

# Prolonged Off-Treatment Efficacy of Barzolvolumab in Chronic Spontaneous Urticaria

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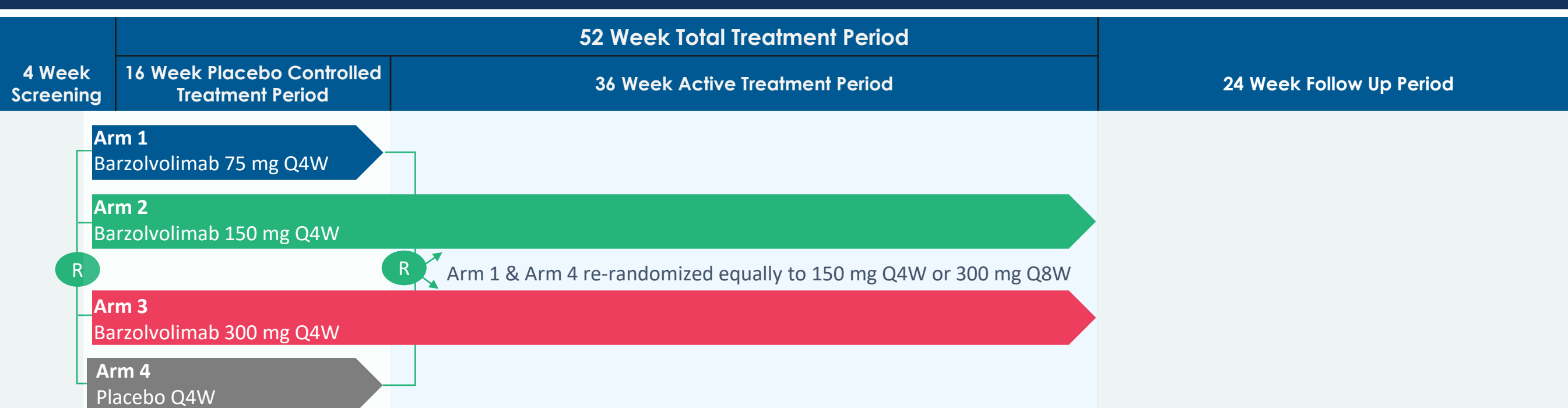
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## INTRODUCTION

