Positive Efficacy and Favorable Safety of Barzolvolimab in Chronic Inducible Urticaria: Phase 2 Trial Results

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ACAAI 2024, Boston, MA

Disclosures

Dr. Jonathan Bernstein has been a principal investigator, consultant and speaker for Novartis, Genentech, Astra Zeneca, Sanofi, Regeneron, Biocryst, CSL Behring, Takeda/Shire, Pharming, GSK

He has been a principal investigator and consultant for Celldex, Cogent, Escient, Jasper Amgen, Roche, Ionis, Kalvista, Allakos, Biomarin, Blueprint Medicine

He has been a principal investigator for Teva; consultant for Incyte, Astria, ONO, Cycle, Escient, Pharvaris, and TLL

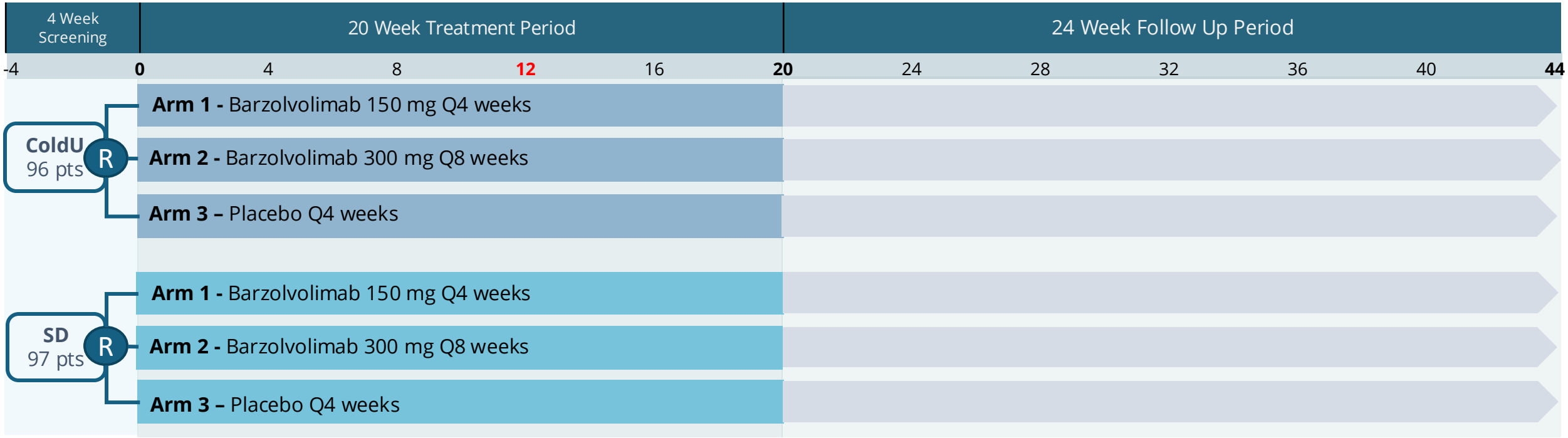
Introduction

- Chronic inducible urticaria (CIndU) is a mast cell (MC)-driven disease characterized by itch and wheals, triggered by cold in cold urticaria (ColdU), or pressure on the skin in symptomatic dermographism (SD)
  - There are currently no approved therapies for CIndU beyond antihistamines

- Barzolvolimab (CDX-0159), an anti-KIT monoclonal antibody, has demonstrated clinically meaningful and statistically significant improvement in itch and urticarial lesions accompanied by depletion of skin mast cells in chronic urticarias

- Here we report the primary analysis (Week 12) of a Phase 2 study evaluating the efficacy and safety of barzolvolimab compared with placebo in patients with cold urticaria and symptomatic dermographism whose disease is inadequately controlled by antihistamines (NCT05405660)

Phase 2 CIndU Study Design and Key Eligibility



Randomized, double-blind, placebo-controlled, dose-finding study

Key Eligibility Criteria:

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< 12

Primary Endpoint:

% of patients with a negative provocation test at Week 12 ColdU (TempTest®) & SD (FricTest®)

Secondary Endpoints:

CTT (Critical Temperature Threshold)

CFT (Critical Friction Threshold)

WI-NRSprovo (Worst Intensity of Itch at Testing)

Safety

Exploratory Endpoints:

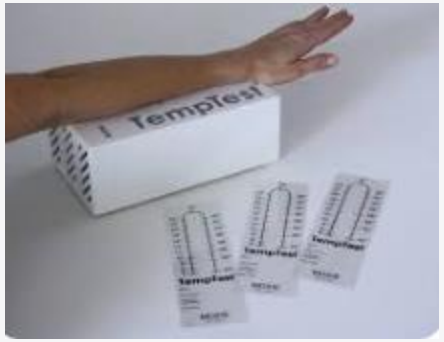
UCT (Urticaria Control Test)

