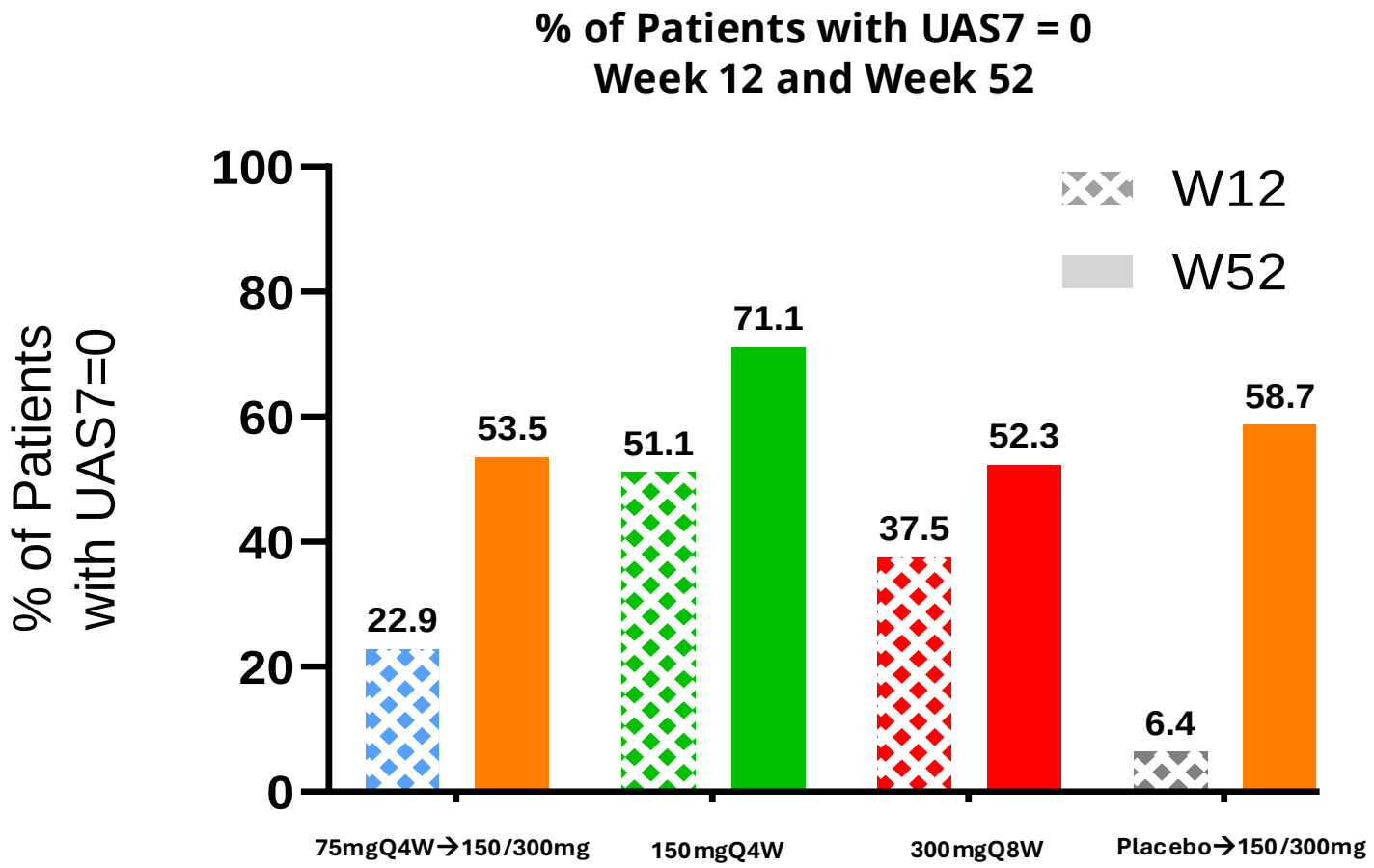


Up to 74% of Patients Achieved Well-Controlled Disease (UAS7≤6) With Barzolvolimab at Week 52