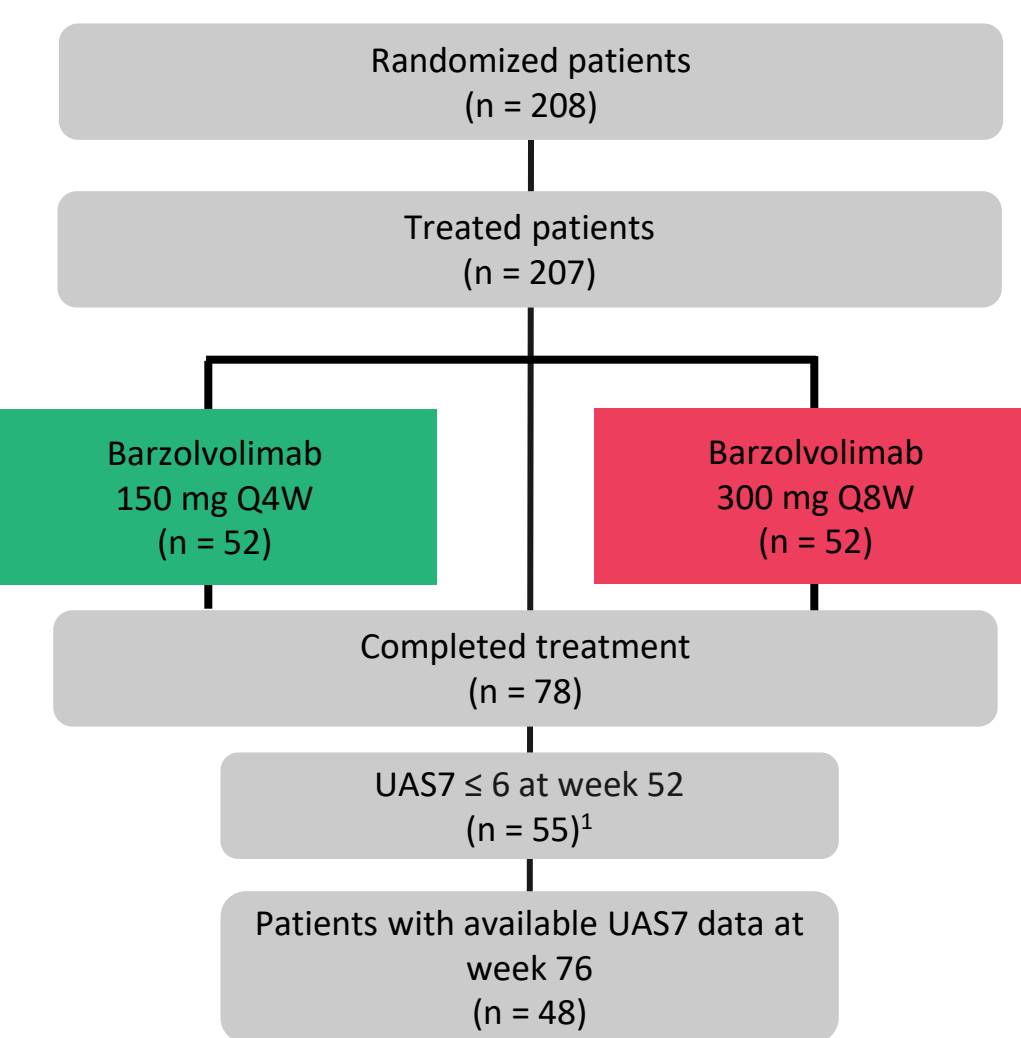
- Mast cells (MCs) are key effector cells in chronic spontaneous urticaria (CSU)
- Barzolvolumab, a humanized monoclonal antibody that inhibits KIT activation by SCF, demonstrated rapid and durable depletion of skin MCs<sup>1</sup>
- We previously reported that barzolvolumab treatment resulted in statistically 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<sup>2</sup>
  - Up to 74% of patients treated with barzolvolumab for 52 weeks achieved well-controlled disease<sup>3</sup>
- The objective of this analysis was to characterize off-treatment efficacy among patients who achieved well-controlled disease (UAS7 ≤ 6) after 52 weeks of barzolvolumab treatment

## STUDY DESIGN



## METHODS

- We conducted a randomized, double-blind, placebo-controlled, dose-finding study in patients with antihistamine-refractory chronic spontaneous urticaria (NCT05368285). Following a 52-week total treatment period, patients entered a 24-week follow-up period
- We performed a post hoc analysis of efficacy in patients during the 24-week follow-up period who randomized to barzolvolumab 150 mg Q4W or 300 mg Q8W for 52 weeks (Arm 2 & 3), completed the full treatment period (52 weeks), achieved at least well-controlled disease (UAS7 ≤ 6) at Week 52 (n = 55) and had a reported UAS7 at Week 76 (n = 48)
- Analyses on barzolvolumab concentrations versus urticaria activity scores and circulating tryptase, a soluble mast cell marker, were conducted. As a comparison, serum tryptase levels (n = 78) from Phase 1 studies in Healthy Volunteers (NCT05031624, NCT04146129, NCT06650761) was used.