Data cut off: July 3, 2024

Methodology

Provocation Tests

Cold Urticaria (ColdU) TempTest®

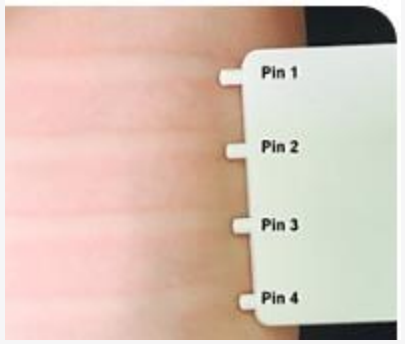


Critical Temperature Threshold (CTT): Threshold temperature at which wheals are triggered assessed at the 10-minute mark

Complete Response: negative test at 4 °C

Partial Response: ≥ 4 °C improvement

Symptomatic Dermographism (SD) FricTest®



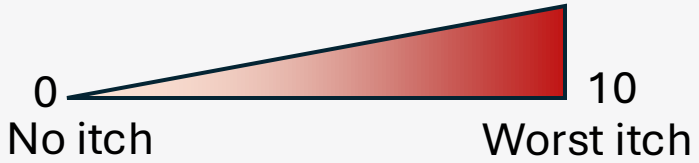
Critical Friction Threshold (CFT): Threshold pin number (out of 4) at which wheals are triggered assessed at the 10-minute mark

Complete Response: 0 pins

Partial Response: ≥ 2 pin improvement

Worst Itch Numeric Rating Scale with provocation test (WI-NRSprovo)

- Patients assess their worst itch triggered by the provocation test via a numerical rating scale (NRS)

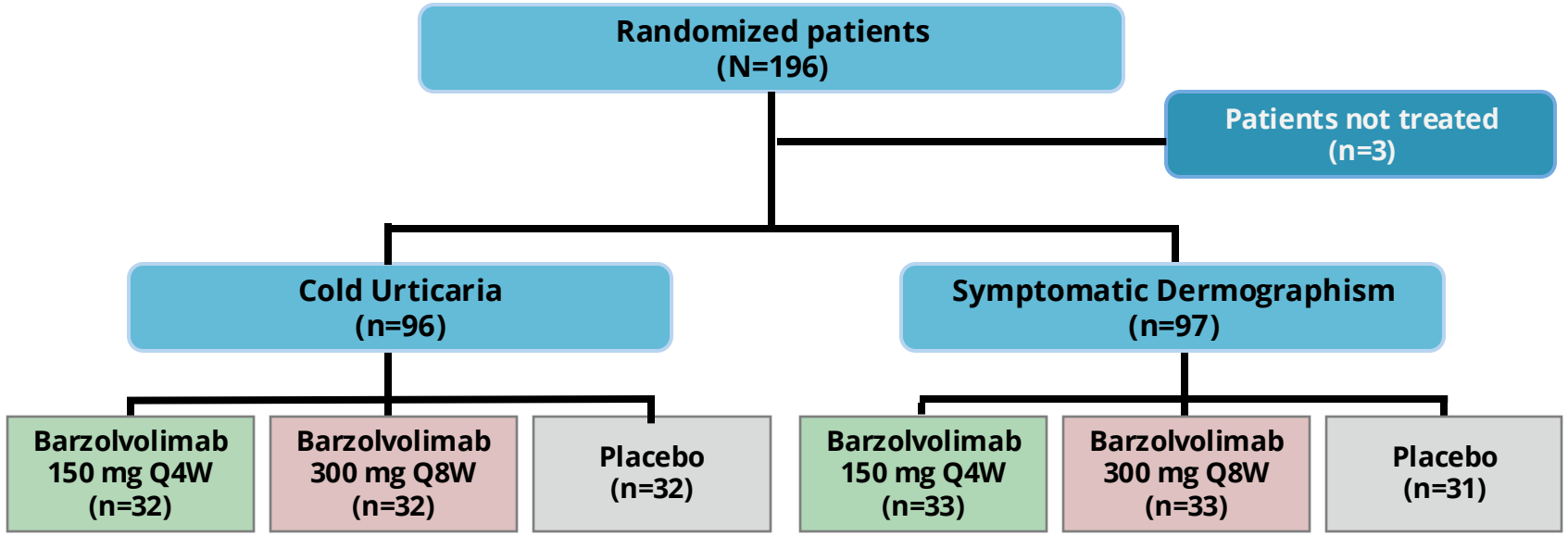


Urticaria Control Test (UCT)

- The UCT is comprised of 4 dimensions including physical symptoms, quality of life, treatment and overall disease control, with each dimension rated on a scale of 0-4 and a total score of 0-16
  - Well-controlled (UCT>12); Complete Response (UCT=16)

Patient Disposition

- In total, 196 patients randomized, 193 included in the full analysis (mITT) and safety set
- Overall, 173 (90%) completed through 12-weeks (primary endpoint)
  - 8% of patients treated with barzolvolimab discontinued treatment compared with 14% of patients treated with placebo



