Multi-dosed Barzolvolimab is Effective in Chronic Spontaneous Urticaria

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Conflict of Interest Disclosure

- ❑ I have **no**, real or perceived, direct or indirect conflicts of interest that relate to this presentation.
- ❑ I have the following, real or perceived direct or indirect conflicts of interest that relate to this presentation:

Type of affiliation / financial interest	Name of commercial company
Receipt of grants/research supports:	
Receipt of honoraria or consultation fees:	
Participation in a company sponsored speaker's bureau:	
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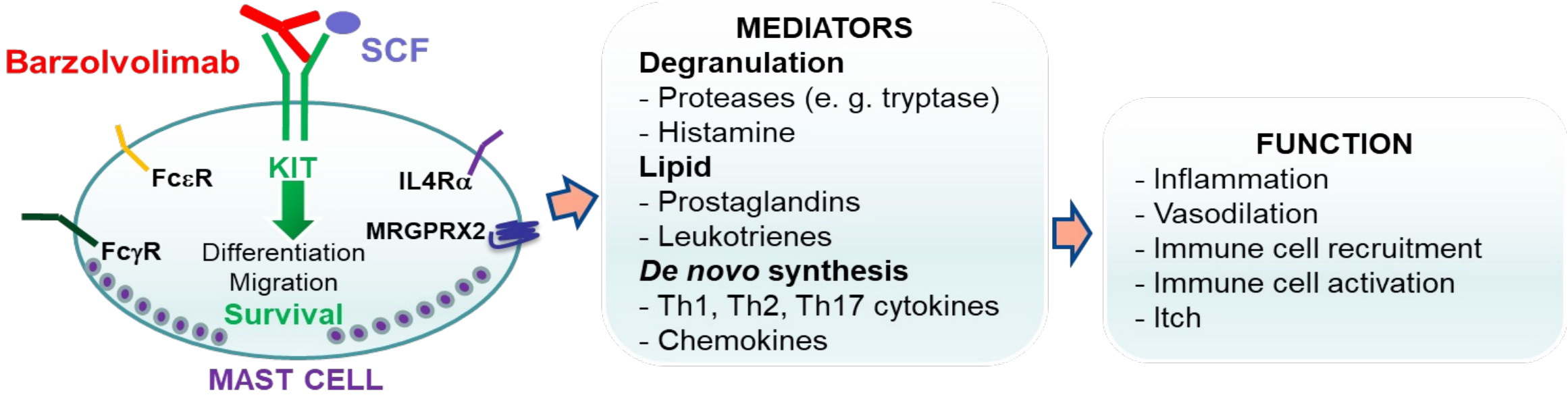
Background

- CSU is a mast cell driven disease characterized by itch and wheals
- Barzolvolimab inhibits SCF-dependent KIT activation which is essential for differentiation, proliferation, and survival of mast cells



- In healthy volunteers, barzolvolimab induced a dose-dependent reduction in circulating tryptase[1]
- 95% complete response (CR; negative provocation test) rate observed in patients with cold urticaria and symptomatic dermographism following a single dose of barzolvolimab 3 mg/kg[2]

[1] Alvarado et al Allergy. 2022 Aug;77(8):2393-2403; [2]Terhorst-Molawi et al Allergy. 2022 Nov 16. doi: 10.1111/all.15585.

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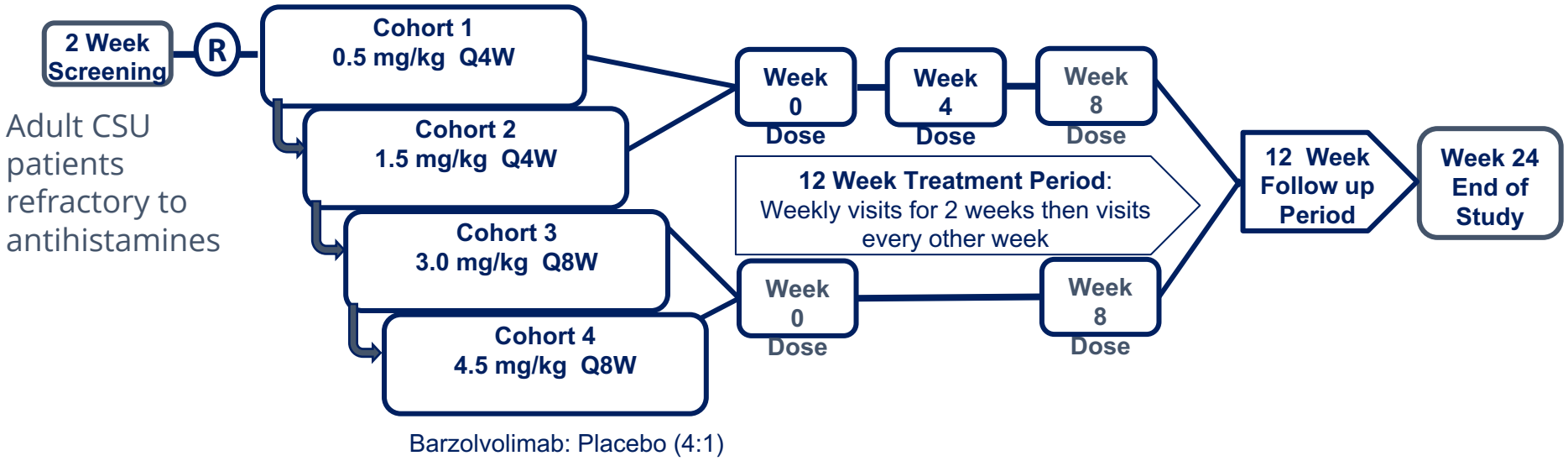
Study Design and Methods

