Patients With Chronic Spontaneous Urticaria Experience Improvement in Quality of Life When Treated With Barzolvolimab

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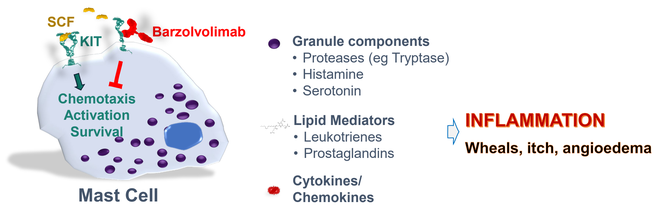
Background

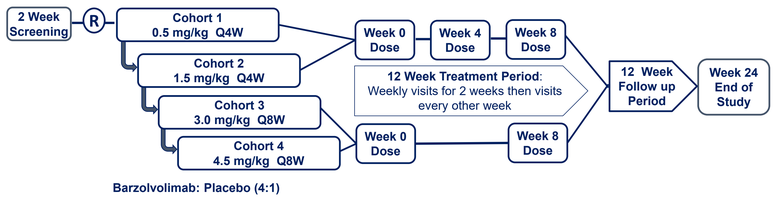
- Mast cells (MCs) are key effector cells of chronic spontaneous urticaria (CSU) and chronic inducible urticaria (CIndU).
- MCs require activation of their KIT receptors by stem cell factor (SCF) for survival, proliferation, and differentiation.
- Circulating tryptase, a protease secreted specifically by MCs, is a biomarker that correlates with MC burden.
- Barzolvolimab (CDX-0159) is a monoclonal anti-KIT antibody that selectively inhibits SCF-dependent KIT activation.
- In prior single IV dose studies, barzolvolimab doses of up to 9 mg/kg were generally well tolerated and demonstrated a profound suppression of circulating tryptase in adult healthy volunteers.[1]
- A single 3 mg/kg IV dose of barzolvolimab demonstrated significant clinical response in patients with antihistamine-refractory CIndU, which mirrored profound reductions in circulating tryptase and skin mast cells.[2]
- We report results from the first multiple dose study of barzolvolimab in CSU patients.



References
1. Alvarado D et al, Allergy. 2022;00:1–11;
2. Terhorst-Molawi D et al, J Allergy Clin Immunol. 2022; 149(2) Suppl. AB178

Study Design and Methods

Double-blind, Placebo-controlled Multiple Ascending Dose Study (NCT04538794)



Barzolvolimab: Placebo (4:1)

Assessments: Safety, 7-day Urticaria Activity Score (UAS7; range 0-42), Urticaria Control test (UCT; range 0-16) , Dermatology Life Quality Index (DLQI; range 0-30), Physician Global Assessment (PhysGA; range 0-3), circulating tryptase, plasma SCF and pharmacokinetics.

Analysis: All patients who received at least one dose of study treatment are included. Data presented through Week 24 for all Cohorts.

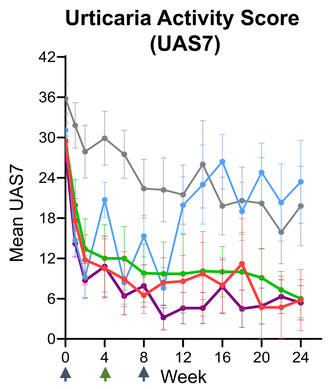
Demographics and Baseline Characteristics