### Baseline Demographics and Disease Characteristics

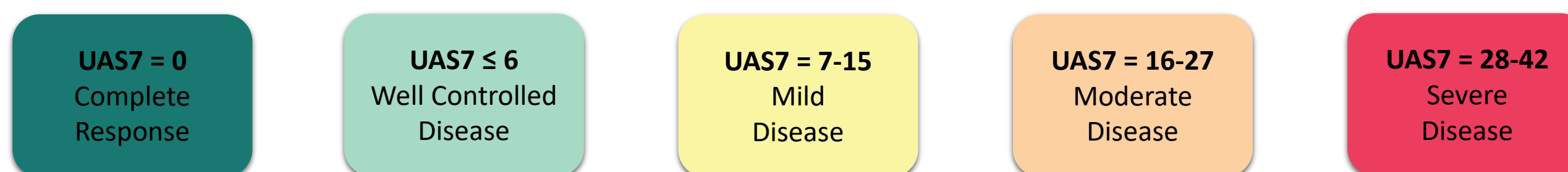
- Baseline demographics/disease characteristics are similar to overall study population
- 66.7% and 68.9% of patients had severe CSU and angioedema, respectively, at baseline

Patients With Well Controlled Disease at Week 52 n = 48 <sup>2</sup>		
Age, years (SD)	47.5 (14.1)	
Female, n (%)	35 (72.9)	
Race, n (%)	African American	2 (4.2)
	Asian	4 (8.3)
	Mixed Race	2 (4.2)
	White	40 (83.3)
Weight, kg (SD)	81.9 (22.5)	
UAS7 (SD)	31.1 (7.7)	
UAS7, severe disease, <sup>3</sup> n (%)	32 (66.7)	
UCT7 score (SD)	4.5 (3.1)	
DLQI score (SD)	16.4 (7.8)	
Tryptase, ng/mL (SD)	5.8 (2.9)	
Angioedema at baseline, n (%)	33 (68.9)	
Duration of Disease, months (SD)	69.6 (81.0)	
Prior omalizumab stratum	Omalizumab Experienced, n (%) <sup>4</sup>	9 (18.7)
	Omalizumab Naive, n (%)	39 (81.3)

<sup>1</sup>55/78 (71%) had UAS7 ≤ 6 (well controlled disease) at W52; <sup>2</sup> Baseline demographics in subpopulation used for analysis were similar to the overall population and are consistent with CSU patient populations from other studies; <sup>3</sup>Severe UAS7 range 28-42; <sup>4</sup>Includes patients with inadequate response or intolerance to omalizumab and patients that have received prior omalizumab but are not refractory, or with unknown status. Unless otherwise stated, all values represent means.

## Prolonged off-treatment efficacy in barzolvolumab-treated patients

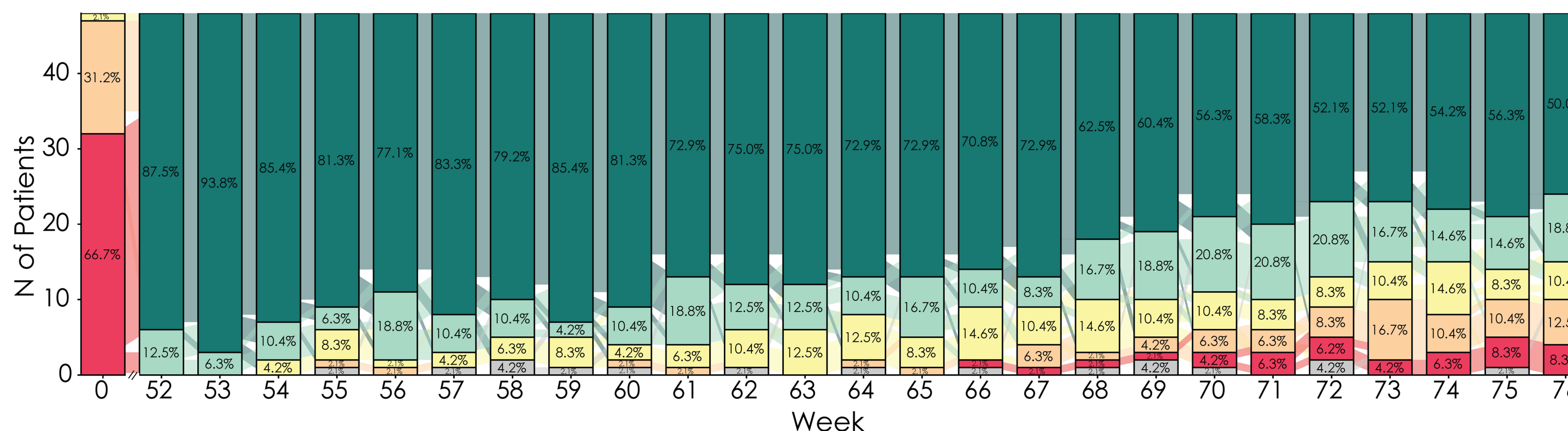
### CSU Disease Activity is Defined Using 5 Distinct Health States



