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Barzolvolimab Demonstrates Clinical Activity in Antihistamine Refractory Cholinergic Urticaria

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Conflict Of Interest Statement

Eva Grekowitz has received research funds and was an advisor for Novartis

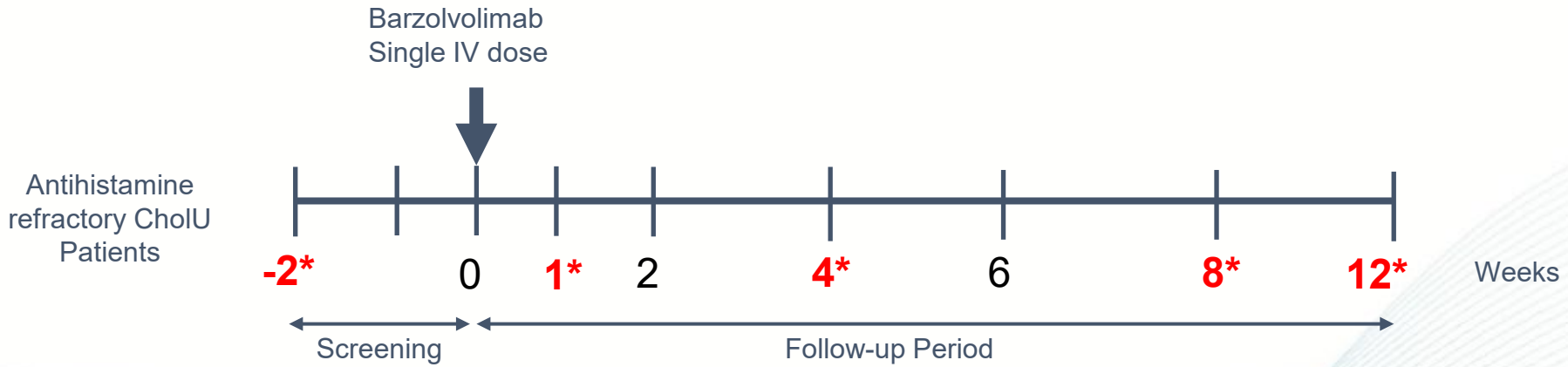
Background

- Cholinergic urticaria (CholU) is a chronic inducible urticaria (CIndU) triggered by physical exercise or passive warming and characterized by itchy wheals that appear upon sweating.
- Mast cells may play an important role in the pathophysiology of CholU in many patients.
- Barzolvolimab (CDX-0159) is a monoclonal anti-KIT antibody that selectively inhibits SCF-dependent KIT activation, which is required for mast cell survival.
- In patients with cold urticaria and symptomatic dermographism, a single dose of 3.0 mg/kg barzolvolimab demonstrated a 95% complete response to provocation testing and corresponding symptom improvement[1].
- Here, we report the safety, clinical activity, and pharmacodynamic response of CholU patients to treatment with 3.0 mg/kg barzolvolimab.

[1]Terhorst-Molawi et al *Allergy*. 2023; 78: 1269- 1279.

Study Design and Methods

- Open label study with single IV dose of barzolvolimab 3 mg/kg and 12 week follow up.
- Patients with antihistamine-refractory cholinergic urticaria were tested using positive pulse controlled ergometry (PCE)[1] test.



*** Visits where PCE testing was conducted**.

[1] Altrichter et al *J Dermatol Sci*. 2014;75(2):88-93

Study Assessments

Safety:

- Adverse events, Laboratory tests.

Clinical activity:

- **Pulse-controlled Ergometry (PCE) test**[1]: UASprovo = 0 – 6 (↑severity with score).
    - UASprovo = Itching (0-3) + Whealing (0-3); Assessed ≤40 min of PCE start.
    - Complete response = UASProvo = 0.
- **Urticaria control test (UCT):** Score = 0-16.
    - UCT< 12 Poorly controlled.
    - UCT ≥ 12 Well controlled.
    - UCT =16 Completely controlled.

Biomarkers:

- Tryptase, SCF, skin mast cell numbers.

