Treatment with Barzolvolimab Improves Urticaria Control and Quality of Life in Patients with Chronic Inducible Urticaria: Phase 2 12 Week Results

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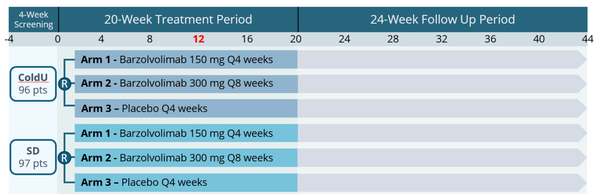
Background

- Chronic inducible urticaria (CIndU) is a mast cell-driven disease characterized by itch and wheals, triggered by cold in cold urticaria (ColdU), or pressure on the skin in symptomatic dermographism (SD).
- In a Phase 2 study (NCT05405660), barzolvolimab (anti-KIT monoclonal antibody) significantly improved complete response rates (negative provocation tests) with a favorable safety profile at 12 weeks in patients with ColdU or SD inadequately controlled by antihistamines.
- Here we report the impact of barzolvolimab treatment versus placebo on urticaria control and quality of life in patients with antihistamine-refractory ColdU or SD. Urticaria control was measured using the Urticaria Control Test (UCT), and quality of life was assessed using the Dermatology Life Quality Index (DLQI).

Study Design

A Randomized, Double-blind, Placebo-controlled, Dose-finding Study



Data cut off: July 3, 2024.

Key Inclusion Criteria

- Patients aged ≥ 18 years with diagnosis of ColdU or SD for more than 3 months
- Recurrent wheals despite stable antihistamine regimen. Prior biologics permitted
- Positive provocation test at screening and randomization
- UCT score < 12 at screening and randomization

Study Outcomes

- **Primary efficacy endpoint:**
  - % of patients with a negative provocation test at Week 12 for ColdU (TempTest®) or SD (FricTest®)
- **Exploratory endpoints:**
  - Mean change in UCT and DLQI scores from baseline to Week 12
  - % of patients with UCT ≥ 12 or UCT = 16 at Week 12
  - % of patients with ≥ 4-point difference in DLQI, or DLQI score of 0 or 1 at Week 12
  - **UCT:** total score of 0 to 16. Scores ≥ 12 indicate well-controlled urticaria, and a score of 16 indicates complete response. Minimum clinically important difference is 3 points.
  - **DLQI:** scores of 0 to 30, with higher scores indicating greater impact of disease on QoL. The minimal clinically important difference is a 4-point reduction. A score of 0 or 1 indicates no impact on the patient's QoL

Results

Demographics and Baseline Characteristics

- Well balanced across groups

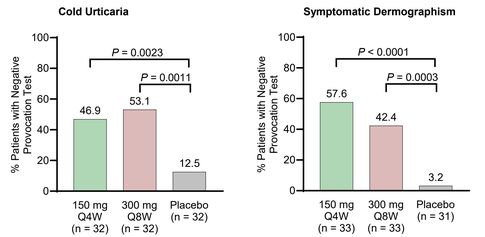
	Cold Urticaria			Symptomatic Dermographism		
	Barzolvolimab		Placebo (n=32)	Barzolvolimab		Placebo (n=31)
	150 mg Q4W (n=32)	300 mg Q8W (n=32)		150 mg Q4W (n=33)	300 mg Q8W (n=33)	
Age, years	40 (18-72)	40 (18-64)	41 (20-69)	41 (19-70)	42 (21-70)	42 (18-71)
Female, n (%)	27 (84)	23 (72)	19 (59)	18 (55)	26 (79)	19 (61)
Weight, kg	83 (55-124)	82 (49-140)	83 (47-129)	84 (58-121)	85 (55-139)	83 (53-115)
CIndU duration, years	7 (0.3-31)	11 (0.3-49)	10 (0.3-34)	7 (0.3-53)	6 (0.3-41)	5 (0.4-23)
Prior antihistamine therapy, n (%)	32 (100)	32 (100)	32 (100)	33 (100)	33 (100)	31 (100)
Prior omalizumab therapy, n (%)	2 (6.3)	1 (3.1)	1 (3.1)	1 (3)	2 (6)	2 (7)
UCT score	5.56 (0-12)	4.94 (0-11)	5.78 (0-12)	5.3 (0-11)	5.39 (0-13)	5.26 (0-13)
DLQI score	14.1 (1-30)	12.8 (2-26)	12.6 (1-30)	14.1 (3-30)	13.0 (1-28)	13.5 (1-26)

Data shown are mean (range) unless otherwise specified.

