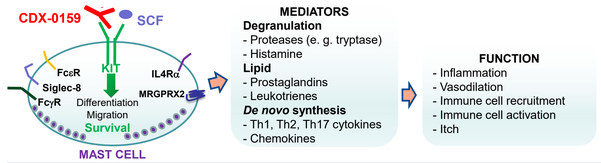
# CDX-0159, an anti-KIT Antibody, Demonstrates Rapid and Sustained Clinical Response and Improved Quality of Life in Patients with Chronic Inducible Urticaria

Tomasz Hawro[1*], Dorothea Terhorst-Molawi[1*], Eva Grekowitz[1*], Lea Kiefer[1], Martin Metz[1], Diego Alvarado[2], Elizabeth Crowley[2], Margo Heath-Chiozzi[2], Marcus Maurer[1]
[1]Dermatological Allergology, Allergie-Centrum-Charité, Department of Dermatology and Allergy, Charité - Universitätsmedizin Berlin, Germany [2],Celldex Therapeutics, Hampton, NJ, USA
*Contributed equally, co-first authors

Study Identifiers: CDX0159-03; EUDRACT2020-

## BACKGROUND

- Chronic inducible urticaria (CIndU) is a mast cell (MC)-driven disease characterized by itch and wheals triggered by cold in cold urticaria (ColdU), or skin scratching in symptomatic dermographism (SD).
- The activation of KIT receptors by stem cell factor is essential for differentiation, proliferation and survival of MCs.
- CDX-0159 is a monoclonal anti-KIT antibody that is engineered to selectively inhibit SCF-dependent KIT activation.
- In healthy volunteers, CDX-0159 induced a profound dose-dependent reduction in circulating tryptase, a biomarker of MC burden, and was overall well-tolerated.
- A single dose of CDX-0159 (3 mg/kg) was generally well-tolerated and resulted in rapid and durable complete responses (negative provocation test) in antihistamine-refractory CIndU (ColdU and SD) patients as previously reported[1]. Data presented here show the effect of CDX-0159 on urticaria control and quality of life (QoL) of these patients.




## STUDY DESIGN AND METHODS

CDX0159-03 is an ongoing open-label, Phase 1b trial in patients with CIndU (including ColdU and SD) refractory to antihistamine treatment, who receive a single IV infusion of CDX-0159 at 3 mg/kg with a 12-week follow-up.

- Primary objective is to evaluate safety/tolerability of CDX-0159 (adverse events and clinical lab tests).
- Secondary objectives include evaluating the effect of CDX-0159 on clinical effect and serum tryptase.
- Clinical effect assessments include provocation test [TempTest/ColdU; FricTest/SD], urticaria control test (UCT) and dermatology life quality index (DLQI).

## STUDY STATUS

- Study is ongoing; current data cut as of 13Aug2021.
- 21 ColdU and SD patients received study drug and are included in the safety analysis.
- 20 ColdU and SD patients received a full dose of study drug and are included in UCT, DLQI, and provocation test data.
- 20 of 21 ColdU and SD patients completed the 12-week observation period; 1 is ongoing.