Discontinued Treatment, n (%)	3 (9%)	1 (3%)	2 (6%)	2 (6%)	5 (15%)	7 (23%)
Patient Decision	1 (3%)	1 (3%)	1 (3%)	1 (3%)	2 (6%)	4 (13%)
Adverse Event	1 (3%)				2 (6%)	2 (6%)
Other	1 (3%)		1 (3%)	1 (3%)	1 (3%)	1 (3%)

Demographics and Baseline Characteristics

- Well balanced across the treatment groups

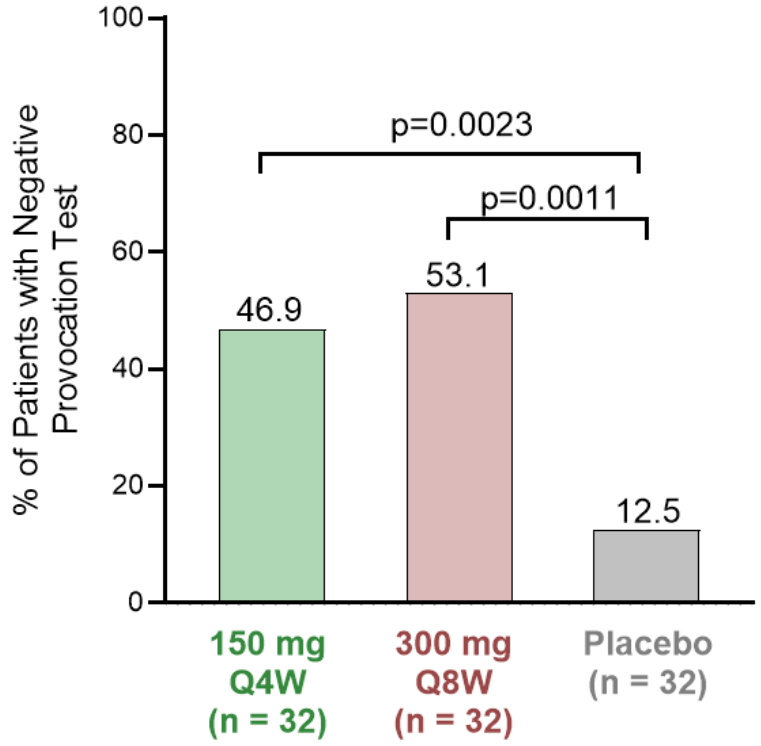
	Cold Urticaria			Symptomatic Dermographism		
	Barzolvolimab 150 mg Q4W (n=32)	**Barzolvolimab 300 mg Q8W (n=32)**	**Placebo (n=32)**	**Barzolvolimab 150 mg Q4W (n=33)**	**Barzolvolimab 300 mg Q8W (n=33)**	**Placebo (n=31)**
Age (years)	40 (18-72)	40 (18-64)	41 (20-69)	41 (19-70)	42 (21-70)	42 (18-71)
Gender, Female, n (%)	27 (84%)	23 (72%)	19 (60%)	18 (55%)	26 (79%)	19 (61%)
Race						
White, n (%)	26 (81%)	31 (97%)	28 (88%)	29 (88%)	29 (88%)	27 (87%)
Black, n (%)	4 (13%)	1 (3%)	2 (6.3%)	3 (9%)	2 (6%)	1 (3%)
Weight (kg)	83 (55-124)	82 (49-140)	83 (47-129)	84 (58-121)	85 (55-139)	83 (53-115)
CINDU Duration, yr	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 angioedema, n (%)	9 (28%)	11 (34%)	11 (34%)	9 (27%)	7 (21%)	7 (23%)
Prior anti-histamine 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%)
CTT (°C)	18.7 (4-38)	20.7 (8-40.5)	18.6 (4-44)	NA	NA	NA
CFT (pins)	NA	NA	NA	3.64 (2-4)	3.58 (2-4)	3.55 (3-4)
WI-NRSprovo	6.28 (0-10)	5.47 (0-10)	5.41 (0-9)	5.73 (1-9)	5.70 (2-9)	5.23 (1-9)
UCT	5.56 (0-12)	4.94 (0-11)	5.78 (0-12)	5.3 (0-11)	5.39 (0-13)	5.26 (0-13)

CTT, Critical Temperature Threshold; CFT, Critical Friction Threshold; WI-NRSprovo, Numerical Rating Scale of Worst Itch at the time of provocation testing; UCT, Urticaria Control Test
Data shown are Mean (range) unless otherwise specified