[1] Altrichter et al *J Dermatol Sci*. 2014;75(2):88-93

Demographics and Baseline Characteristics

		CholU 3 mg/kg (N=9*)
Age mean (range) years		35.4 (23 - 52)
Gender Male, n (%)		7 (78%)
Race	White, n (%)	7 (78%)
	Black, n (%)	2 (22%)
Weight mean (range) kg		83 (56– 107)
Disease Duration	< 5 yr, n (%)	4 (44%)
	≥ 5 yr, n (%)	5 (56%)
History of Angioedema		1 (11%)
Prior Medication H1 Antihistamines		9 (100%)
Biologics[†]		2 (22%)
UASProvo Mean (range)		4.3 (2-6)
UCT Mean (range)		6.3 (1-11)
Tryptase mean (range) ng/mL		4.4 (3.1-6.6)

*Nine patients received a complete dose of study drug and are included in the safety and clinical activity analysis, 8 patients have completed the 12-week follow-up, one patient withdrew early from the study

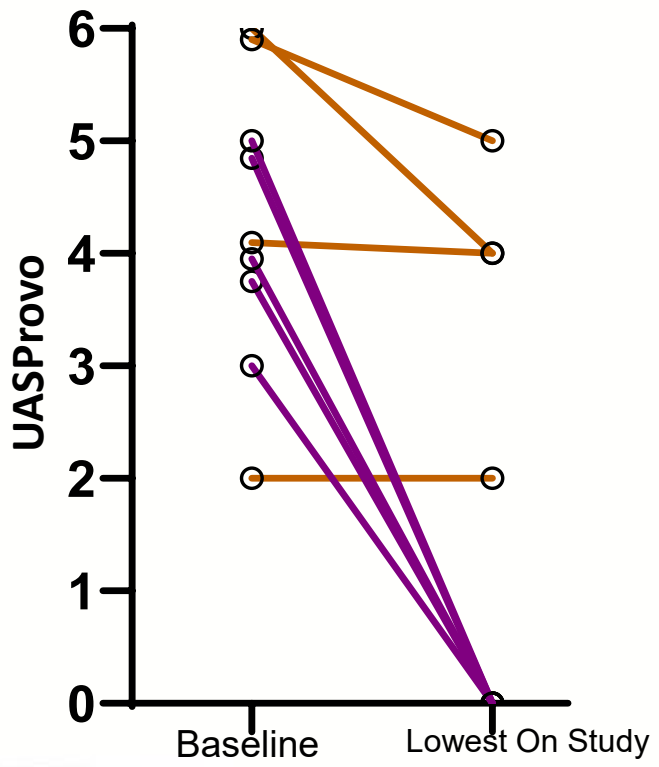
[†]One patient was refractory to omalizumab, and one patient was refractory to omalizumab and dupilumab

Barzolvolimab Demonstrates Favorable Safety and Tolerability

- Barzolvolimab was generally well tolerated in patients with CholU, with a similar safety profile to that reported previously[1].
- AE reported were mainly mild.
- The most common AEs reported were hair color changes (78%), nasopharyngitis (67%), taste changes (44%), and infusion related reactions (33%).
- Hematology parameters were consistent with previous observation and generally remained within the normal ranges. Mild, transient, and asymptomatic decreases in hemoglobin and WBC parameters were noted.