UAS7 score-based health states were used to describe CSU disease activity throughout the 24-week follow-up period (W52 – W76)

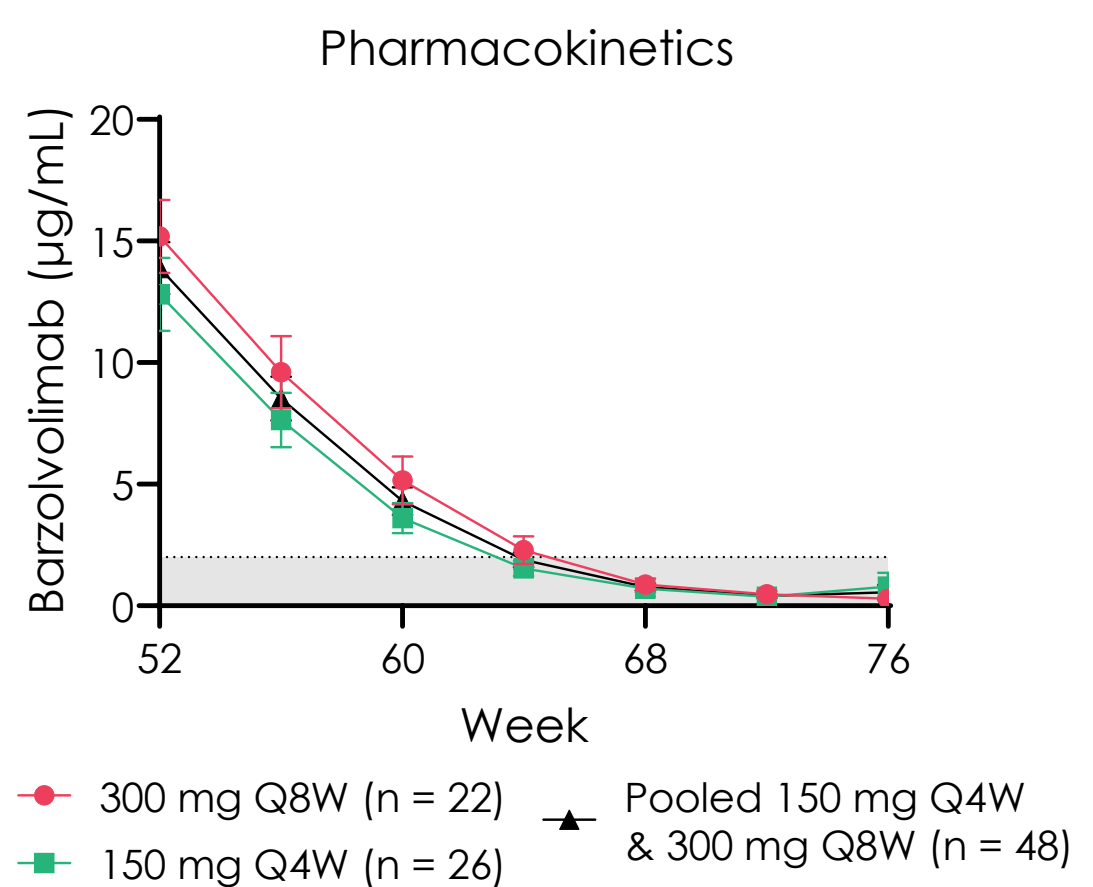
Based on: Stull D, et al. Br J Dermatol 2017;177(4):1093-1101.

