The anti-KIT antibody, CDX-0159, reduces disease activity and tryptase levels in patients with chronic inducible urticaria

**BACKGROUND**

- Chronic inducible urticaria (CIndU) is characterized by mast cell (MC)-driven events and clinical lab tests.
- MCs require activation of their KIT receptors by stem cell factor (SCF), proliferation, and differentiation. MC burden is correlated with circulating tryptase, a protease secreted specifically by MCs.
- CDX-0159 is a monoclonal anti-KIT antibody that is engineered to selectively inhibit SCF-dependent KIT activation.

**STUDY DESIGN AND METHODS**

- **Primary objective:** to evaluate safety/tolerability of CDX-0159 (adverse events and clinical lab tests).
- **Secondary objectives:** include evaluating the effect of CDX-0159 on clinical activity and serum tryptase.
- **Activity endpoints:** include provocation test (TempTest/ColdU; FricTest/SD), physician’s global assessment (Phys-GA), and patient’s global assessment (Pat-GA) of disease severity.

**STUDY STATUS**

- **Study is ongoing:** date cut as of 11.La2021.
- **20 patients** received study drug and are included in the safety analysis. 19 patients received full dose and are included in the analysis. 14 patients completed the 12-week observation period; 5 are ongoing.

**DEMOGRAPHICS AND BASELINE DISEASE CHARACTERISTICS**

- **CDX-0159:** on an open-label, Phase 1b trial in patients with CIndU (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:** to evaluate safety/tolerability of CDX-0159 (adverse events and clinical lab tests).
- **Secondary objectives:** include evaluating the effect of CDX-0159 on clinical activity and serum tryptase.
- **Activity endpoints:** include provocation test (TempTest/ColdU; FricTest/SD), physician’s global assessment (Phys-GA), and patient’s global assessment (Pat-GA) of disease severity.
- **Mean ± SD:** are displayed for provocation tests, biomarkers, and hematological parameters.

**RESULTS**

- **CDX-0159** was generally well tolerated and patients with CIndU.
- The most common AEs were hair color changes (14/20 [70%]), injection reactions (9/20 [45%]), and local reactions (8/20 [40%]). Most AEs were mild.
- Hair color changes improved upon longer observation period.
- Injection reactions, generally manifested as hives and itching, resolved spontaneously. A single severe infusion reaction occurred that was not attributable to MC activation.
- Taste disorders were selective and transient.
- Hematological parameters generally remained within the normal ranges. Mild, transient, and asymptomatic decreases in hemoglobin and WBC parameters were noted.

**SUMMARY AND DISCUSSION**

- **A single dose of CDX-0159 (3 mg/kg) results in a rapid, profound, and durable depletion of skin MCs and serum tryptase.**
- **Complete response was achieved in 95% patients (100% in ColdU and 89% in SD patients) including in patients who had received prior omalizumab and was sustained for a median duration of 57+ days in ColdU and 57 days in SD patients who completed the 12 week follow-up period.**
- **Improved disease activity assessed by Phys-GA and Pat-GA is consistent with the complete response per the provocation test.**
- **A single 3 mg/kg CDX-0159 dose resulted in a rapid, marked, and durable depletion of skin MCs and serum tryptase.**
  - The kinetics of skin MC and serum tryptase depletion mirror clinical activity.
  - Serum tryptase level is a robust pharmacodynamic biomarker for assessing MC burden and clinical activity in patients with CIndU.
- **CDX-0159** was generally well tolerated. There was no evidence of clinically significant decreases in hematological parameters. Hair color changes and taste disorders are consistent with inhibiting KIT signaling in other cell types and are expected to be transient.

**CDX-0159 demonstrates favorable safety and tolerability.**

**CDX-0159 was generally well tolerated in patients with CIndU.**

**Tryptase values below LLoQ normalized to 0.**

**Critical temperature thresholds values below 4°C (negative test) assigned a value of 3°C.**

**CDX-0159 demonstrated unpreceded MC depletion with a favorable safety profile, providing significant potential as a therapy for CIndU and opening opportunities for the evaluation of MC involvement across many diseases.**