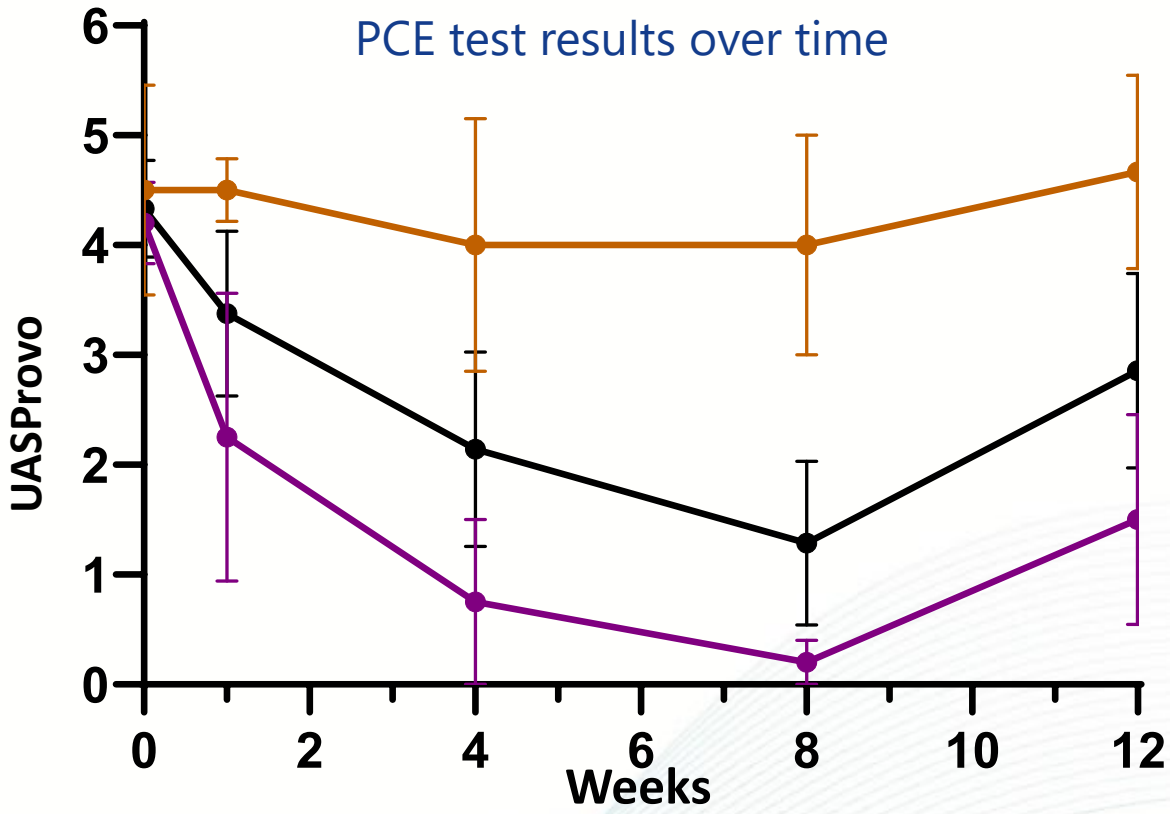
[1]Terhorst-Molawi et al *Allergy*. 2023; 78: 1269- 1279.