## Sustained well controlled disease observed 7 months after the last dose of barzolvolumab in 69% of patients who achieved well controlled disease at week 52

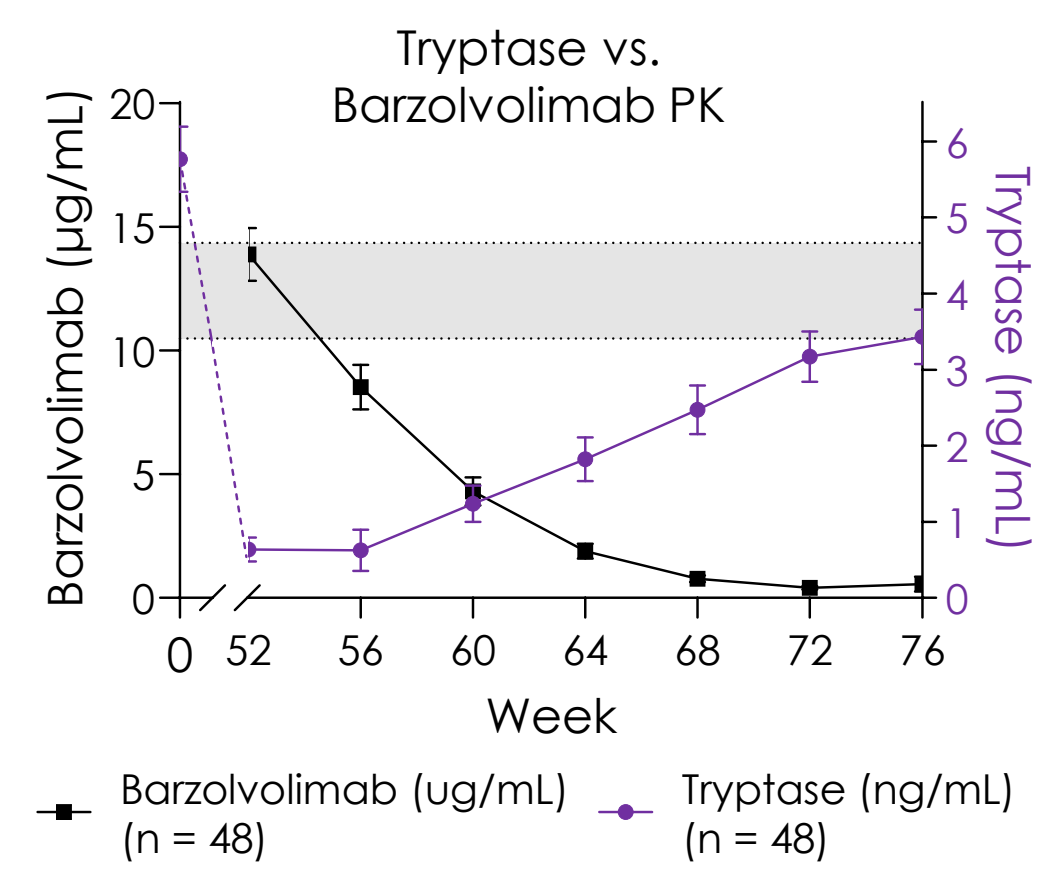