Barzolvolimab Drives Rapid and Durable Improvement in Urticaria Control and Quality of Life in Patients with Antihistamine-Refractory ColdU or SD

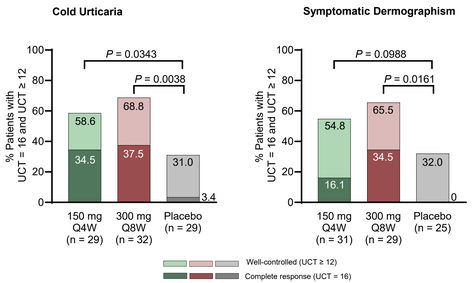
Primary Endpoint Achieved: Statistically Significant Improvement in Rate of Complete Response at Week 12

- Up to 53% of patients with ColdU and 58% of patients with SD treated with barzolvolimab achieved a complete response with negative provocation tests

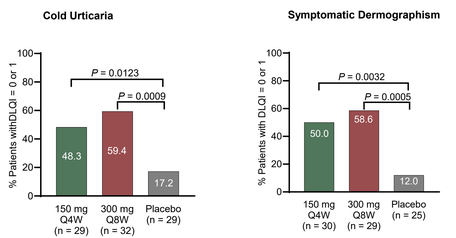


ColdU: Complete Response (CR) = negative provocation test at ≤ 4°C
Symptomatic Dermographism: CR = 0 pins
Non-responder imputation approach; mITT population

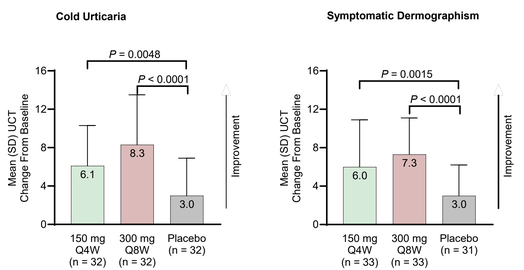
Up to 69% of Patients Achieved Well-controlled Urticaria as Measured by UCT at Week 12



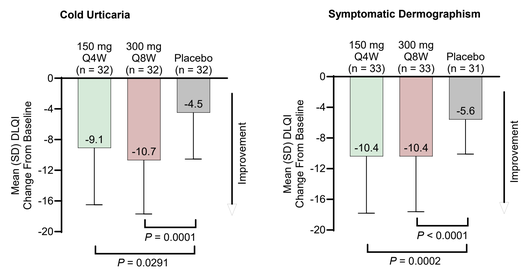
Up to 60% of Patients Reported "No Impact" of Urticaria on Quality of Life (DLQI = 0 or 1) at Week 12



Clinically Meaningful Improvement in Urticaria Control at Week 12

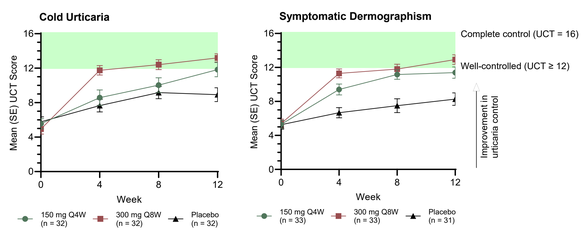


Clinically Meaningful Improvement in Quality of Life at Week 12



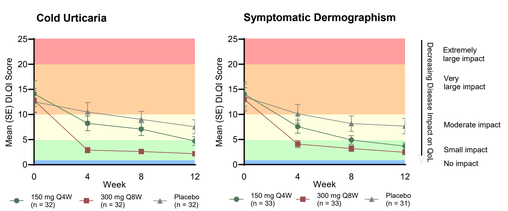
Marked Improvement in Urticaria Control Over 12 Weeks

- At Week 12, mean UCT scores indicated well-controlled urticaria.



Rapid and Sustained Improvement in Quality of Life Over 12 Weeks

- Patients reported that ColdU and SD had a "very large" impact on quality of life at baseline. At Week 12, patients reported a "small" impact on quality of life.



Barzolvolimab Was Well Tolerated

- No difference between active treatment and placebo groups in rate of discontinuations due to adverse events.
- Most adverse events were mild. Adverse events reported by ≥ 10% of patients in any treatment group were hair color changes (13%) and neutropenia (10%).[1]
- Most common events were mechanism-related (KIT) and expected to be reversible.
- No association between infections and neutropenia; neutropenia was transient.

Summary

- First large, randomized, placebo-controlled study to demonstrate clinical benefit in patients with CIndU.
- Up to 53% of patients with ColdU and 58% of patients with SD achieved complete response (negative provocation tests).
- Barzolvolimab treatment resulted in clinically meaningful improvement in urticaria control (UCT) and quality of life (DLQI) in both ColdU and SD patients.
- Improvement was marked and rapid across UCT and DLQI and was sustained through the 12-week period.
- Barzolvolimab potentially provides patients with a fast-acting and durable treatment option that offers a meaningful opportunity for complete disease control.
- Barzolvolimab was well tolerated with a safety profile consistent with previous studies.
- Plan to advance barzolvolimab into Phase 3 development for CIndU.

Reference: 1. Maurer et al. Positive Efficacy and Favorable Safety of Barzolvolimab in Chronic Inducible Urticaria: Phase 2 Trial Results. Presented at the American College of Allergy Asthma and Immunology Annual Scientific Meeting, Boston, MA, October 24-28, 2024.

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