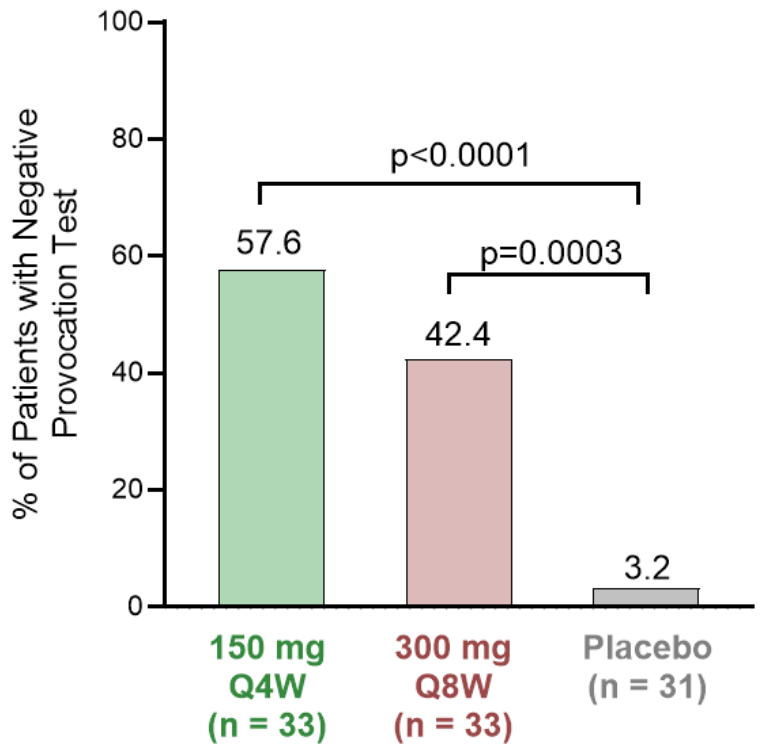
Statistically Significant Improvement in Rate of Complete Response at Week 12

- Up to 53% of ColdU and 58% of Symptomatic Dermographism patients treated with barzolvolimab achieved a Complete Response

Cold Urticaria
% of patients with negative provocation test



Symptomatic Dermographism
% of patients with negative provocation test



ColdU: Complete Response (CR) =negative provocation test at ≤4°C
Symptomatic Dermographism: CR=0 pins

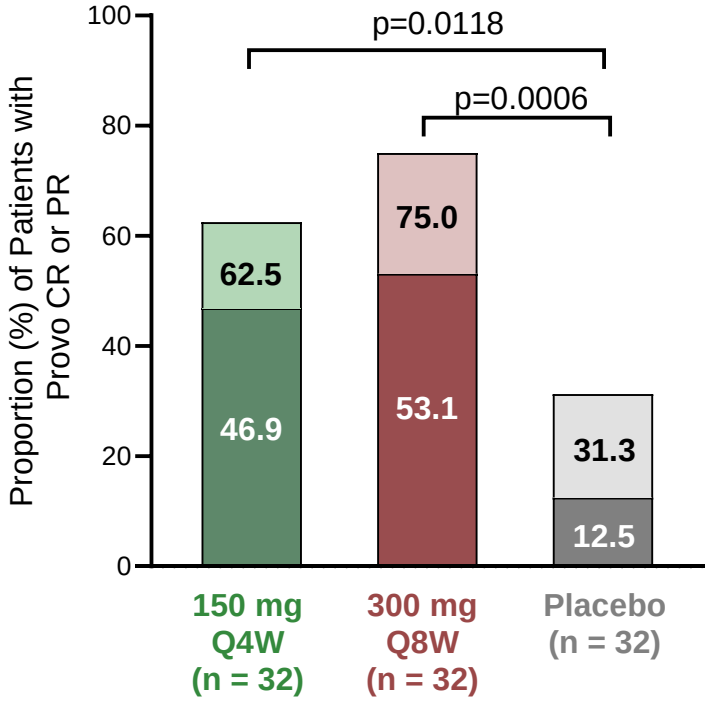
Non-responder imputation approach; mITT population

Statistically Significant Improvement in Rates of Complete and Partial Response at Week 12

- Up to 75% of ColdU and 67% of Symptomatic Dermographism patients treated with barzolvolimab achieve a Complete or Partial Response