- Last dose of barzolvolumab was at W48

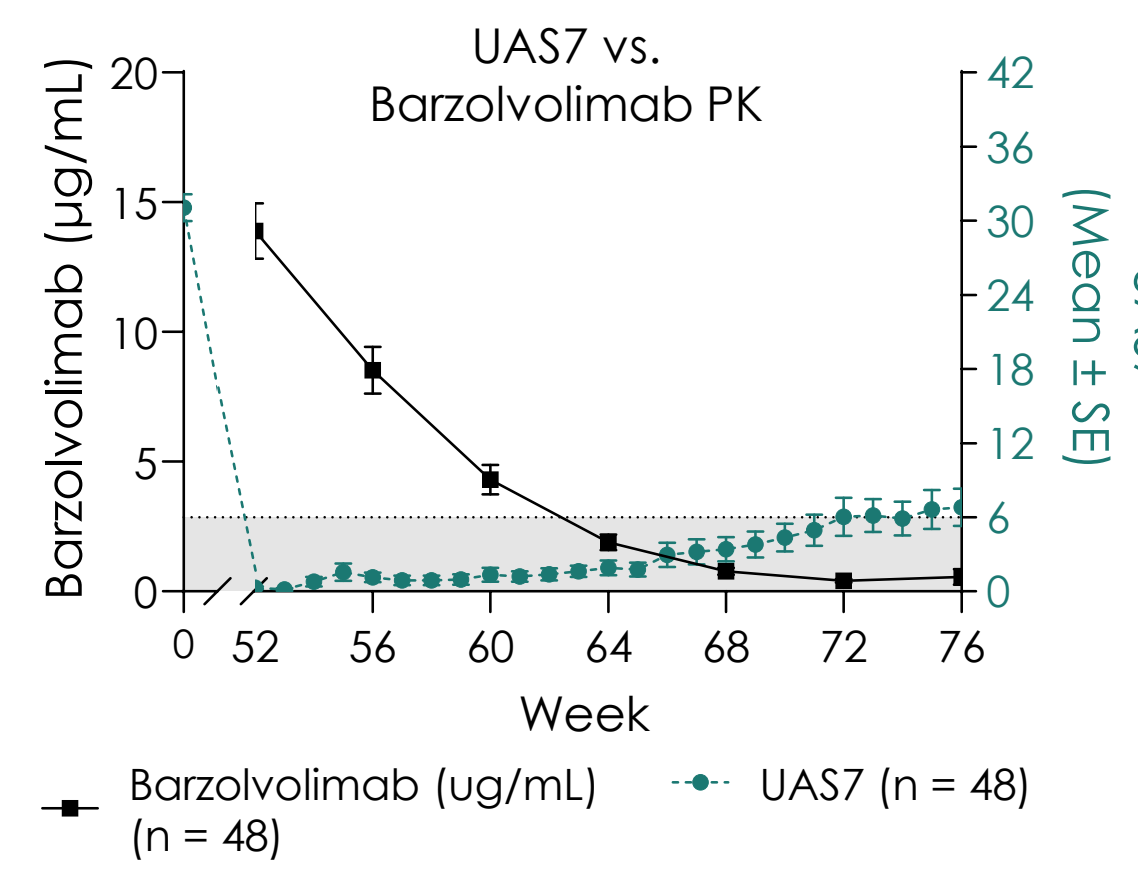
### Concentration of barzolvolumab falls below therapeutic levels by week 64