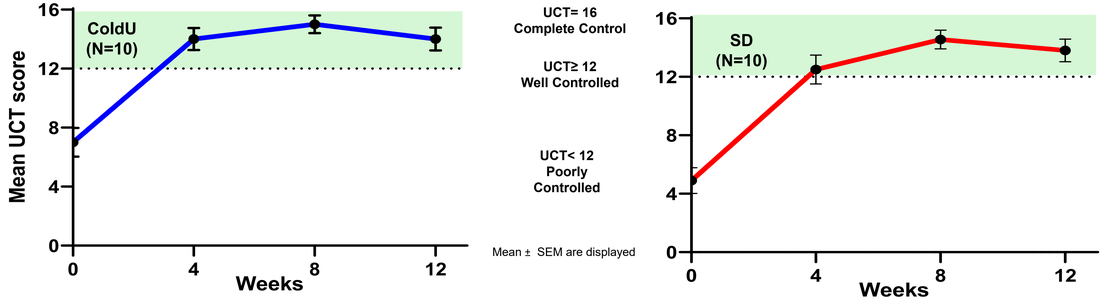
## DEMOGRAPHICS AND BASELINE DISEASE CHARACTERISTICS

| | | ColdU (N=11) | SD (N=10) | All (N=21) |
|---|---|---|---|---|
| **Age** median (range) years | | 43 (27- 65) | 39 (25- 56) | 41 (25 - 65) |
| **Gender** Female, n (%) | | 6 (54.5%) | 4 (40.0%) | 10 (47.6%) |
| **Race** | White, n (%) | 10 (90.9%) | 10 (100%) | 20 (95.2%) |
| | Asian, n (%) | 1 (9.1%) | 0 (0%) | 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) | 85.7 (57.0 – 122.0) | 81.5 (57.0 – 122.0) |
| **Disease Duration** | < 5 yr, n (%) | 5 (45.5%) | 4 (40%) | 9 (42.9%) |
| | ≥ 5 yr, n (%) | 6 (54.5%) | 6 (60%) | 12(57.1%) |
| **History of Angioedema** | | 6 (54.5%) | 0 | 6 (28.6%) |
| **Provocation Threshold** Mean (range) | | 18.9 (5-27) °C | 3.5 (2-4) Pins | |
| **UCT** Mean (range) | | 7 (2-13) | 4.9 (0-10) | 6.0 (0-13) |
| **DLQI** Mean (range) | | 10.8 (3-17) | 11.4 (2-21) | 11.1 (2-21) |
| **Prior Medication** H1 Antihistamines | | 11 (100%) | 10 (100%) | 21 (100%) |
| | Biologics (omalizumab) | 1 (9%) | 2 (20%) | 3 (14.3%) |
| **Tryptase** median (range) ng/mL | | 3.8 (2.4-5.5) | 4.6 (1.3-8.6) | 4.2 (1.3-8.6) |

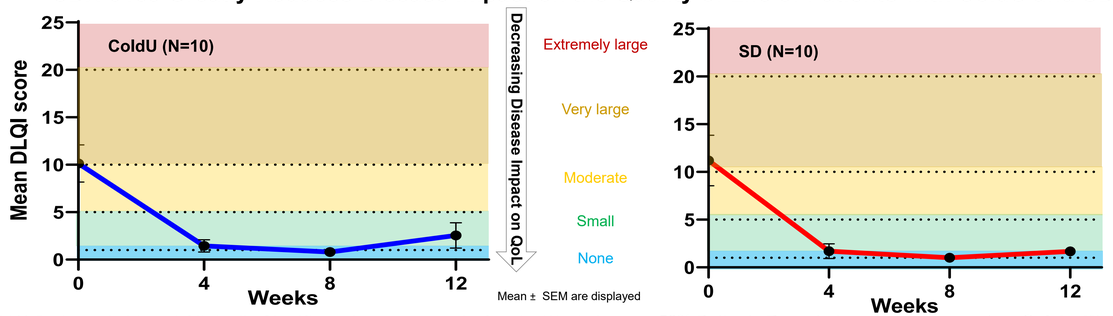
[1]Terhorst-Molawi et al, presented at EAACI 2021

## RESULTS

### A Single 3 mg/kg Dose of CDX-0159 Results in Rapid and Sustained Improvement in Urticaria Control and the QoL in ColdU and SD Patients




### CDX-0159 Greatly Reduces Disease Impact on the Quality of Life of Patients with ColdU and SD




**93% Patients Achieved Clinically Significant Improvement in QoL by Week 4**

| ≥4-point reduction† in DLQI from baseline * | Week4 | Week8 | Week12 |
|---|---|---|---|
| ColdU Patients % (n/ N) | 100% (6/6) | 100% (6/6) | 83% (5/6) |
| SD Patients % (n/ N) | 88% (7/8) | 86% (6/7) | 86% (6/7) |
| All Patients % (n/ N) | 93% (13/14) | 92% (12/13) | 85% (11/13) |

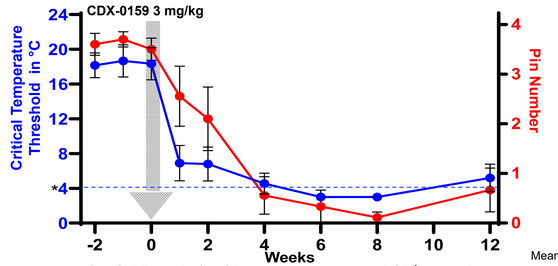
† MCID for DLQI is ≥4
*Only patients whose baseline score was ≥4 were included
† All responses provided for each week were included

**58% Patients Reported no Disease Impact on QoL by Week 4**

| DLQI score =0-1† | Week4 | Week8 | Week12 |
|---|---|---|---|
| ColdU Patients % (n/ N) | 56% (5/9) | 70% (7/10) | 67% (6/9) |
| SD Patients % (n/ N) | 60% (6/10) | 67% (6/9) | 44% (4/9) |
| All Patients % (n/ N) | 58% (11/19) | 68% (13/19) | 56% (10/18) |