Here we report interim results from the first multiple dose study of barzolvolimab in CSU patients

Double-blind, Placebo-controlled Multiple Ascending Dose Study



Assessments: Safety, UAS7: HSS7 and ISS7, UCT, and serum tryptase

Analysis: All patients who received at least one dose of study treatment are included. Data presented through Week 12 for Cohorts 1 and 2, and through Week 8 for Cohort 3 (single dose only).

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Demographics and Baseline Characteristics

Characteristics	Barzolvolimab 0.5 mg/kg Q4W (N= 9)	Barzolvolimab 1.5 mg/kg Q4W (N= 8)	Barzolvolimab 3.0 mg/kg Q8W (N= 9)	All Barzolvolimab (N= 26)	Pooled Placebo (N= 8)
Age years	43.8 (21.0 - 73.0)	53.3 (29.0 - 75.0)	49.4 (26.0 - 65.0)	48.7 (21.0 - 75.0)	47.4 (18.0 - 70.0)
Gender Female, n (%)	6 (67)	7 (88)	6 (67)	19 (73)	5 (63)
Race White, n (%)	6 (67)	7 (87.5)	9 (100)	22 (85)	6 (75)
African American n (%)	3 (33)	1 (12.5)	0 (0)	4 (15)	2 (25)
BMI kg/m^2	31.1 (26.0 - 36.0)	37.8 (28.6 - 58.9)	29.4 (22.3 - 36.9)	32.6 (22.3 - 58.9)	32.1 (16.4 - 55.2)
CSU Duration years	7.5 (0.6 - 41.1)	17.1 (2.6 - 61.3)	5.3 (0.6 - 21.3)	9.8 (0.6 - 61.3)	6.0 (1.4 - 13.1)
History of Angioedema n (%)	5 (56)	5 (63)	5 (56)	15 (58)	4 (50)
Prior Omalizumab* n (%)	4 (44)	3 (38)	4 (44)	11 (42)	5 (63)
UAS7	31.1 (20.0 - 39.0)	29.4 (20.0 - 40.6)	29.4 (16.3 - 42.0)	30.0 (16.3 - 42.0)	36.6 (19.0 - 42.0)
HSS7	15.4 (8.0 - 21.0)	14.0 (8.0 - 21.0)	14.8 (8.0 - 21.0)	14.7 (8.0 - 21.0)	17.5 (7.0 - 21.0)
ISS7	15.7 (11.0 - 21.0)	15.5 (12.0 - 21.0)	14.6 (1.2 - 21.0)	15.2 (1.2 - 21.0)	19.1 (12.0 - 21.0)
UCT	1.7 (0.0 - 4.0)	2.4 (1.0 - 8.0)	3.1 (0.0 - 7.0)	2.4 (0.0 - 8.0)	3.4 (0.0 - 11.0)
Tryptase ng/mL	5.1 (2.0 - 10.3)	6.4 (2.8 - 15.1)	8.6 (3.3 - 28.8)	5.4 (2.0 - 28.8)	6.1 (3.6 - 7.7)

Mean (range) is presented unless otherwise indicated, *The majority had inadequate response to omalizumab

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Multiple IV Doses of Barzolvolimab Were Well Tolerated in CSU Patients

Adverse Events Reported in ≥ 10% Barzolvolimab Treated Patients

	Barzolvolimab 0.5 mg/kg Q4W (N= 9)	Barzolvolimab 1.5 mg/kg Q4W (N= 8)	Barzolvolimab 3.0 mg/kg Q8W (N= 9)	All Barzolvolimab (N= 26)	Pooled Placebo (N= 8)
All AEs	8 (89)	7 (88)	6 (67)	21 (81)	6 (75)
Urinary Tract Infection*	1 (11)	2 (25)	2 (22)	5 (19)	1 (13)
Headache	2 (22)	0 (0)	2 (22)	4 (15)	1 (13)
Neutropenia	2 (22)	2 (25)	0 (0)	4 (15)	0 (0)
Back pain	0 (0)	1 (13)	2 (22)	3 (12)	0 (0)