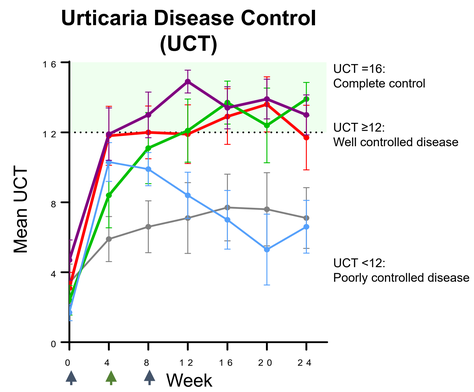
Characteristics	Barzolvolimab 0.5 mg/kg Q4W (N= 9)	Barzolvolimab 1.5 mg/kg Q4W (N= 8)	Barzolvolimab 3.0 mg/kg Q8W (N= 9)	Barzolvolimab 4.5 mg/kg Q8W (N= 9)	All Barzolvolimab (N= 35)	Pooled Placebo (N= 10)
Age years	43.8 (21 - 73)	53.3 (29 - 75)	49.4 (26 - 65)	51.1 (29 - 68)	49.3 (21 - 75)	49.8 (18 - 70)
Gender Female, n (%)	6 (67)	7 (88)	6 (67)	9 (100)	28 (80)	7 (70)
BMI kg/m^2	31.1 (26.0 - 36.0)	37.8 (28.6 - 58.9)	29.4 (22.3 - 36.9)	27.1 (21.5 - 34.4)	31.2 (21.5 - 58.9)	31.8 (16.4 - 55.2)
CSU Duration years	7.5 (0.6 - 41.1)	17.1 (2.6 - 61.3)	4.8 (0.6 - 21.3)	10.4 (1.0 - 35.4)	9.7 (0.6 - 61.3)	5.6 (1.4 - 13.1)
Prior Omalizumab* n (%)	4 (44)	3 (38)	4 (44)	2 (22)	13 (37)	6 (60)
UAS7	31.1 (20.0 - 39.0)	29.5 (20.0 - 40.6)	29.4 (16.3 - 42.0)	28.3 (22.0 - 38.0)	29.6 (16.3 - 42.0)	35.8 (19.0 - 42.0)
DLQI	13.2 (7-24)	15.1 (5-24)	7.8 (1-15)	9.7 (1-16)	11.3 (1-24)	13.5 (1-26)
PhysGA	1.9 (1-3)	2.3 (1-3)	2.7 (2-3)	2.1 (1-3)	2.2 (1-3)	2.1 (1-3)
UCT	1.7 (0 - 4)	2.4 (1- 8)	3.1 (0 - 7)	4.7 (1 -12)	3.0 (0 - 12)	3.4 (0 - 11)
Tryptase ng/mL	5.0 (2.0 - 10.3)	6.3 (2.8 - 15.1)	8.6 (3.3 - 28.8)	5.5 (2.3 - 10.2)	6.2 (2.0 - 28.8)	5.3 (3.2 - 7.5)

Mean and range are presented unless otherwise indicated.
*The majority had inadequate response to omalizumab.

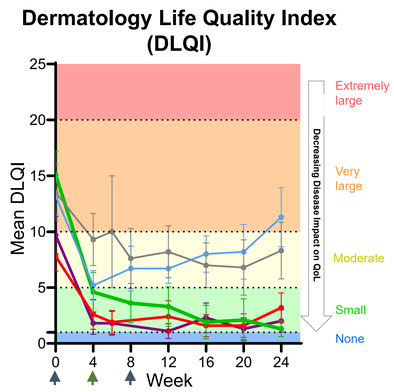
Results

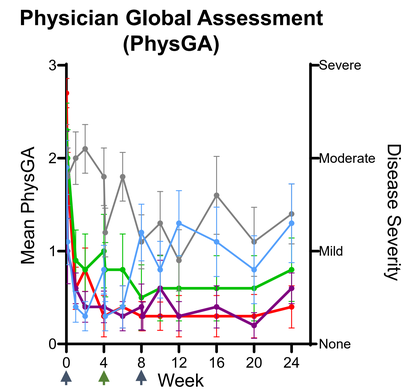
Barzolvolimab Drives Rapid and Durable Clinical Symptom and Quality of Life Improvement in Patients with Antihistamine Refractory CSU





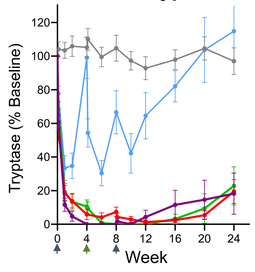
Doses ≥ 1.5 mg/kg drive rapid and durable UAS7 improvement and well-controlled disease by UCT

