Cold Urticaria Patients Achieve Complete Response with 1.5 mg/kg Barzolvolimab

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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:	
Stock shareholder:	
Other support (please specify):	

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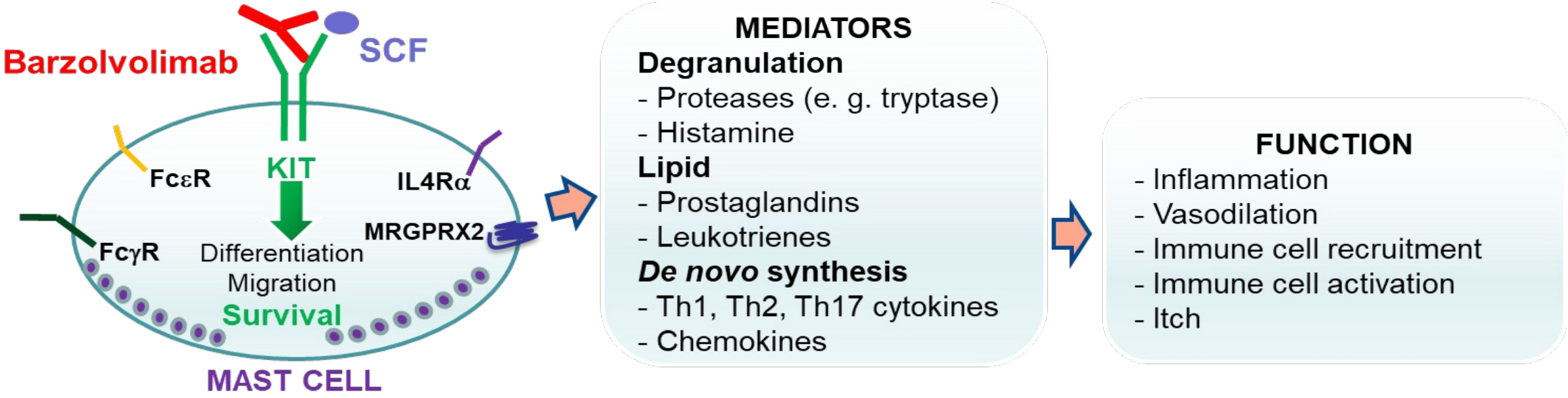
Background

- Chronic inducible urticaria 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]
- 100% complete response (CR; negative TempTest®) rate observed in patients with cold urticaria 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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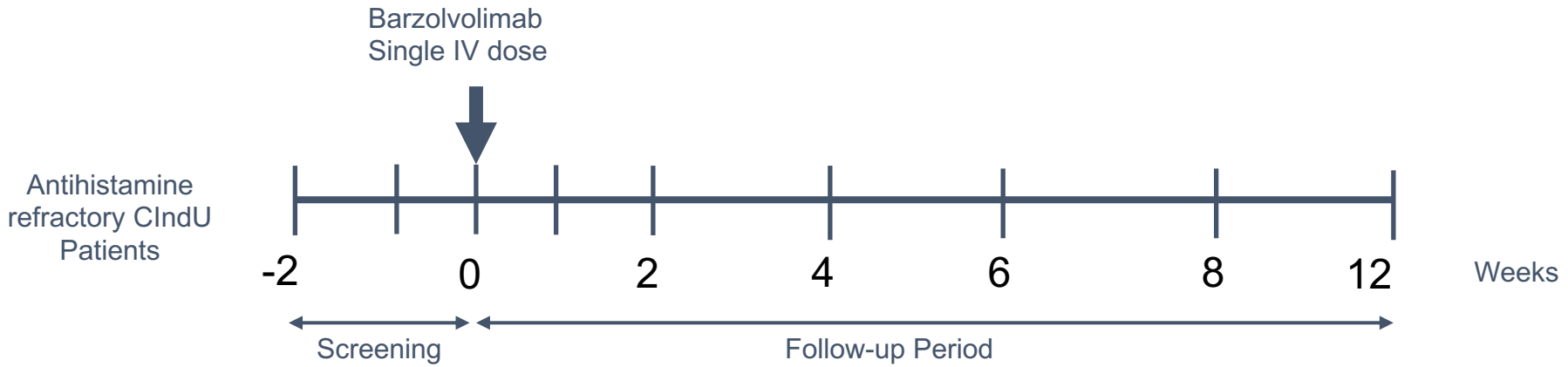
Study Design and Methods

Here, we assessed the clinical and pharmacodynamic response to a 1.5 mg/kg dose of barzolvolimab in an additional ColdU cohort:

- All patients (N=10) have completed the 12-week follow-up and are included in the safety analysis
  - One patient excluded from activity analysis due to receipt of partial dose (infusion related reaction)



Assessments included adverse events, clinical laboratory testing, provocation testing (TempTest®), UCT, and circulating tryptase.