### Rapid and Durable Improvement in Provocation Tests with a 95% Complete Response and Profound Tryptase Reduction

**TempTest and FricTest Over Time in ColdU and SD Patients**

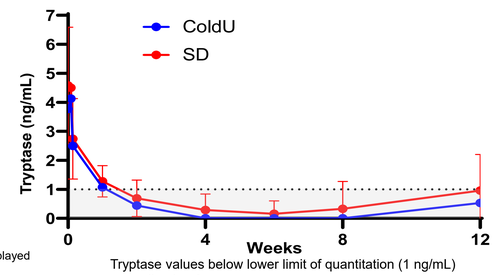



10/10 ColdU and 9/10 SD patients experienced CR‡ on study.

*Critical temperature threshold values below 4°C (negative test) assigned a value of 3°C
‡CR=complete response, negative provocation test, ≤4°C or 0 pins.

Mean ± SEM are displayed

**CDX-0159 Treatment Markedly Depletes Serum Tryptase**




Tryptase values below lower limit of quantitation (1 ng/mL) normalized to 0.

**100% Patients Achieved "Well Controlled" Status (UCT≥12) by Week 8**

| UCT Scores ≥ 12 | Predose | Week4 | Week8 | Week12 |
|---|---|---|---|---|
| ColdU Patients % (n/ N) | 10% (1/10) | 90% (9/10) | 100% (10/10) | 80% (8/10) |
| SD Patients % (n/ N) | 0% (0/10) | 70% (7/10) | 100% (9/9) | 78% (7/9) |
| All Patients % (n/ N) | 5% (1/20) | 80% (16/20) | 100% (19/19) | 79% (15/19) |

**63% Patients Achieved "Complete Control" Status (UCT=16) by Week 8**

| UCT Score = 16 | Predose | Week4 | Week8 | Week12 |
|---|---|---|---|---|
| ColdU Patients % (n/ N) | 0% (0/10) | 50% (5/10) | 70% (7/10) | 40% (4/10) |
| SD Patients % (n/ N) | 0% (0/10) | 20% (2/10) | 56% (5/9) | 33% (3/9) |
| All Patients % (n/ N) | 0% (0/10) | 35% (7/20) | 63% (12/19) | 37% (7/19) |

### CDX-0159 Was Generally Safe and Well Tolerated

- CDX-0159 was generally well tolerated in patients with CIndU (ColdU and SD).
- The most common AEs were hair color changes (15/21 [71%]), infusion reactions (9/21 [43%]), and taste disorders (8/21 [38%]). Most AEs were mild.
- Hair color changes improved upon longer observation period.
- Infusion reactions were mostly mild, generally manifested as hives and itching and resolved spontaneously. A single severe infusion reaction occurred that was not attributed to MC activation.
- Taste disorders were selective and transient.
- Hematology parameters generally remained within the normal ranges. Mild, transient, and asymptomatic decreases in hemoglobin and WBC parameters were noted.

## SUMMARY AND DISCUSSION

- In patients with CIndU refractory to antihistamines, a single dose of CDX-0159 (3 mg/kg) resulted in rapid, profound, and durable responses in 100% of patients with 95% achieving complete response, as previously reported[1].
- We now demonstrate that this noteworthy response to provocation testing was also accompanied by markedly improved urticaria control and QoL.
  - Rapid improvement in the UCT score was noted within 4 weeks and sustained to Week 12.
  - 80% and 100% patients achieved "well controlled" status (UCT≥12) by Week 4 and 8, respectively.
  - 63% of patients achieved "complete control" status (UCT=16) by Week 8.
  - 93% and 92% patients achieved ≥4-point reduction (minimal clinically important difference [MCID]) in DLQI by Week 4 and 8, respectively.
  - 58% and 68% patients achieved DLQI score of 0-1 (no impact of disease on quality of life) by Week 4 and 8 respectively.
- Rapid and durable improvement in provocation response mirrors reduction in tryptase.
- CDX-0159 was generally well tolerated. There was no evidence of clinically significant decreases in hematology parameters. Hair color changes and taste disorders are consistent with inhibiting KIT signaling in other cell types and are expected to be fully reversible.
- CDX-0159 has significant potential as a therapy for CIndU, and other mast cell-related diseases.