PHASE 1B/2A SPOTLIGHT STUDY IN CHRONIC INDUCIBLE URTICARIA*
Open Label, Dose Escalation Study of Briquilimab Subcutaneously Administered

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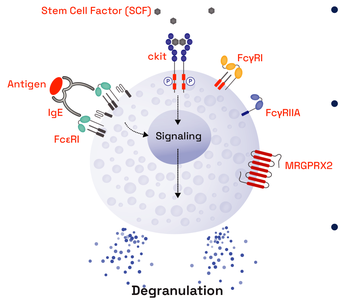
*Protocol Title: A Phase 1b/2a, Dose Escalation Trial of Safety, Pharmacokinetic/Pharmacodynamic and Preliminary Clinical Activity of Briquilimab in Adult Patients with Chronic Inducible Urticaria (CIndU) Who Remain Symptomatic Despite Treatment with H1-Antihistamines

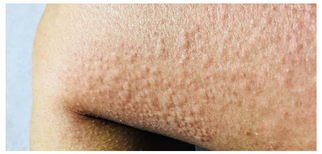
BACKGROUND

Mast cells (MCs) are key drivers of the inflammatory response in a number of allergic and dermatologic diseases[1]



- MCs are potent drivers of inflammation in skin, lungs and gut
- Activated MCs release pro-inflammatory compounds that drive diseases such as CSU, & CIndU
- Current approved therapies targeting mast cell driven diseases have limited efficacy and limited durability of response

Chronic inducible urticaria (CIndU), a subtype of chronic urticaria, is an inflammatory disease driven by the activation of skin mast cells

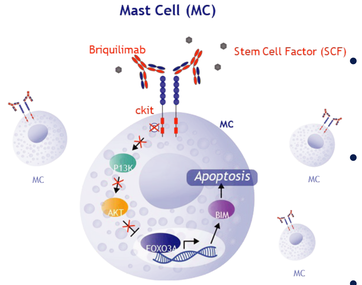


- Devastating disease characterized by severe itching, hives/wheals, inflammation, and/or angioedema **occurring for >6 weeks**
- Patients with CIndU develop symptoms in response to specific stimuli (e.g., cold, heat, pressure)
- Patients suffer numerous physical/ psychological symptoms that **significantly impair quality of life** (sleep/work disturbances, depression)
- The two most common forms of CIndU are **symptomatic dermographism** (SD) and **cold contact urticaria** (ColdU)

References: 1. Theoharides et al. *N Engl J Med.* (2015) **2.** Moller C et al. *Blood* (2005) **3.** Hundley TR et al. *Blood* (2004) **4.** Arnold JN et al. *Annu Rev Immunol* (2007) **5.** Jasper internal data (Phase 1a, healthy volunteer study) **6.** Maurer et al, GA²LEN Global Urticaria Forum; Berlin, December 6, 2022

BRIQUILIMAB

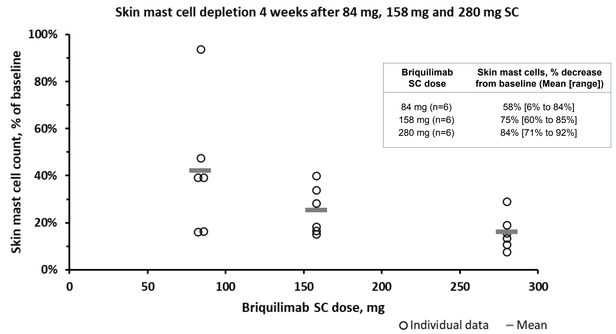
Mechanism of Action[2-4]



Briquilimab-Mediated Mast Cell Apoptosis

- SCF signaling through c-Kit prevents mast cells apoptosis via the Bim-mediated pathway[1]
- Blockade of c-Kit signaling on MCs leads to apoptosis and phagocytic clearance[2]
- Depletion of cutaneous MCs are C_{max} dependent, whereas unwanted effects appear AUC driven
- Once MC are depleted, unwanted effects minimized by intermittent dosing

Single subcutaneous injection of briquilimab significantly depletes human skin MCs[5,6]



Briquilimab SC dose	Skin mast cells, % decrease from baseline (Mean [range])
84 mg (n=6)	58% [6% to 84%]
158 mg (n=6)	75% [60% to 85%]
280 mg (n=6)	84% [71% to 92%]

- SC dose above 80mg, potently depletes skin MCs
- Dose dependent MC depletion
- MC depletion by day 7, with durable response lasting at least 29 days
- MCs take at least 3 months to recover, potentially leading to durable disease control[2]

BRIQUILIMAB PHASE 1B/2A SPOTLIGHT STUDY IN PATIENTS WITH CHRONIC INDUCIBLE SPONTANEOUS URTICARIA (CINDU)

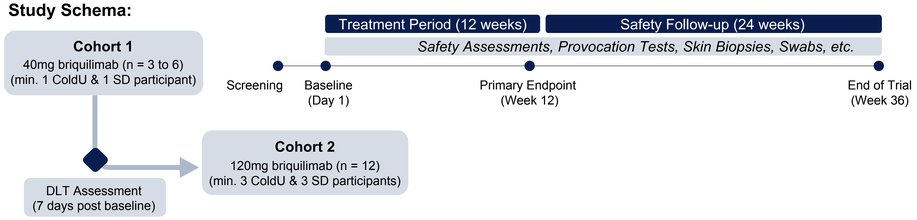
Open label, Dose Escalation Study of Briquilimab Subcutaneously Administered

Screening/Eligibility
- ColdU or SD diagnosis ≥ 3 mos.
- H1-antihistamine-failed
- 18+ years

Study Operations
- Countries: 1 (Germany)
- Sites: 4
- Subjects: 15 - 18

Key Assessments
- ✓ **Efficacy:** TempTest® & FricTest®
- ✓ **Mast Cell Depletion & Recovery:** Serum Tryptase, Skin Biopsies, Buccal & Nasal Swabs
- ✓ **Safety:** TEAEs, SAEs

Study Schema:



Status: Patient enrollment ongoing at sites in the EU

Study Goal: evaluate the safety, tolerability, and preliminary efficacy of a single SC dose of briquilimab in patients with Cold Urticaria (ColdU) or Symptomatic Dermographism (SD)

Key Objectives: Single SC dose of briquilimab at two dose levels, 40mg and 120mg, to study the effects of:
- Mast cell depletion and disease symptom/disease modifications
- Briquilimab drug clearance
- Time to return of disease symptoms
- Briquilimab on other c-Kit expressing cell lineages

Our thanks to the patients, site staff and investigators of the Spotlight trial

Briquilimab is an investigational product and not approved for any indication.