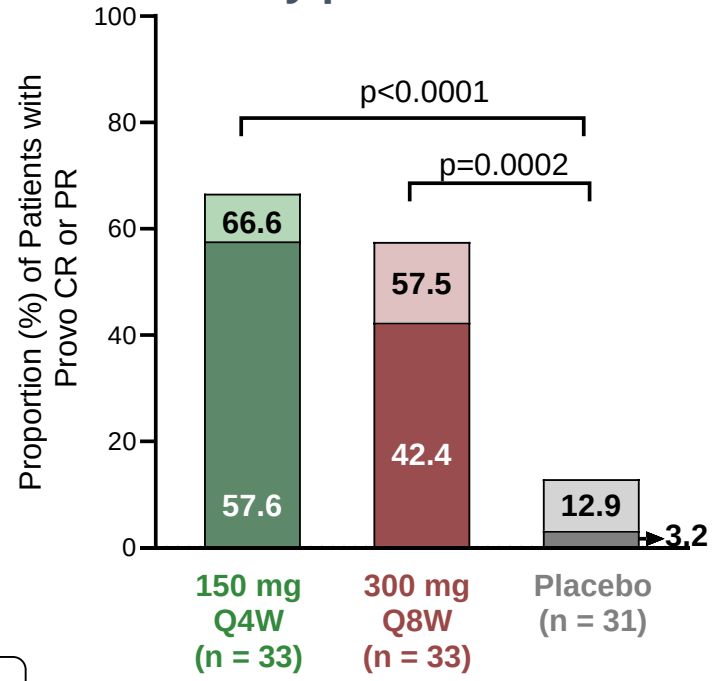
Cold Urticaria

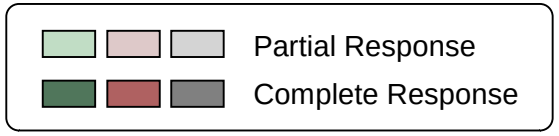
% of patients with Complete and Partial Response by provocation



Symptomatic Dermographism

% of patients with Complete and Partial Response by provocation

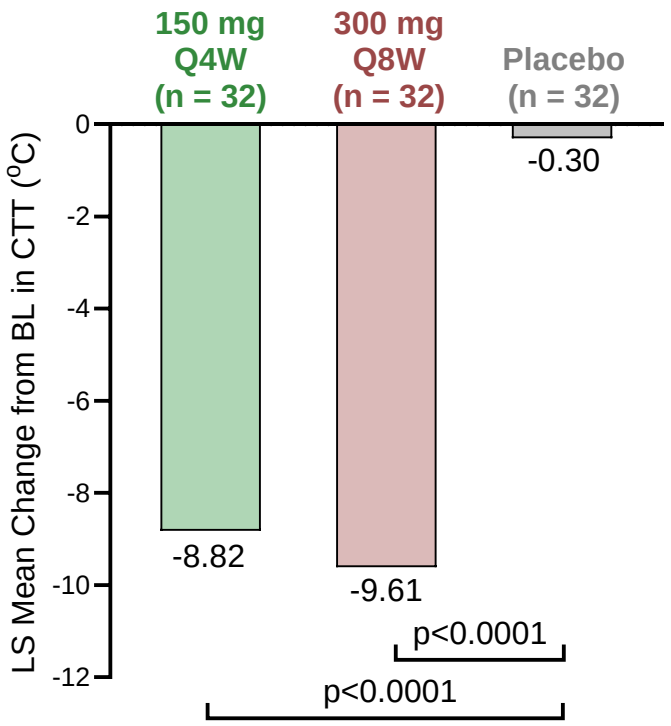




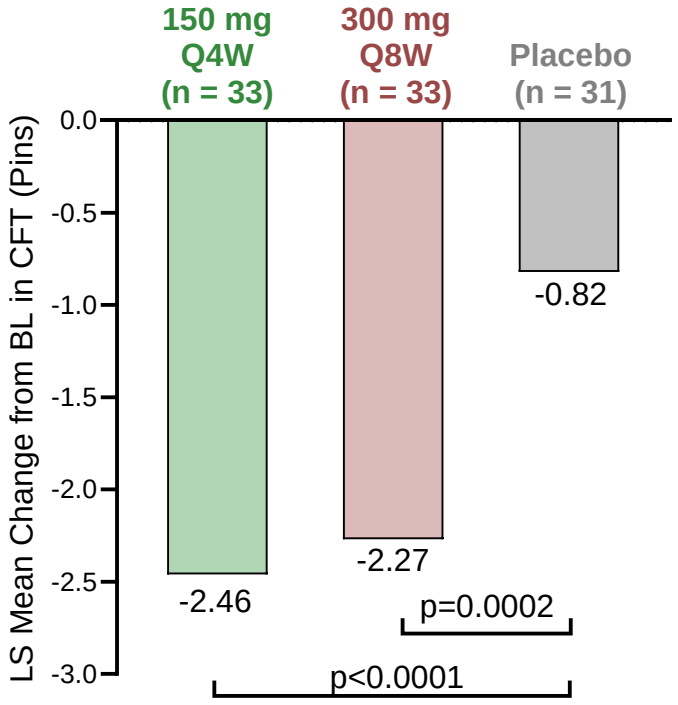
ColdU: Complete Response (CR) =negative provocation test at ≤4°C; Partial Response (PR) ≥ 4°C improvement in provocation test
Symptomatic Dermographism: CR=0 pins; PR ≥ 2 pin improvement in provocation test
Non-responder imputation approach; mITT population

Marked Improvement in Critical Temperature (CTT) and Friction Thresholds (CFT) at Week 12