Improvement in PCE Provocation Results with Single Dose of Barzolvolimab



Complete responders = UASProvo=0, Non-responders = UASProvo> 0

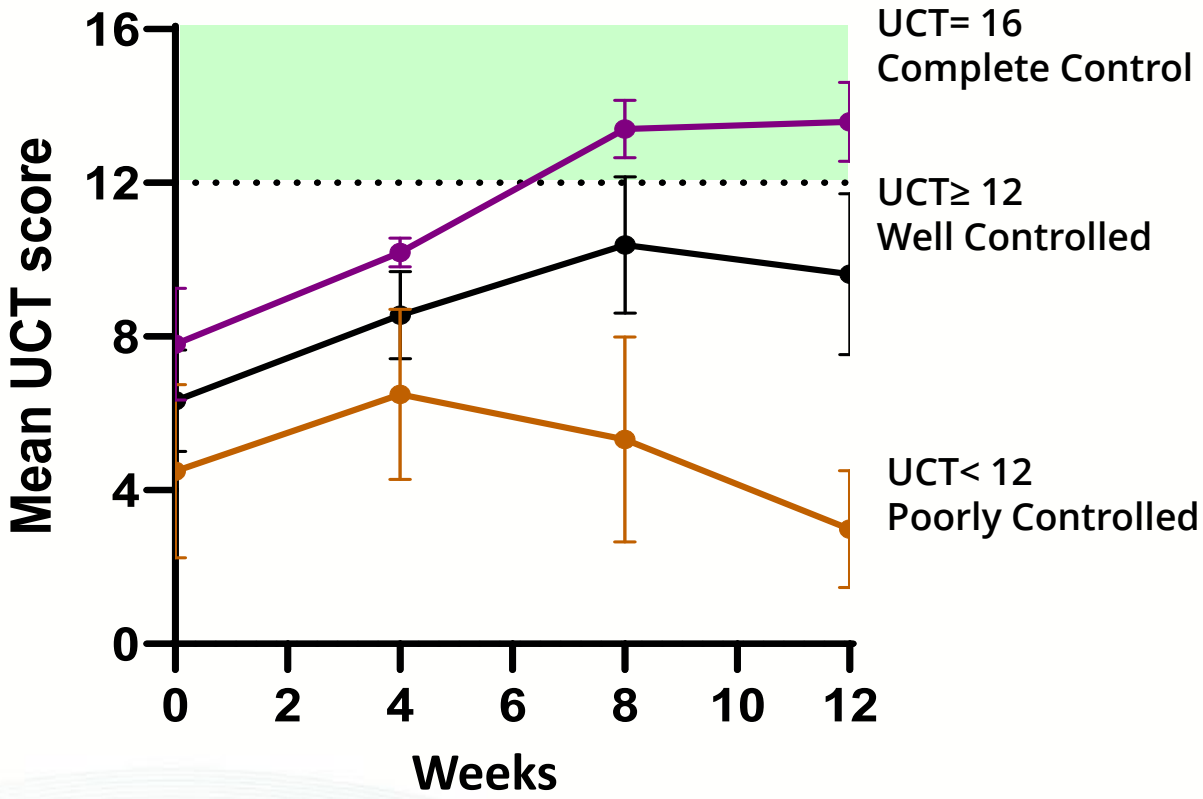
5/9 patients showed a complete response



Mean ± SEM for **all patients (n=9),** **Complete responders (n=5),** and **Non-responders (n=4)** are shown