### Tryptase recovers towards range of healthy subjects by week 76 indicating normal mast cell numbers

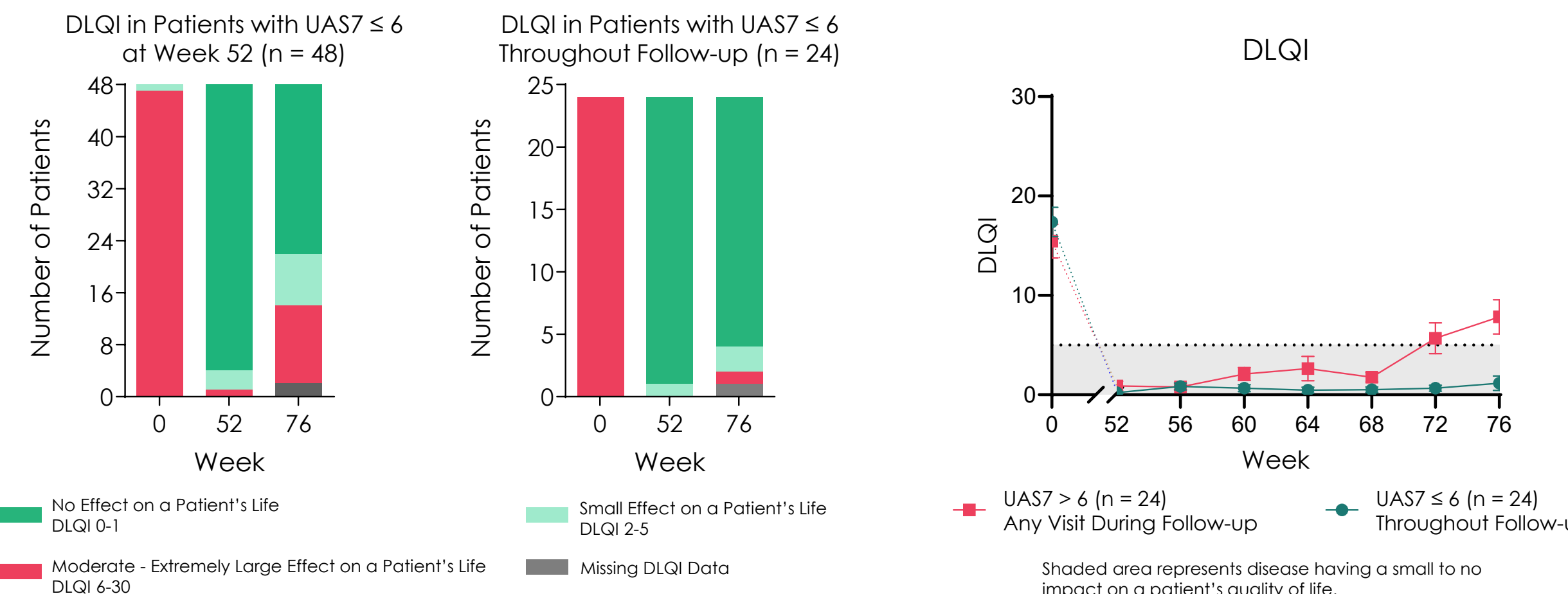


### Maintenance of well-controlled disease despite subtherapeutic concentrations of barzolvolumab



- Despite gradual decreasing concentration of barzolvolumab and tryptase recovery, mean UAS7 scores remained low

## Sustained and marked benefits in quality of life in patients 7 months after the last dose of barzolvolumab



- The mean (SE) DLQI at W76 for patients with well controlled disease at week 52 was 1.2 (0.75)
- 50% of patients that maintained a UAS7 ≤ 6 throughout follow-up had profound benefits on QoL throughout the entire follow-up period
  - 20/24 (83%) reported a DLQI 0/1 (no impact of disease on QoL) at week 76
  - Mean (SE) UAS7 = 0.4 (0.2) at week 76

## CONCLUSIONS

- In a Phase 2 trial of patients with antihistamine-refractory CSU treated with barzolvolumab (150 mg Q4W or 300 mg Q8W for 1 year), 71% had well controlled disease at the end of the treatment period
  - Of those with at least well controlled disease, 88% had a complete response (UAS7 = 0)
- Barzolvolumab induces prolonged clinical efficacy 7 months after the last dose of barzolvolumab in patients with CSU
  - 69% of patients who achieved well controlled disease after 52 weeks of treatment, also achieved well controlled disease at week 76
  - 50% of patients who achieved well controlled disease after 52 weeks of treatment, achieved complete response at week 76
- Sustained off-treatment efficacy was observed despite barzolvolumab clearance and normalization of tryptase, suggesting disease modification<sup>4</sup>
- Barzolvolumab represents a promising treatment for CSU with sustained off-treatment efficacy especially in patients who achieve well controlled disease
- Barzolvolumab is being evaluated in ongoing Phase 3 studies in patients with CSU (NCT06445023 and NCT06445202)

## References

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