Previously reported data for barzolvolimab 3mg/kg included for comparison

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Demographics and Baseline Characteristics

		ColdU 3 mg/kg (N=11)*	ColdU 1.5 mg/kg (N=10)*	All (N=21)
Age median (range) years		43 (27- 65)	51.5 (19- 69)	48 (19-69)
Gender Female, n (%)		6 (54.5%)	6 (60.0%)	12 (57.1 %)
Race	White, n (%)	10 (90.9%)	9 (90%)	19 (90.5%)
	Asian, n (%)	1 (9.1%)	0 (0%)	1 (4.8%)
	Black, n (%)	0 (0%)	1 (10%)	1 (4.8%)
Ethnicity	Hispanic or Latino	1 (9.1%)	0 (0%)	1 (4.8%)
Weight median (range) kg		77.0 (61.0 – 93.0)	97.8 (63.0 – 126.6)	85.4 (61.0 – 126.6)
Disease Duration	< 5 yr, n (%)	5 (45.5%)	6 (60%)	11 (52.4%)
	≥ 5 yr, n (%)	6 (54.5%)	4 (40%)	10 (47.6%)
History of Angioedema		6 (54.5%)	4 (40%)	10 (47.6%)
Prior Medication H1 Antihistamines		11 (100%)	10 (100%)	21 (100%)
Biologics (omalizumab)		1 (9%)	5 (50%)	6 (28.6%)†
Provocation Threshold Mean (range)		18.9 (5-27) °C	18.4 (6-27) °C	18.6 (5-27) °C
UCT Mean (range)		7.0 (2-13)	5.9 (1-11)	6.5 (1-13)
Tryptase median (range) ng/mL		3.7 (2.4-5.5)	4.5 (2.2-10.6)	3.8 (2.2-10.6)

* All patients are included in the safety analysis. 2 patients, one in each cohort, did not receive a full dose and are not included in the clinical/PD analysis
†All 6 patients reported inadequate response (defined as biologic refractory)

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Barzolvolimab Demonstrates Favorable Safety and Tolerability

Adverse Events Reported in at least 3 Patients

Adverse Event n (%)	ColdU 3 mg/kg N=11	ColdU 1.5 mg/kg N=10	Total N=21
Any adverse event	11 (100)	9 (90)	20 (95)
Hair color changes	8 (73)	2 (20)	10 (48)
Infusion related reactions	8 (73)	2 (20)	10 (48)
Taste changes	4 (36)	2 (20)	6 (29)
Malaise	4 (36)	1 (10)	5 (24)
Headache	3 (27)	0 (0)	3 (15)
COVID-19	0 (0)	3 (30)	3 (15)

- AEs were similar across dose groups and mainly mild.
- Hematology parameters generally remained within the normal ranges. Mild, transient, and asymptomatic decreases in hemoglobin and WBC parameters were noted.