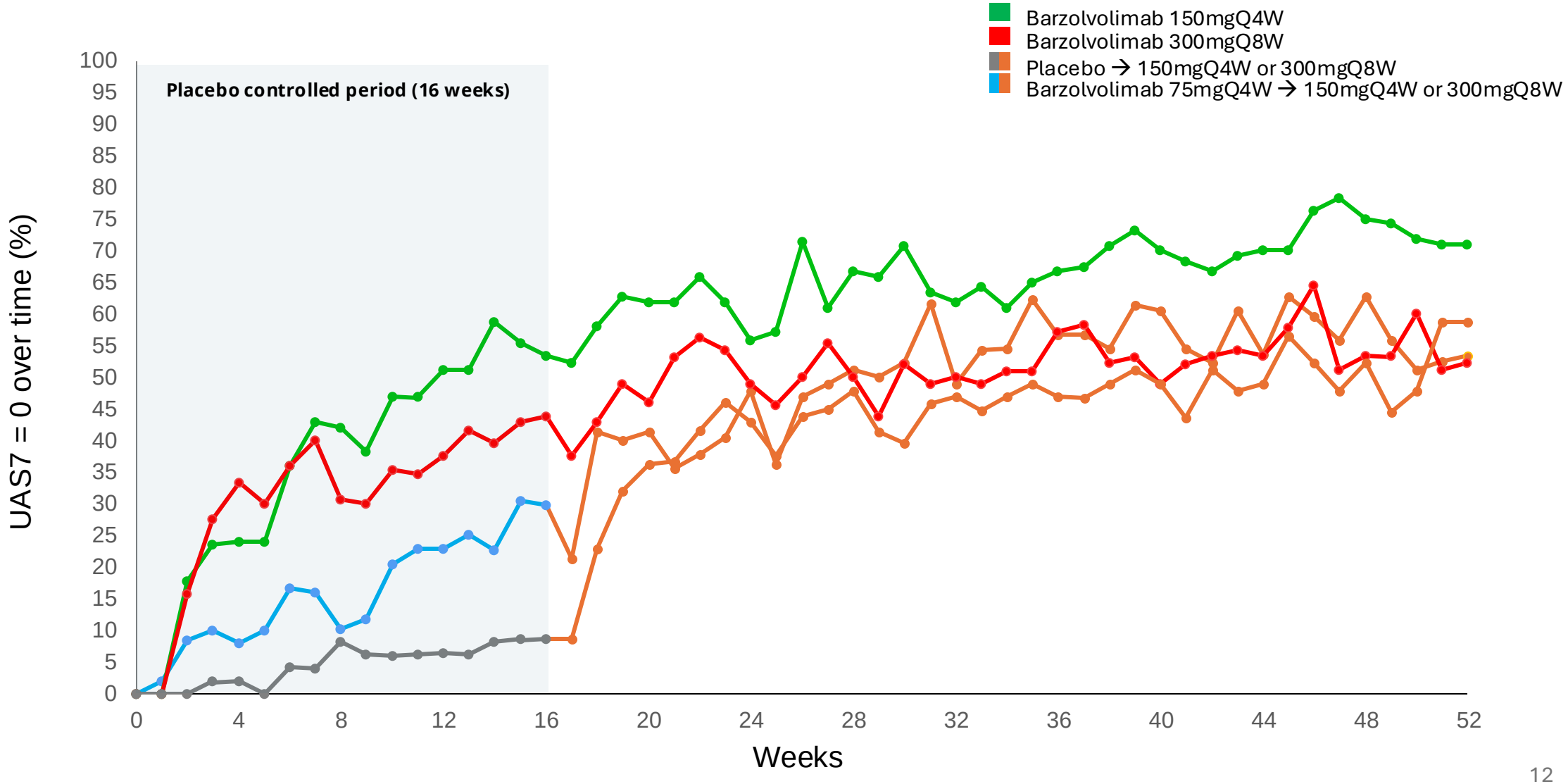
Placebo and 75mg Q4W re-randomized to 150mg Q4W or 300mg Q8W at Week 16

Up to 71% of Patients Achieved Complete Control (UAS7=0) With Barzolvolimab at Week 52