*Includes preferred terms: urinary tract infection, cystitis, and bacteriuria

- Most AEs were mild or moderate in severity and resolved while on study
- No AE led to treatment discontinuation
- One SAE of salmonella colitis, which was considered unrelated to the study treatment was reported

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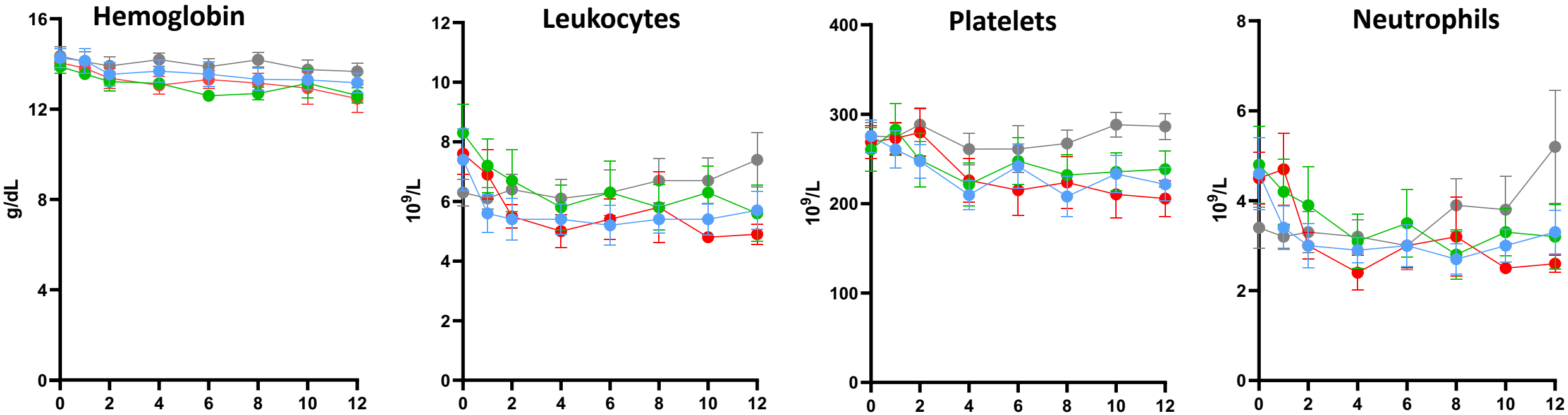
Changes in Hematology Parameters Consistent with Single Dose Studies



Available hematology data through week 12 are presented

- Hematology parameters generally remained within the normal range
- Transient, asymptomatic, mild decreases in neutrophils were reported as AEs in four patients
- Changes were similar to those previously observed in single dose studies, with no pattern of further decreases with multiple doses