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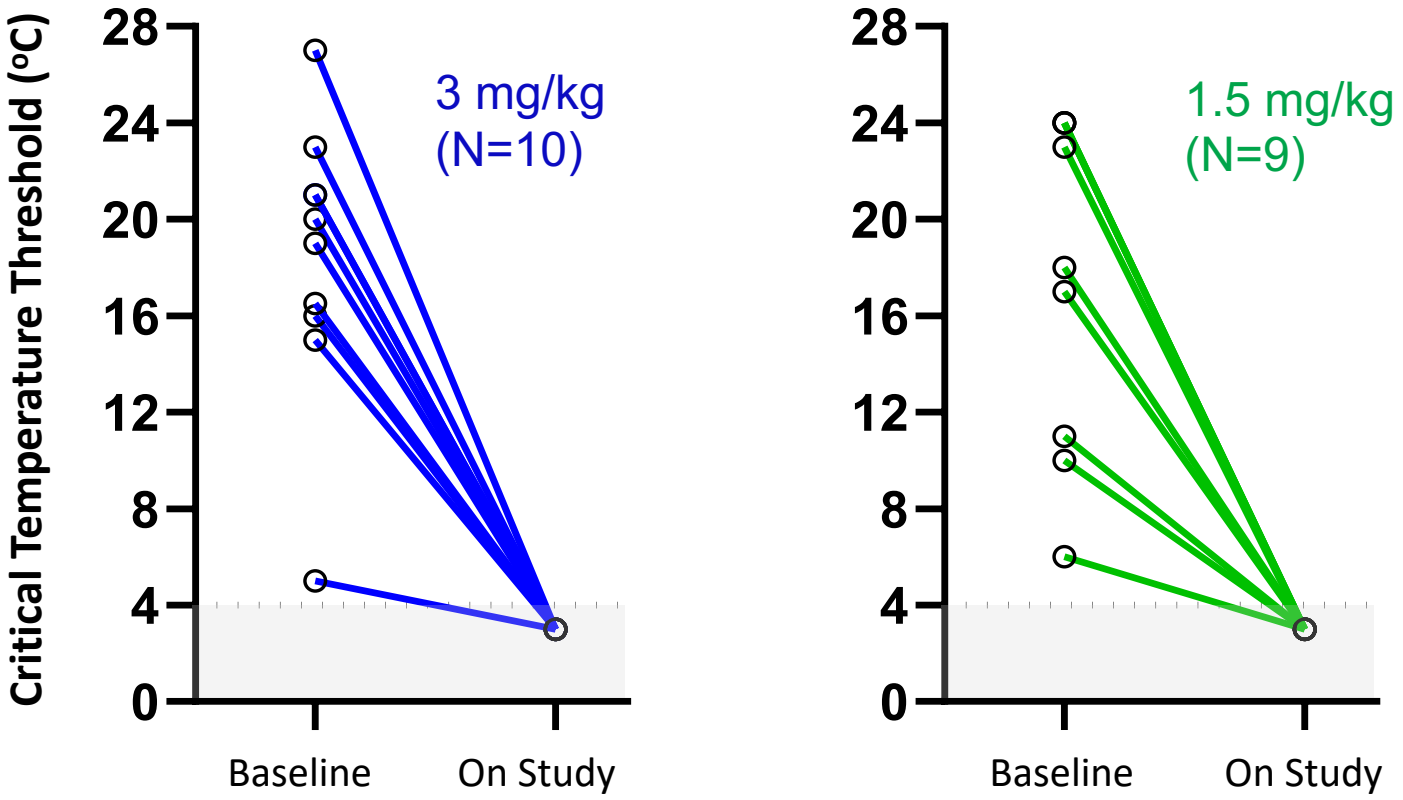
100% Complete Response with Single Dose of Barzolvolimab