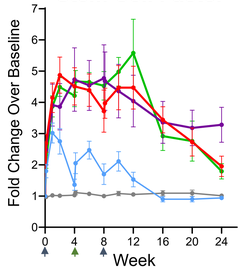


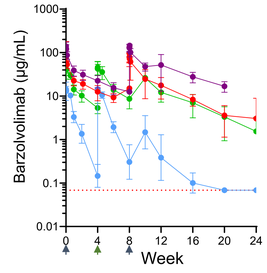


Rapid and sustained improvement by DLQI and PhysGA with barzolvolimab

Kinetics of Tryptase and SCF Modulation and Exposure Mirror Symptom Improvement



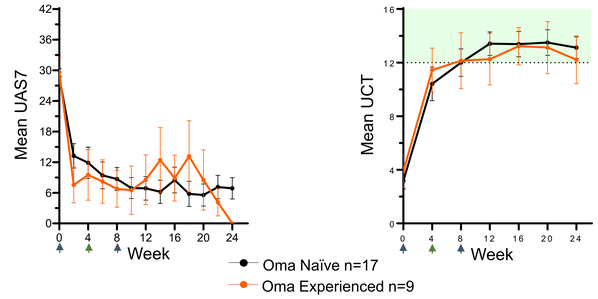




Prolonged tryptase suppression and SCF modulation achieved at doses ≥ 1.5 mg/kg

Sustained exposure through week 24 consistent with prolonged clinical benefit

Robust Clinical Activity in Both Omalizumab Experienced and Naïve Patients



Data shown is an aggregate of high doses (≥ 1.5 mg/kg)

Multiple IV Doses of Barzolvolimab Were Well Tolerated in CSU 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)	Barzolvolimab 4.5 mg/kg Q8W (N= 9)	All Barzolvolimab (N= 35)	Pooled Placebo (N= 10)
Any AE	8 (89)	7 (88)	9 (100)	6 (67)	30 (86)	6 (60)
Hair Color Changes	0 (0)	1 (13)	3 (33)	5 (56)	9 (26)	0 (0)
Urinary Tract Infection*	1 (11)	3 (38)	3 (33)	0 (0)	7 (20)	0 (0)
COVID-19	0 (0)	1 (13)	2 (22)	2 (22)	5 (14)	0 (0)
Headache	2 (22)	0 (0)	2 (22)	1 (11)	5 (14)	2 (20)
Neutropenia	2 (22)	2 (25)	1 (11)	0 (0)	5 (14)	0 (0)
Nasopharyngitis	0 (0)	1 (13)	2 (22)	1 (11)	4 (11)	1(10)

- Most AEs were mild or moderate in severity and resolved while on study.
- *Includes preferred terms: urinary tract infection, cystitis, and bacteriuria.
- One SAE of salmonella colitis, considered unrelated to the study treatment.
- Hematology parameters generally remained within the normal range; changes in neutrophils were similar to those observed in previously reported single dose studies, with no pattern of further decreases with multiple doses.

LEGEND

Placebo · 0.5 mg/kg Q4W · 1.5 mg/kg Q4W · 3.0 mg/kg Q8W · 4.5 mg/kg Q8W

Dosing for all treatment groups

Dosing for the Q4W treatment groups only

- Tryptase values below lower limit of detection normalized to 0

- Data presented are mean ± S.E.

Summary

- Multiple IV doses of barzolvolimab up to 4.5 mg/kg resulted in long-term exposure to 24 weeks with sustained KIT suppression at doses ≥ 1.5 mg/kg in antihistamine refractory patients with moderate to severe CSU.
  - Barzolvolimab was well tolerated and the safety profile is similar to single dose studies.
    - Hematologic parameters showed no pattern of further decreases with multiple doses.
  - Rapid improvement in UAS7 was observed within 1 week.
  - A rapid decrease in the DLQI was noted within 4 weeks in all barzolvolimab treated patients.
    - DLQI improvement was sustained at doses ≥ 1.5 mg/kg.
  - PhysGA for the treated cohorts also decreased by week 1 and was sustained through Week 24.
  - DLQI and PhysGA trended closely with the dose-dependent improvement in UAS7 and UCT, tryptase suppression, and increases in SCF.
  - Durable clinical response and tryptase reduction reflect MC depletion.
  - Patients had similar symptom improvement irrespective of prior omalizumab use.
- This multi-dose study further characterizes barzolvolimab as a promising novel treatment in antihistamine refractory CSU.