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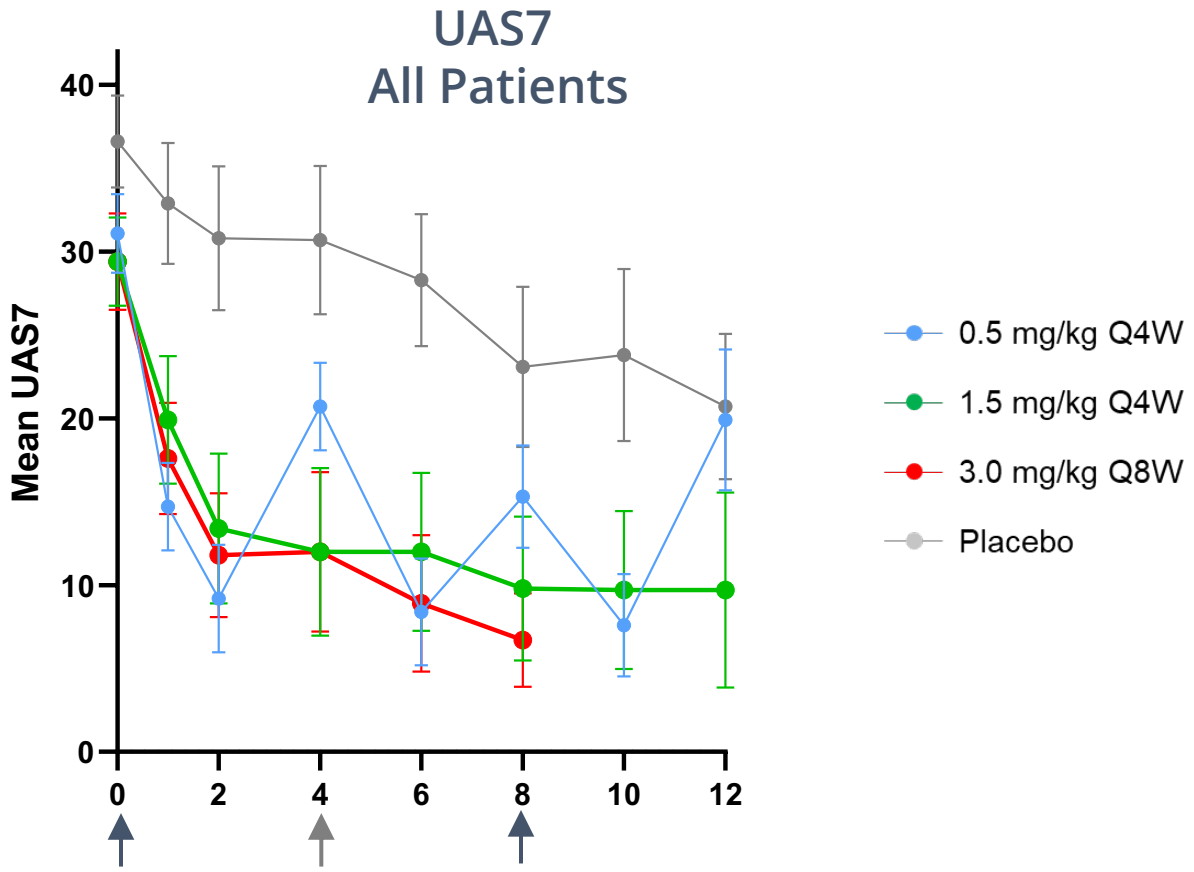
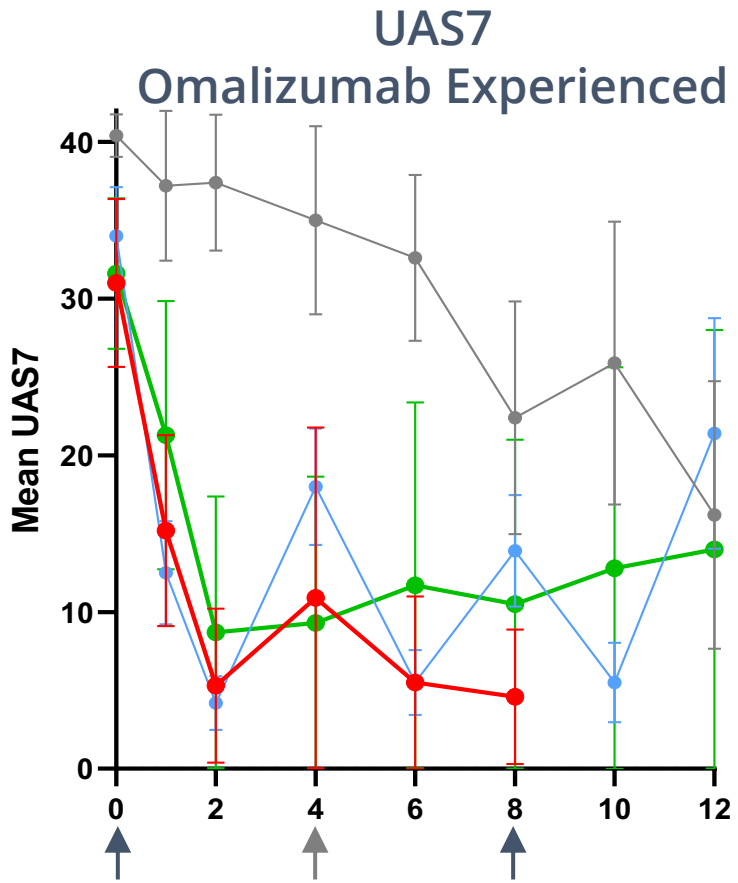
Barzolvolimab Drives Rapid Symptom Improvement in Antihistamine Refractory, Including Omalizumab Experienced, CSU Patients





Dosing for the Q4W treatment groups only

Dosing for all treatment groups

Data presented are mean ± S.E.