Cold Urticaria
LS Mean Change in CTT (°C) at Week 12



Symptomatic Dermographism
LS Mean Change in CFT (pins) at Week 12

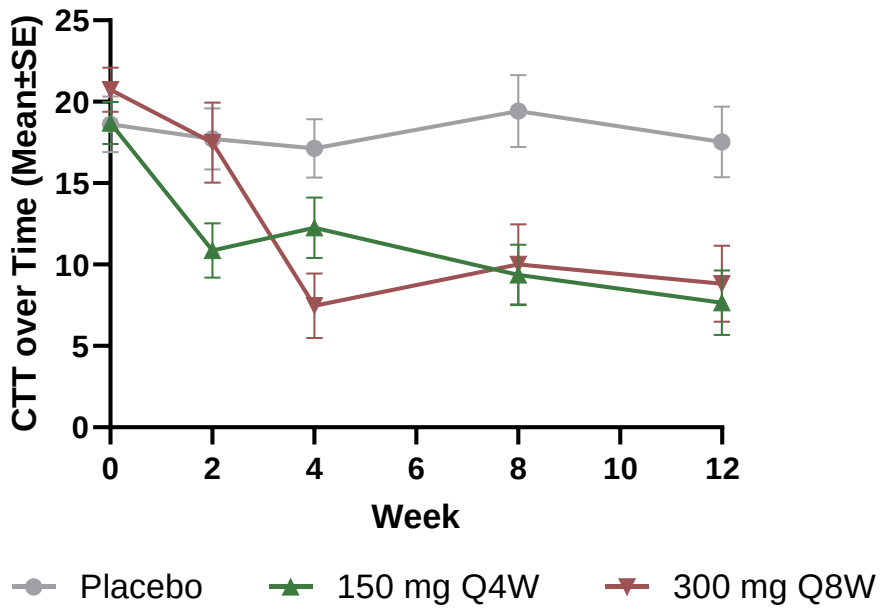


CTT, Critical Temperature Threshold; CFT, Critical Friction Threshold; LS, Least Square
ANCOVA model; multiple imputation; mITT population

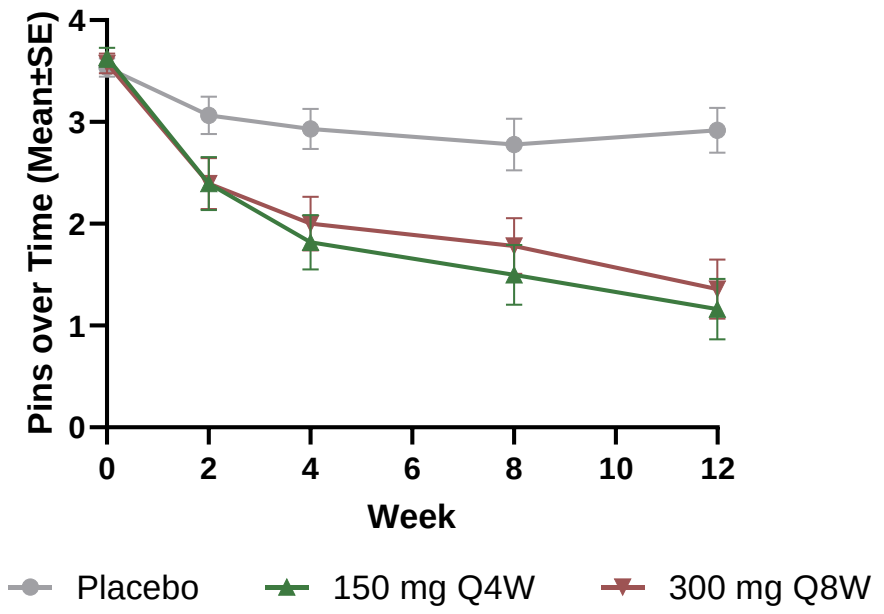
Rapid Reduction in Critical Temperature and Friction Thresholds

- Improvements seen as early as 2 weeks after first dose (first assessment)

Cold Urticaria
TempTest® Results Over Time



Symptomatic Dermographism
FricTest® Results Over Time

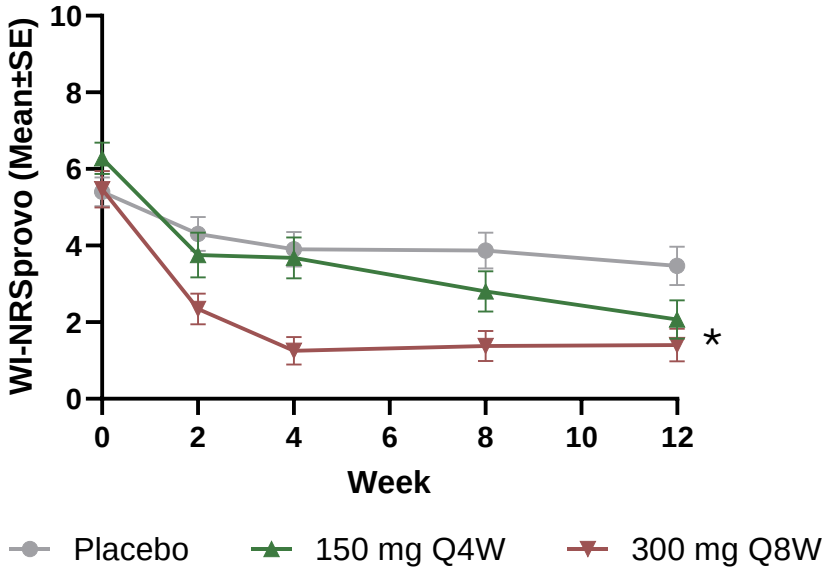


Critical temperature threshold values below 4°C (negative test) assigned a value of 3°C
CTT, Critical Temperature Threshold; CFT, Critical Friction Threshold
Observed Data; mITT population