Most responses remained durable to Week 12

Improvement in Urticaria Control Test with Single Dose of Barzolvolimab

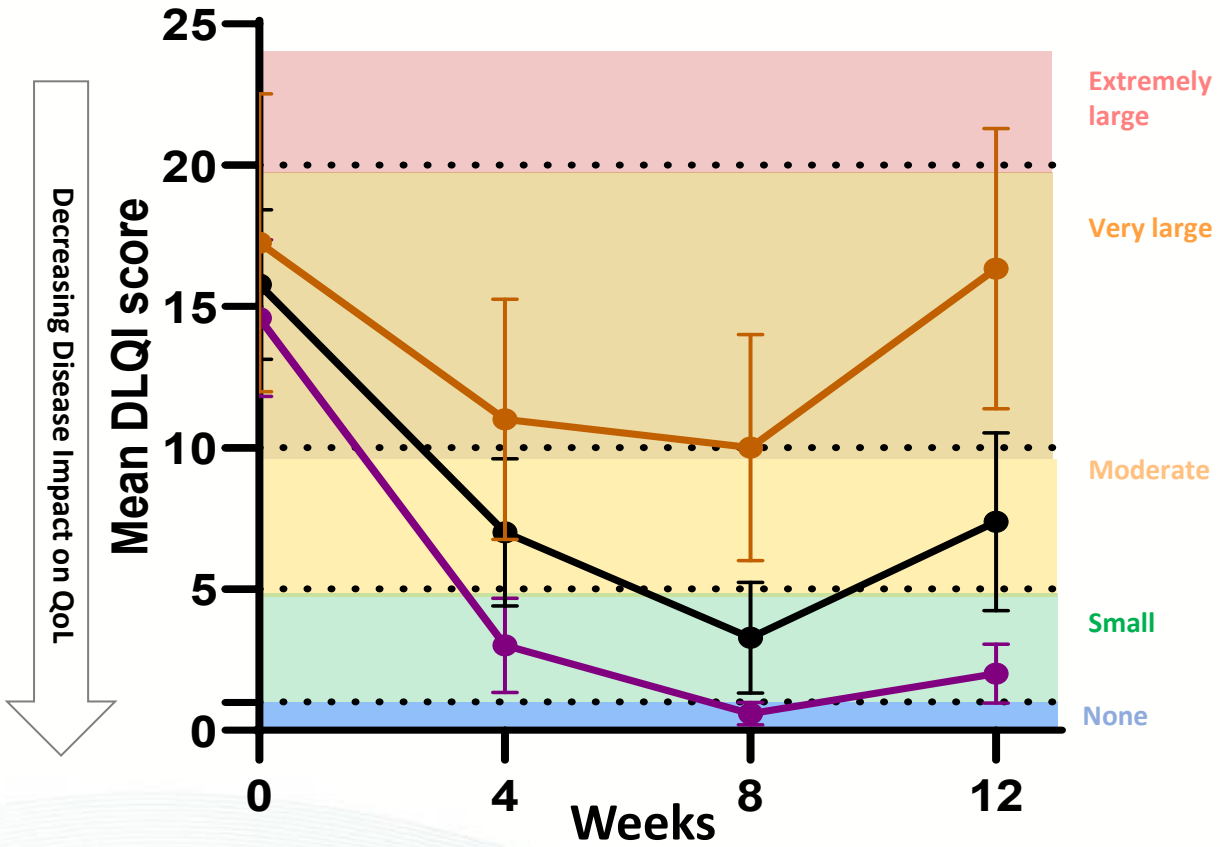


All patients (n=9)
Complete responders (n=5)
Non-responders (n=4)

63% Patients were well controlled (UCT ≥ 12) at Week 8

3 mg/kg barzolvolimab	Predose	4 week	8 week	12 week
UCT≥ 12 n (%)	0/9 (0)	0/9 (0)	5/8 (63)	4/8 (50)

Improvement in Disease Impact on QoL with Single Dose of Barzolvolimab



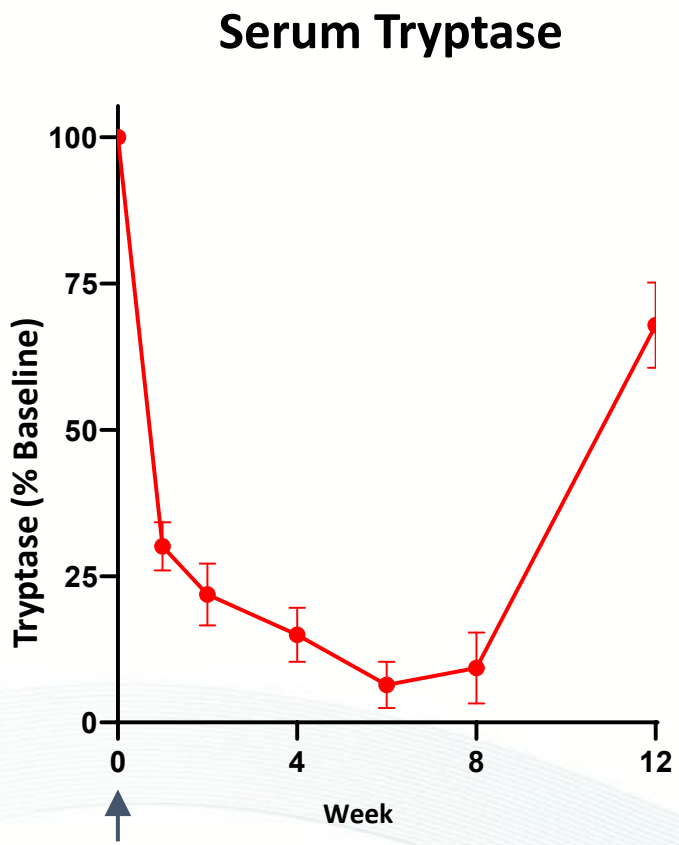
All patients (n=9)
Complete responders (n=5)
Non responders (n=4)