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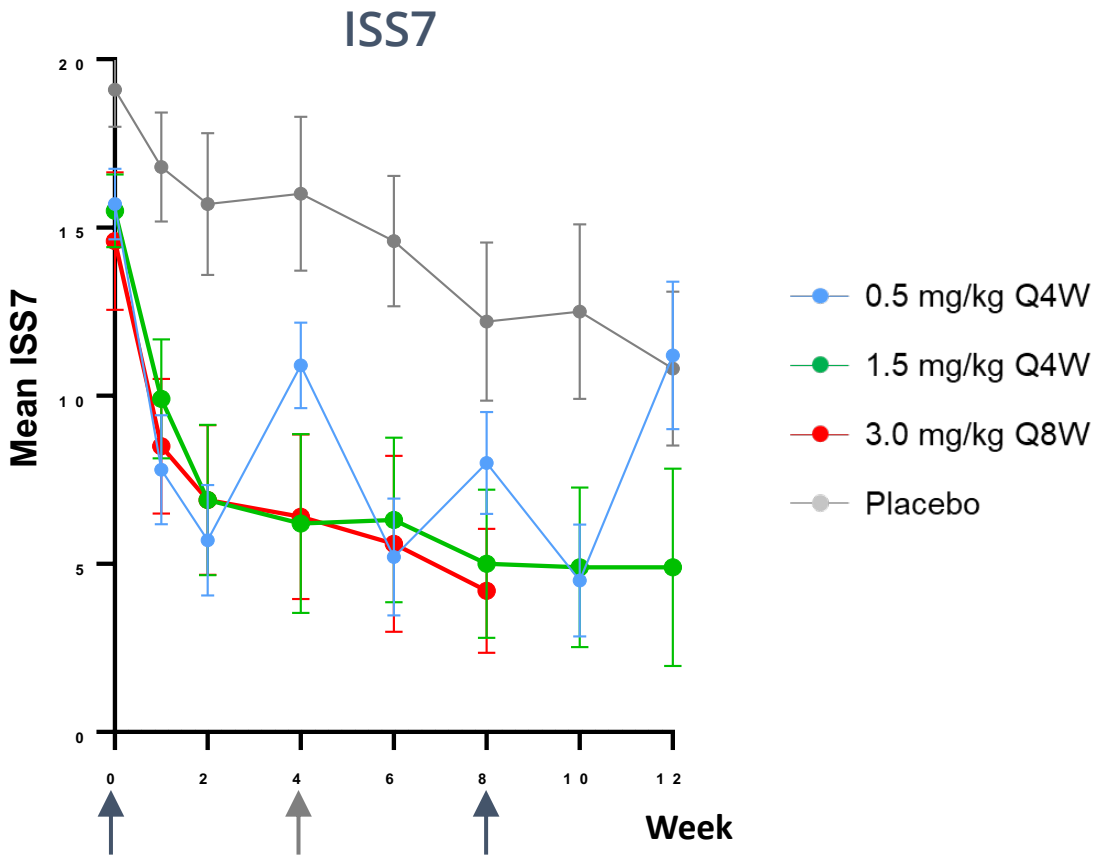
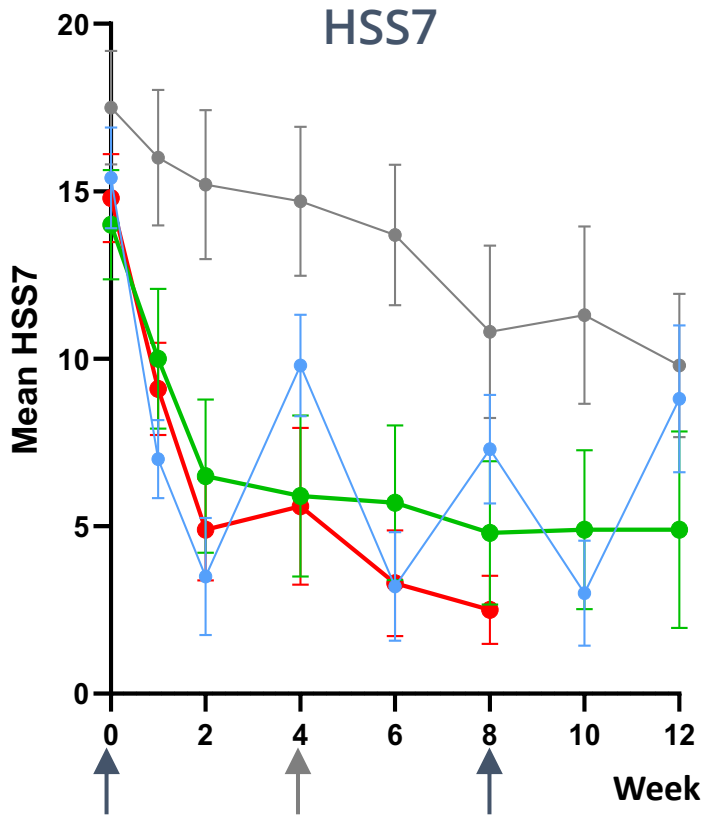
Rapid and Sustained Improvement in Itch and Hives