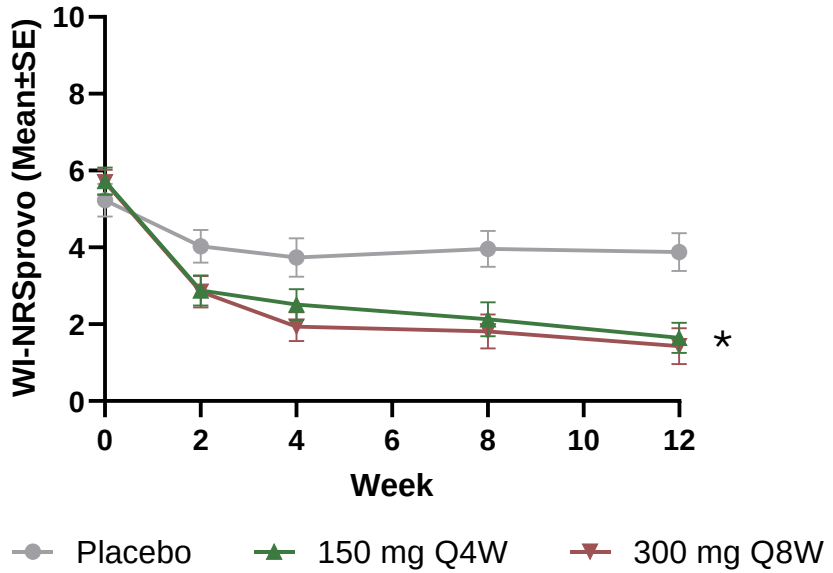
Rapid Reduction in Itch at the Time of Provocation Testing (WI-NRSprovo)

- Improvements seen as early as 2 weeks after first dose (first assessment)

Cold Urticaria
WI-NRSprovo Results Over Time



Symptomatic Dermographism
WI-NRSprovo Results Over Time

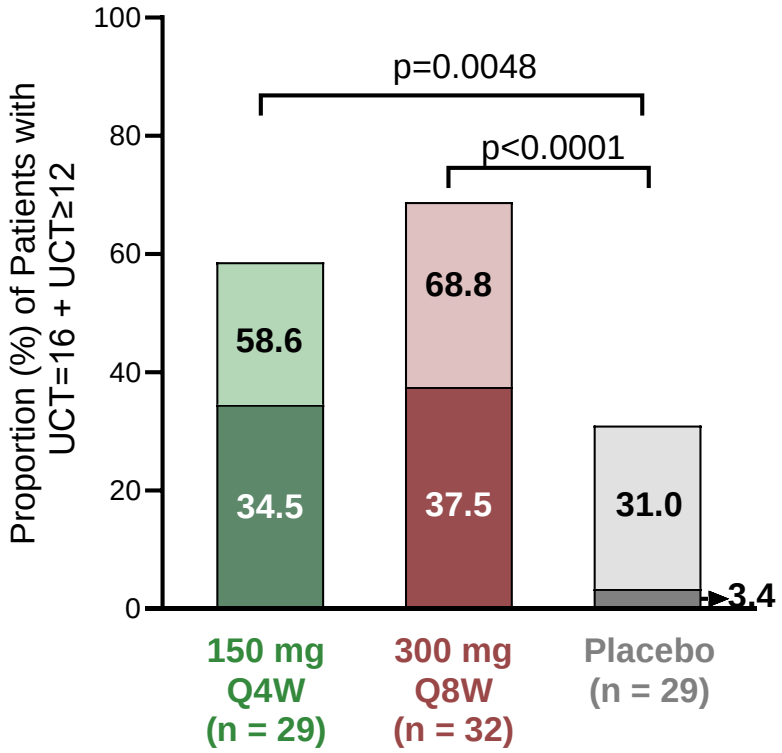


* At Week 12, p=0.0291 and p=0.0016 for barzolvolimab 150mg Q4W and 300mg Q8W compared to placebo for Cold Urticaria and p<0.0001 and p=0.0002 for Symptomatic Dermographism