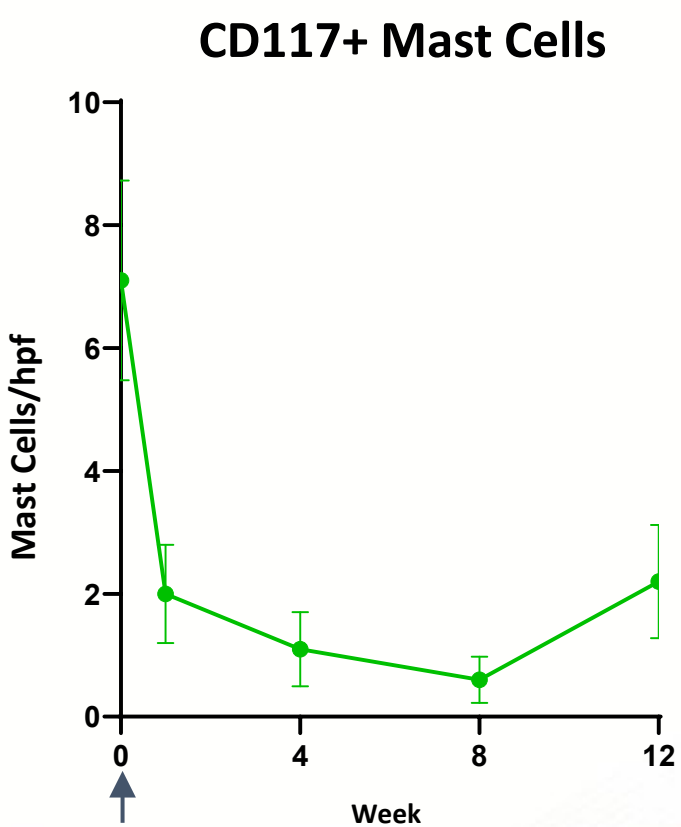
100% Patients Achieved Clinically Significant Improvement in QoL by Week 8

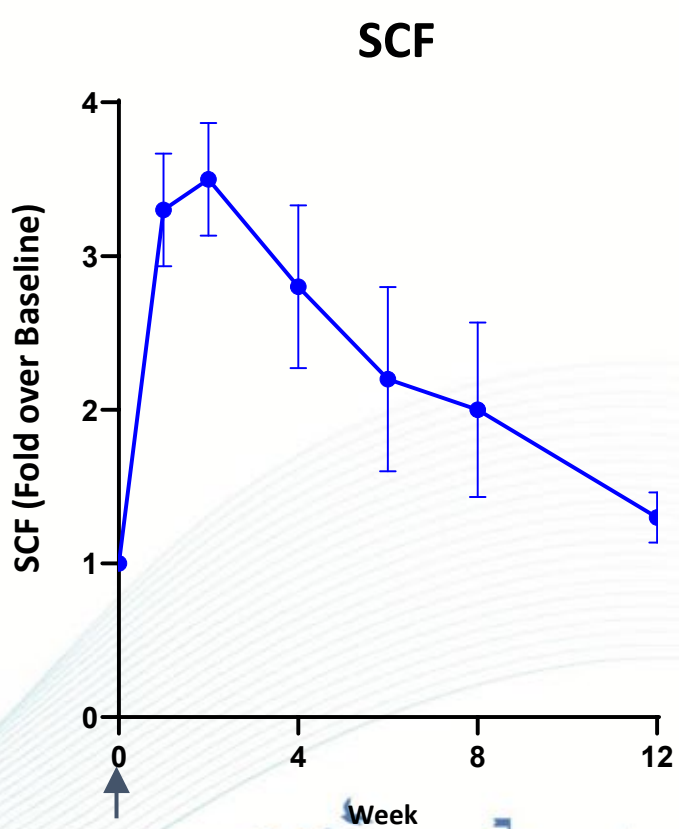
≥4-point reduction† in DLQI from baseline *	Week 4	Week 8	Week 12
CholU Patients % (n/ N)	71% (5/7)	100% (6/6)	71% (5/7)