Dosing for the Q4W treatment groups only

Dosing for all treatment groups

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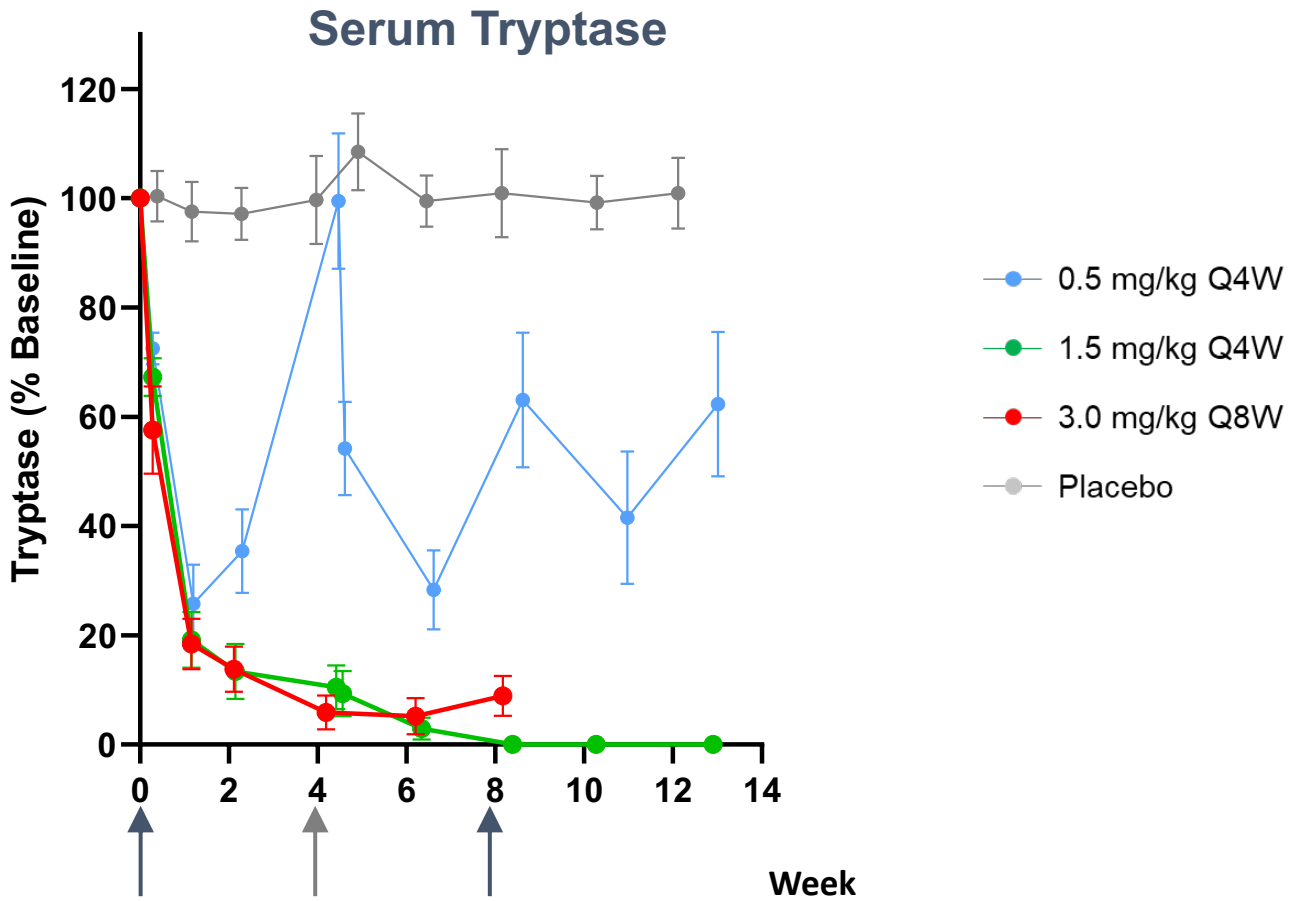
More Profound Tryptase Suppression With Higher Doses



Dosing for the Q4W treatment groups only

Dosing for all treatment groups

- Data presented are mean ± S.E.
- Tryptase values below lower limit of detection normalized to 0