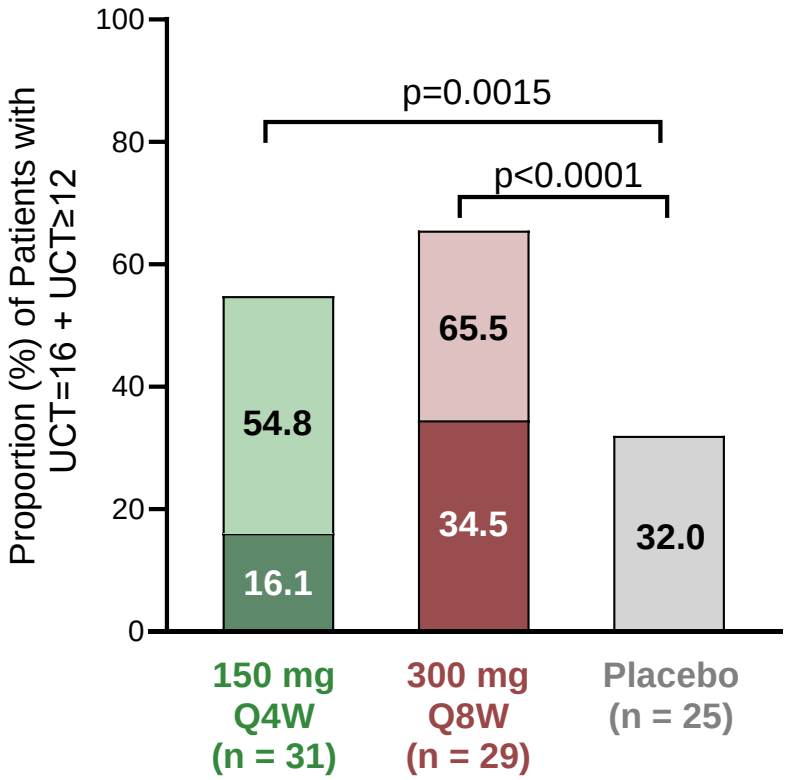
WI-NRSprovo is worst itch at the time of provocation testing
Observed data; mITT population

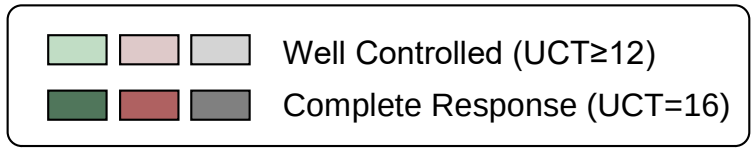
Clinically Meaningful Improvement in UCT at Week 12

Cold Urticaria



Symptomatic Dermographism





UCT, Urticaria Control Test
Observed data; mITT population

Favorable safety profile, consistent with prior studies

- 98% of treatment emergent adverse events were Grade 1 or 2 (mild (66.7%), moderate (31.7%))
- No difference in rate of discontinuations due to AEs between active and placebo
- The most common events are mechanism-related (KIT) and expected to be reversible
- No association between infections and neutropenia; events were mild and transient

Patients, n (%)	Barzolvolimab 150 mg Q4W (n=65)	Barzolvolimab 300 mg Q8W (n=65)	All Barzolvolimab Treated Patients (n=130)	Placebo (n=63)
Patients with any AE	40 (62%)	39 (60%)	79 (61%)	33 (52%)
Patients with treatment related SAE(s)[1]	0	1 (2%)	1 (1%)	0
Discontinued study treatment due to AE(s)[2]	1 (2%)	2 (3%)	3 (2%)	2 (3%)
Most frequent AEs by Preferred Term (≥10% of patients in any treatment group)				
Hair color changes	9 (14%)	8 (12%)	17 (13%)	0
- Grade 1 / Grade 2, n	8 / 1	7 / 1	15 / 2	0
Neutropenia	4 (6%)	9 (14%)	13 (10%)	0
- Grade 1 / Grade 2, n	3 / 1	4 / 5	7 / 6	0

[1] Single treatment related SAE (anaphylaxis) reviewed by independent expert adjudication panel who concluded there was no evidence of anaphylaxis

[2] Other discontinuations due to AEs: urticaria/lip edema (150mg), neutropenia (300mg), cystic acne/aphthous ulcer (placebo) and paraesthesia oral/swollen tongue (placebo)

Conclusions

- First large, randomized, placebo-controlled study to demonstrate **clinical benefit** in patients with chronic inducible urticaria
- Study met all primary and secondary endpoints at Week 12 with **statistically significant and clinically meaningful improvements** observed with barzolvolimab 300mg Q8W and 150mg Q4W compared to placebo
  - Up to **53% ColdU and 58% of SD achieved complete response** (negative provocation test)
  - Up to 75% of ColdU and 67% of SD achieved complete or partial response
  - **Marked and rapid improvement** in provocation thresholds and associated itch
  - Clinically meaningful improvement in overall urticaria control (UCT)
- Barzolvolimab was **well tolerated** with safety profile consistent with previous studies
- Phase 3 studies are planned in CIndU

Acknowledgements

We wish to thank all the investigators and their patients who contributed to this trial.

We are especially grateful to Professor Dr. Marcus Maurer for his partnership in advancing barzolvolimab. Dr. Maurer's steadfast commitment to improving the lives of patients with chronic urticarias was at the forefront of every interaction we had with him and was a source of inspiration to our team and the field. His legacy will live on.