All biologic refractory (omalizumab) patients had a complete response

- CR=negative provocation test at ≤4°C

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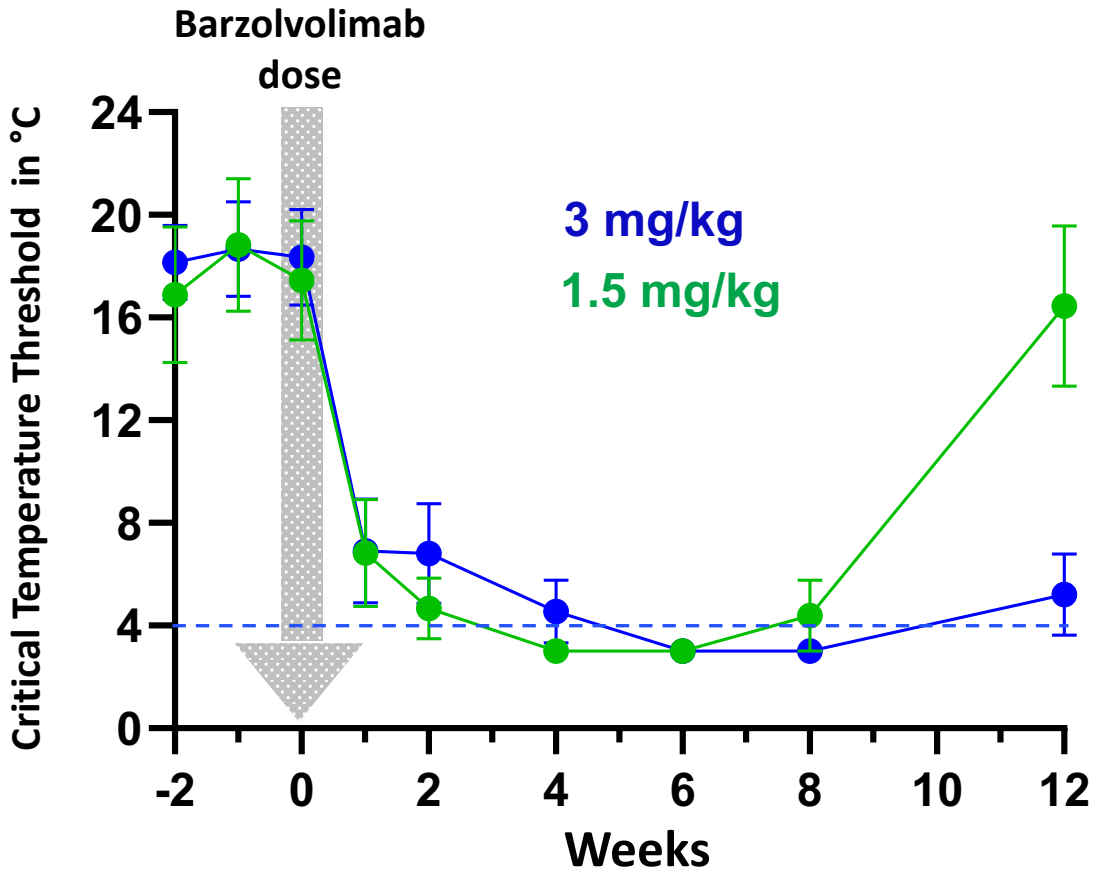
A Single Dose Results in Rapid and Durable Clinical Response



- 68% patients achieved CR within 1 week
- Duration of response is dose proportional at 51+ days for 1.5 mg/kg compared with 77+ days for 3 mg/kg

*Critical temperature threshold values below 4°C (negative test) assigned a value of 3°C

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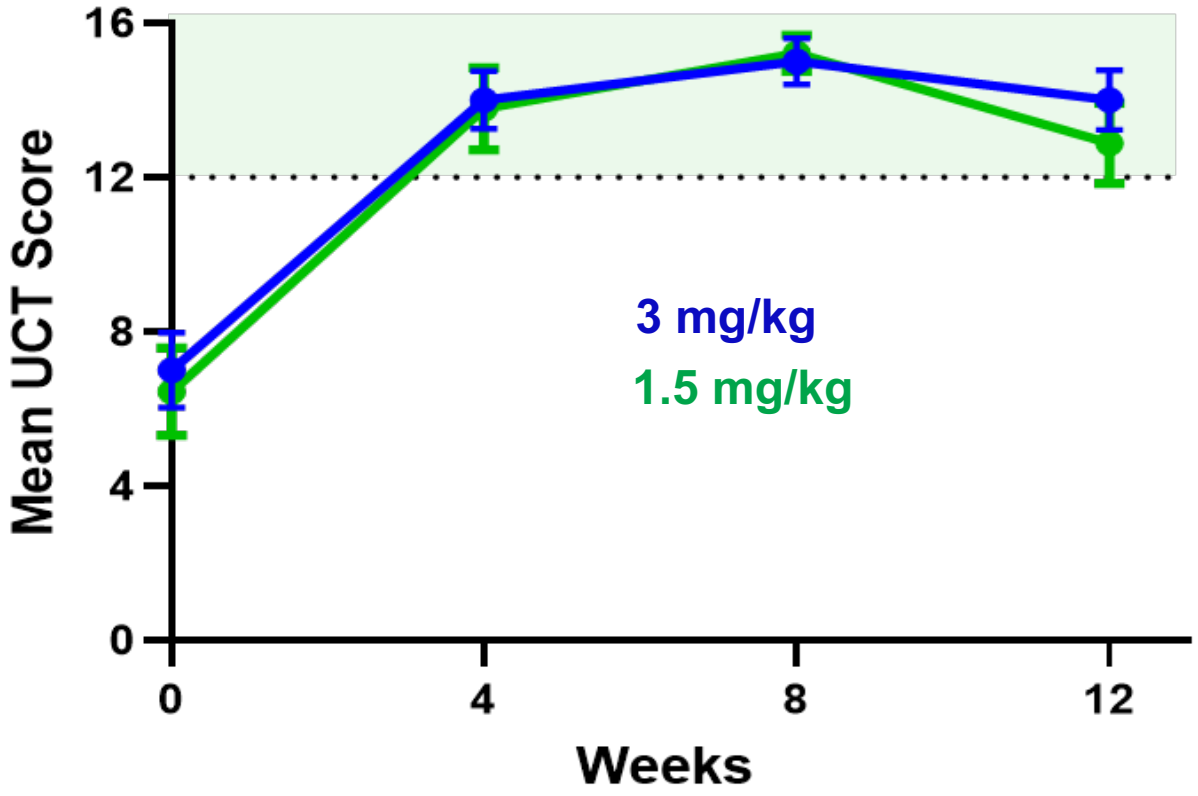
100% Well Controlled Urticaria following a Single Dose of Barzolvolimab