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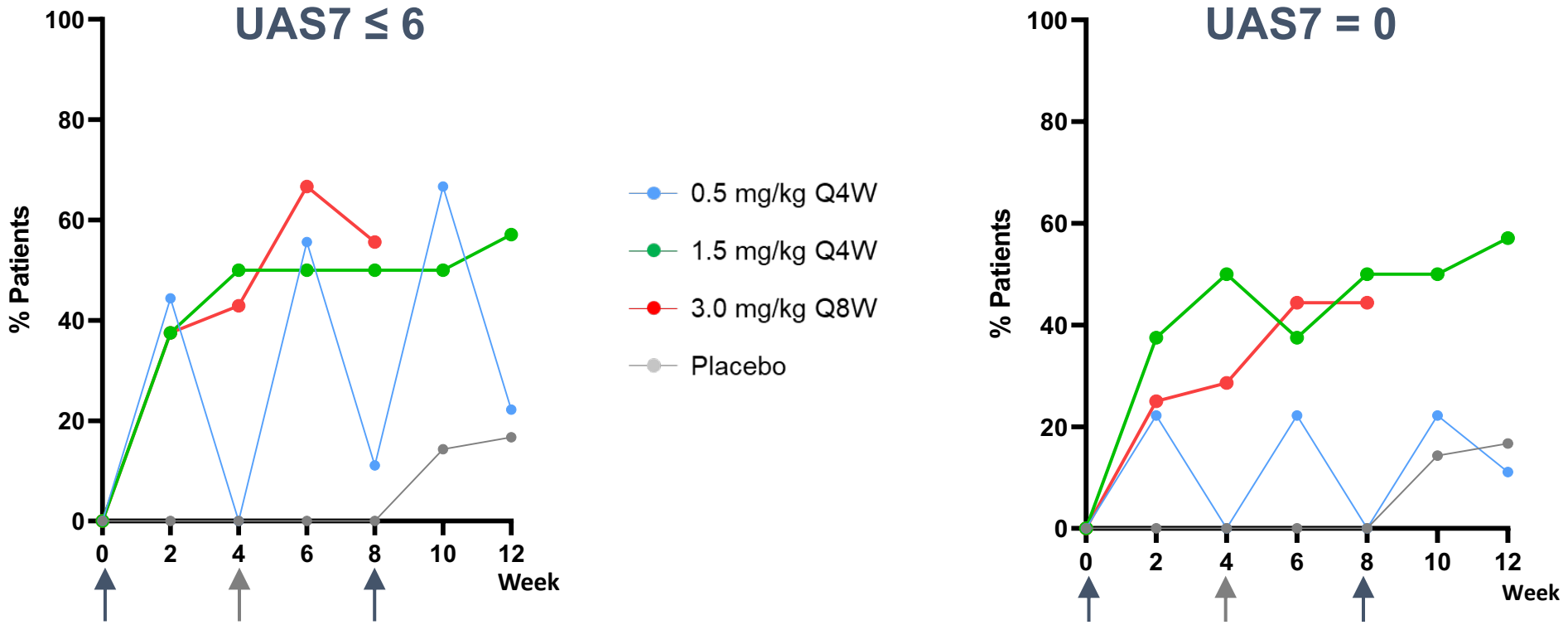
Higher Doses of Barzolvolimab Resulted in More Durable Responses by UAS7



- 57% of patients treated with 1.5 mg/kg achieved complete response (UAS7=0) at week 12
- 44% of patients treated with a single dose of 3 mg/kg achieved complete response at week 8 (follow-up ongoing)

Dosing for the Q4W treatment groups only

Dosing for all treatment groups

Data presented are mean ± S.E.