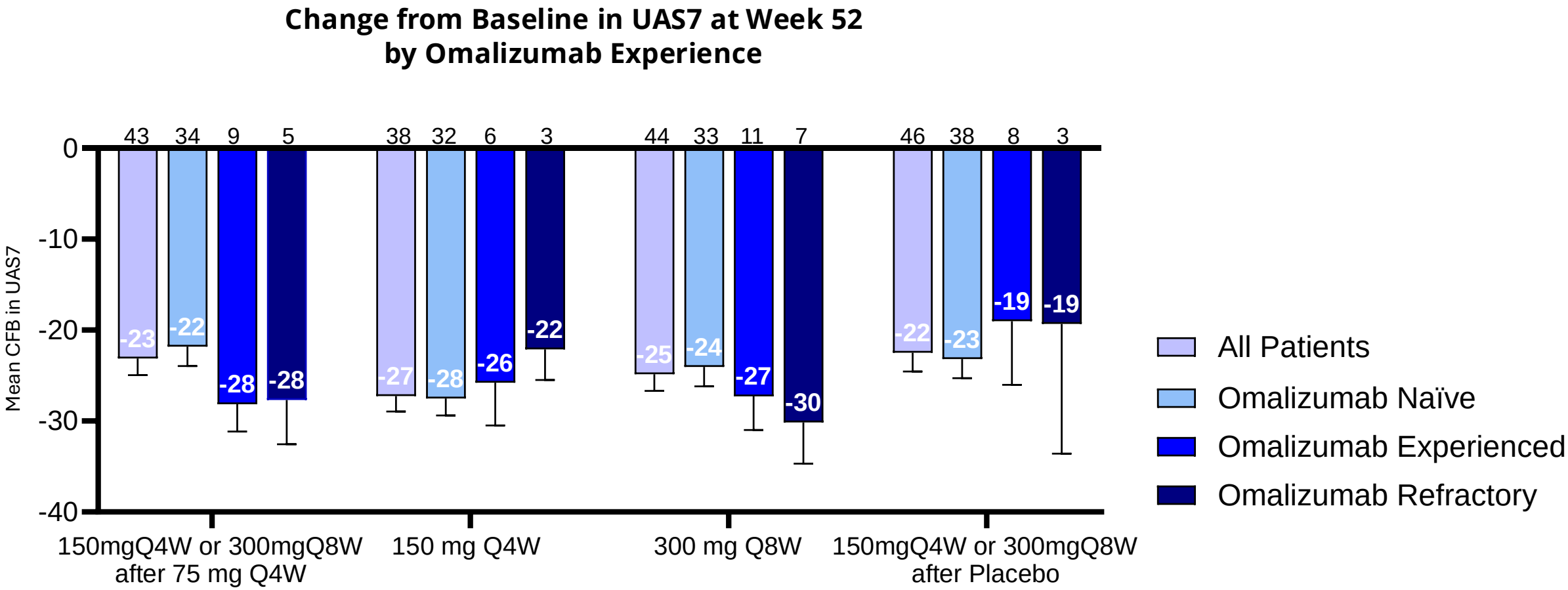


Placebo and 75mg Q4W re-randomized to 150mg Q4W or 300mg Q8W at Week 16

Complete Responses (UAS7=0) With Barzolvolimab Were Observed Early and Were Sustained or Improved to Week 52



Robust Response Seen Regardless of Prior Omalizumab Experience



Placebo and 75mg Q4W re-randomized to 150mg Q4W or 300mg Q8W at Week 16

Barzolvolimab was well tolerated through 52 weeks of treatment

- Most events were grade 1 (mild), mechanism-related (KIT) and expected to be reversible
- Adverse events were not dose dependent
- No association between infections and neutropenia/decreased neutrophil counts

	Placebo Controlled Period (16 weeks)		Full Treatment Period (52 weeks)	Placebo → Barzolvolimab (36 weeks)
Patients, n (%)	**Barzolvolimab[1] (N= 156)**	**Placebo (N= 51)**	**Barzolvolimab[2] (N= 156)**	**Transitioned to Barzolvolimab[3] (N=48)**
At least one AE	103 (66)	20 (39)	139 (89)	32 (67)
Treatment Related SAEs	0	0	2 (1)[4]	0
Most frequent AEs by Preferred Term (≥10% of patients in any treatment group)				
Hair color changes	22 (14)	0	40 (26)	8 (17)
Neutropenia / Neutrophil Count Decreased	14 (9)	0	26 (17)	2 (4)
Urticaria	15 (10)	5 (10)	23 (15)	3 (6)
Skin hypopigmentation	2 (1)	0	21 (13)	9 (19)
Nasopharyngitis	6 (4)	3 (6)	15 (10)	4 (8)

[1] All dose levels (75mgQ4W, 150mgQ4W, 300mgQ8W) combined; [2] All dose levels combined; patients randomized to 75mgQ4W were re-randomized to 150mgQ4W or 300mgQ8W at week 16; [3] Patients received 36 weeks of barzolvolimab 150mgQ4W or 300mgQ8W after 16 weeks of placebo; data are shown for 36 week barzolvolimab experience; [4] SAEs of worsening urticaria symptoms

Conclusions

- Barzolvolimab treatment resulted in **rapid, profound and durable improvement in UAS7** with a **deepening of response** over 52 weeks in patients with antihistamine refractory CSU
  - Up to **71% of patients achieved complete response**
  - Similar robust improvement seen in patients previously treated with omalizumab, including refractory patients
- Barzolvolimab was **well tolerated** through 52 weeks
- Barzolvolimab has the potential to be an important new treatment option. Global Phase 3 studies are actively enrolling

Acknowledgements

We wish to thank all the investigators and their patients who contributed to this trial.

We are especially grateful to Professor Dr. Marcus Maurer for his partnership in advancing barzolvolimab. Dr. Maurer's steadfast commitment to improving the lives of patients with chronic urticarias was at the forefront of every interaction we had with him and was a source of inspiration to our team and the field. His legacy will live on.