UCT= 16
Complete Control

UCT≥ 12
Well Controlled

UCT< 12
Poorly Controlled

% Patients with UCT ≥ 12

3 mg/kg barzolvolimab	Predose	4 week	8 week	12 week
UCT =16 n (%)	0	5/10 (50)	7/10 (70)	4/10 (40)
UCT≥ 12 n (%)	1/10 (10)	9/10 (90)	10/10 (100)	8/10 (80)

1.5 mg/kg barzolvolimab	Predose	4 week	8 week	12 week
UCT =16 n (%)	0	5/9 (56)	6/9 (67)	3/9 (33)
UCT≥ 12 n (%)	0	7/9 (78)	9/9 (100)	7/9 (78)

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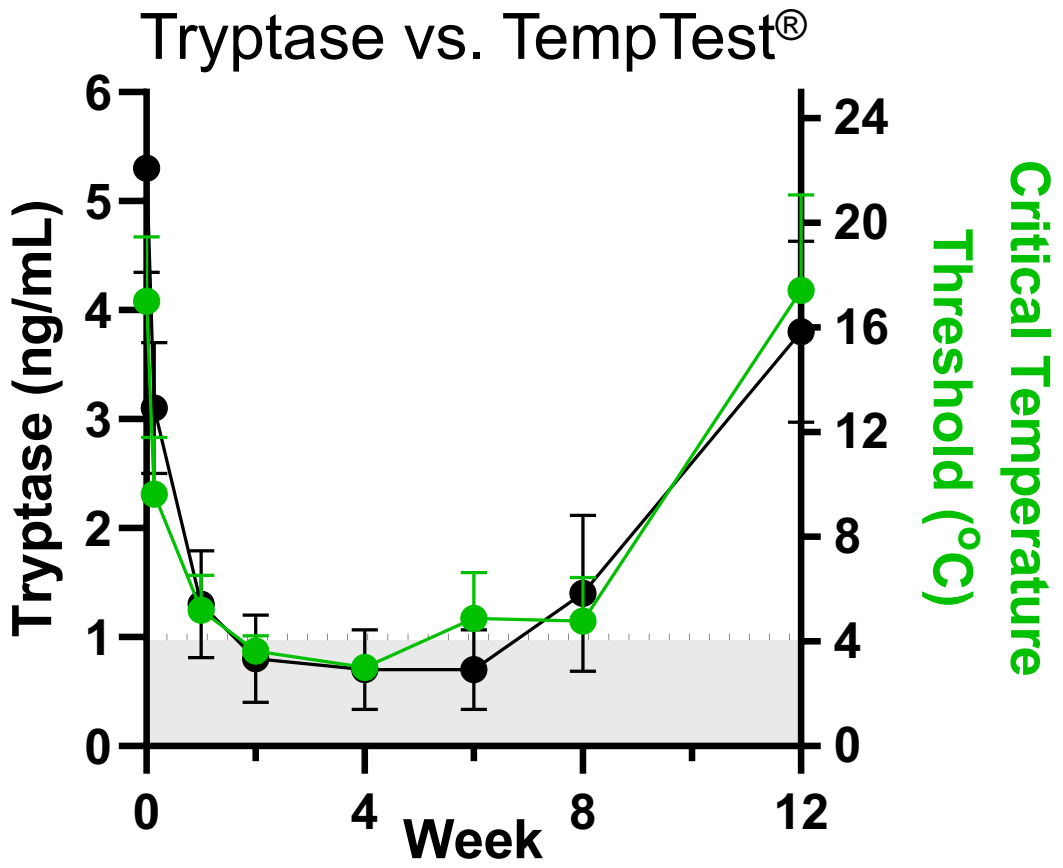
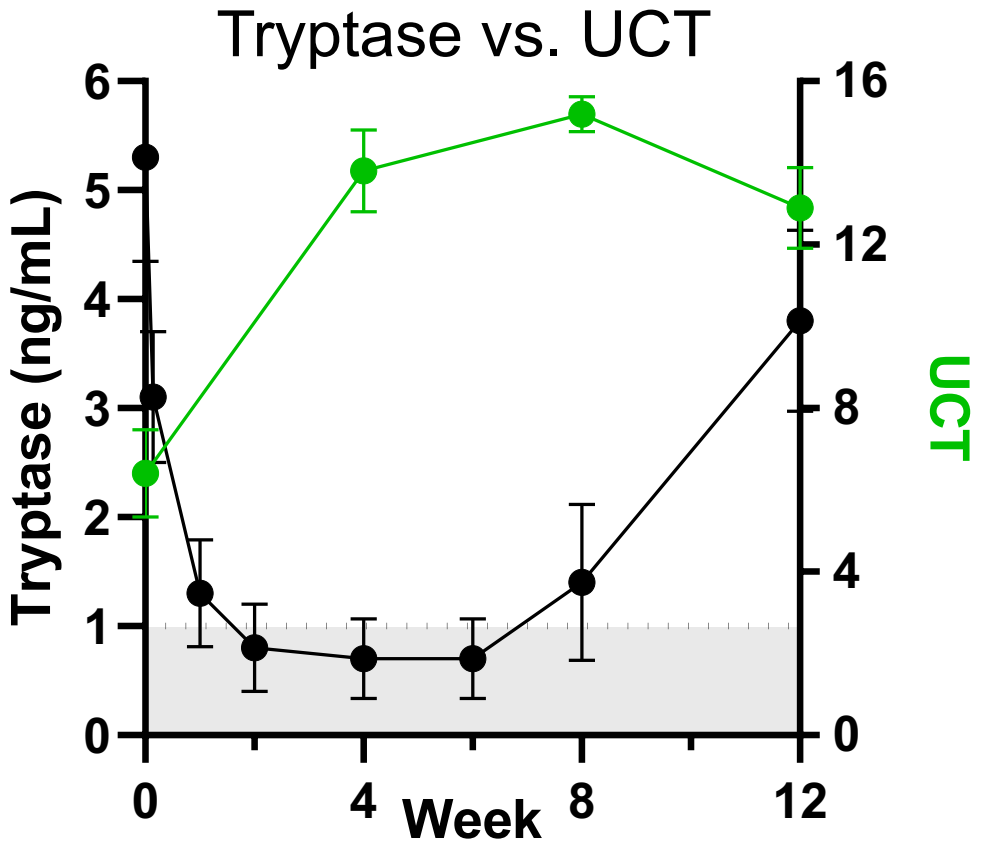
Kinetics of Tryptase Depletion Mirror Changes in Provocation Threshold and UCT





- Data shown for 1.5 mg/kg only; similar kinetics observed at 3 mg/kg

•Tryptase values below LLoQ normalized to 0.
•Critical temperature threshold values below 4°C (negative test) assigned a value of 3°C.

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Summary and Conclusions

- In patients with ColdU refractory to antihistamines, a single dose of barzolvolimab 1.5 mg/kg resulted in a rapid and profound clinical response similar to the 3 mg/kg dose
  - 100% of patients achieved complete response including biologic refractory patients
  - 100% of patients achieved well controlled disease (UCT ≥12)
- The durability of clinical response and tryptase suppression were dose proportional
- Kinetics of tryptase reduction mirrored clinical activity at both doses
- Barzolvolimab was well tolerated with a similar adverse event profile across dose levels
- These results support ongoing Phase 2 subcutaneous study in patients with CIndU

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Thank you!
Questions?

Abstract ID: 79998 poster presentation:
"**Barzolvolimab-induced response and mast cell suppression are durable and linked**"

Results from patients who participated in an optional long term follow up period from the initial 3.0 mg/kg cohorts in ColdU and SD patients are being presented on Thursday, 8 December 2022