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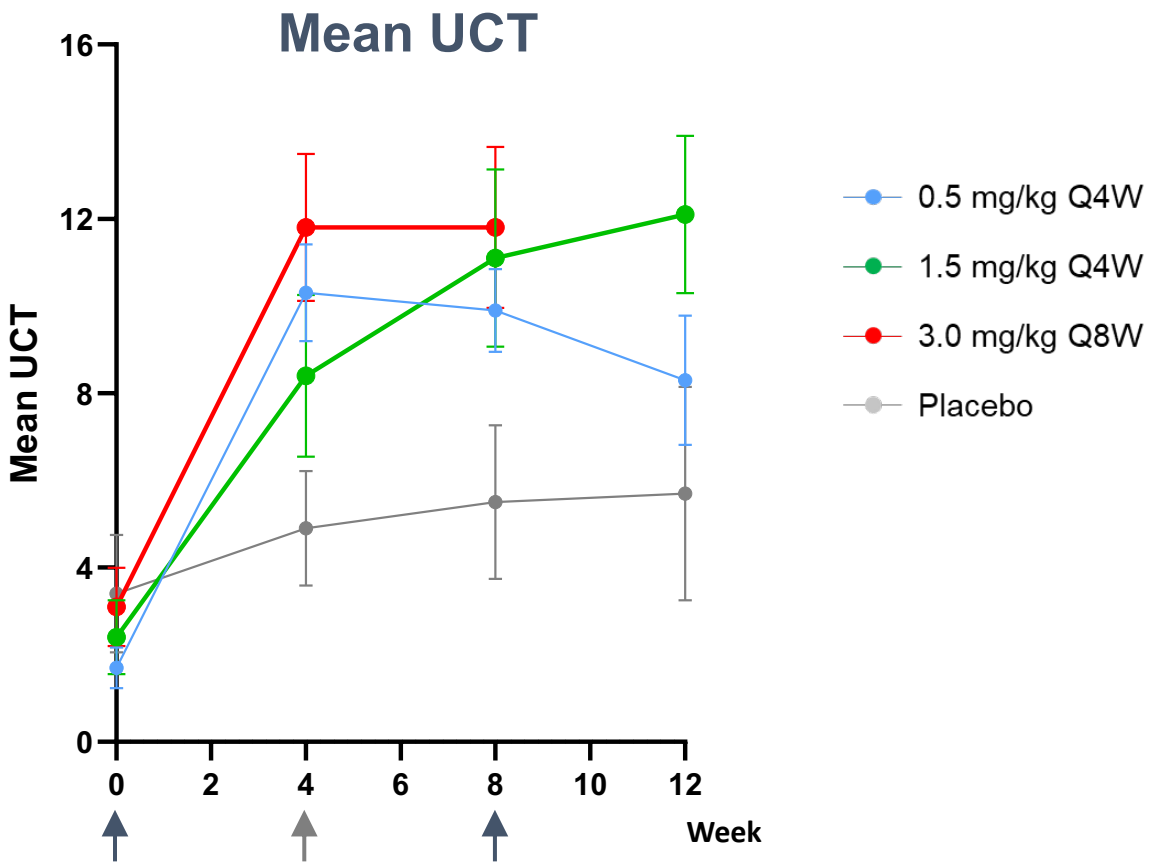
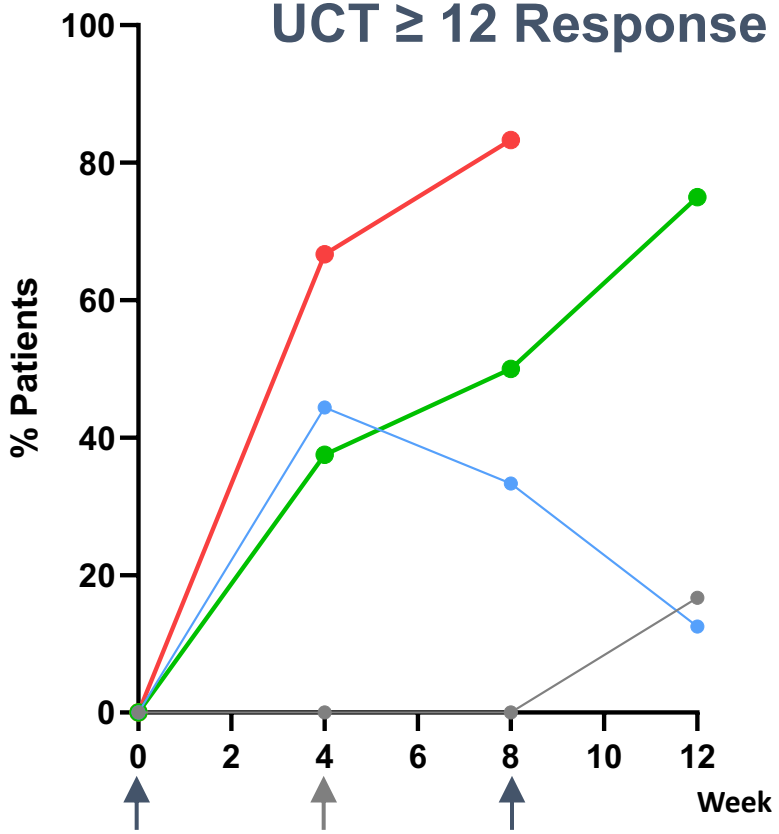
Greater Urticaria Disease Control (UCT ≥ 12) with Higher Doses of Barzolvolimab





Dosing for the Q4W treatment groups only

Dosing for all treatment groups

Data presented are mean ± S.E.

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Summary and Discussion

In patients with moderate to severe CSU refractory to antihistamines:

- Multiple IV doses of barzolvolimab for up to 12 weeks were well tolerated
- Barzolvolimab results in rapid, marked and durable response, including in patients with prior omalizumab treatment
  - More sustained clinical activity observed in two higher dose groups
- Tryptase suppression paralleled symptom improvement
- Results support the ongoing Phase 2 subcutaneous study in chronic spontaneous urticaria

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Thank you!
Questions?

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