† MCID for DLQI is ≥4 ; *Only patients whose baseline score was ≥4 were included

Profound Tryptase and Skin MC Reduction







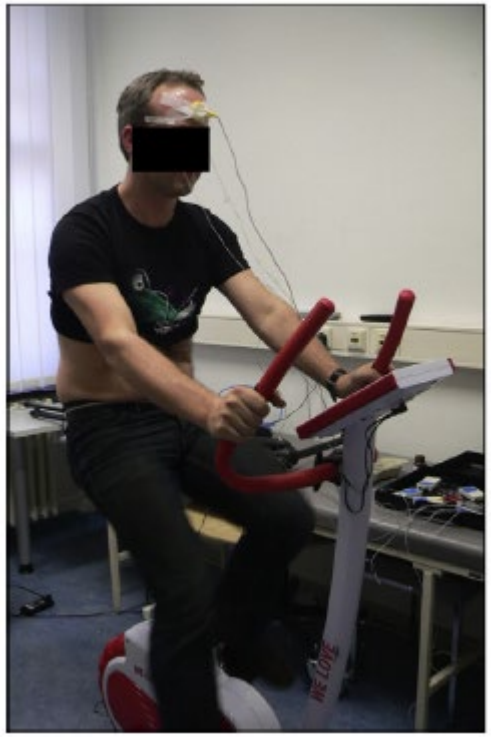
Summary and Conclusions

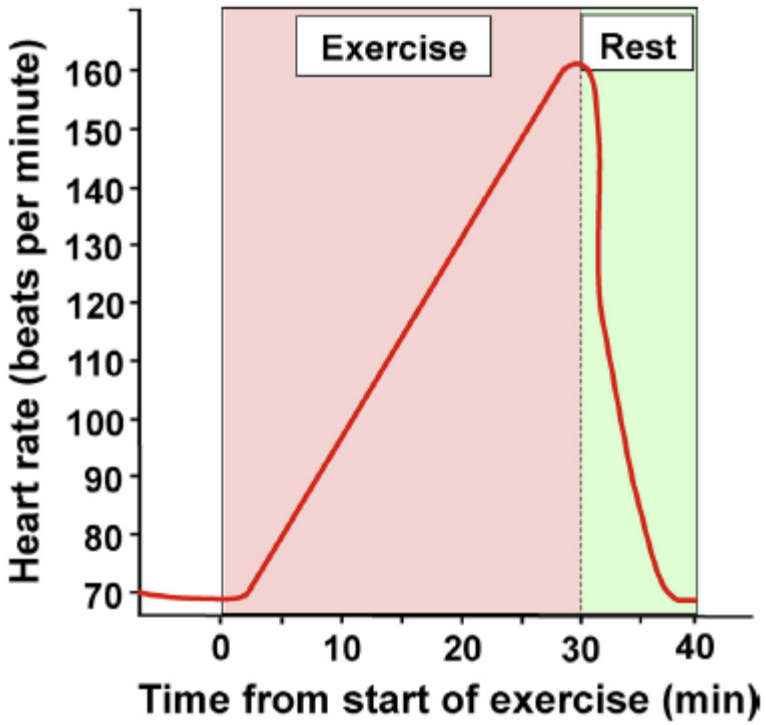
- In patients with CholU refractory to antihistamines, a single dose of barzolvolimab 3.0 mg/kg was well tolerated and demonstrated remarkable clinical activity.
  - The adverse event profile was similar to that observed in other CIndU patients.
  - 56% (5/9) patients achieved a complete response (negative provocation test).
  - 63% (5/8) patients achieved well controlled disease at Week 8.
  - Improvements in QoL were sustained through Week 12 for the majority of patients.
  - The kinetics of tryptase and mast cell reduction mirrored clinical activity.
- Overall, barzolvolimab has demonstrated broad clinical activity in the most common CIndU (ColdU, SD and CholU), with a profound and durable reduction in symptoms, tryptase and mast cells.

Thank you!

Backup

Pulse Controlled Ergometry Test





- Peddling controlled to achieve:
  - Increase in pulse rate of 15 beats/min, every 5 min to 90 beats/min above baseline.
- The following were recorded during exercise (start to end [30 min] + recovery period [10 min]):
  - Core and skin temperature
  - Heart rate
  - Times to sweating (Miner's/iodine test)
  - Time to appearance of wheals
  - Time to disappearance of wheals
  - Itching as reported by patients.

Patient seated on exercise bike and fitted with temperature sensor and pulse heart rate monitor

From Altrichter et al *J Dermatol Sci*. 2014;75(2):88-93