The BEACON Study: A Phase 1b/2a, Dose Escalation Study of Safety, Pharmacokinetic/Pharmacodynamic and Preliminary Clinical Activity of the c-Kit Mab Briquilimab in Adults with symptomatic Chronic Spontaneous Urticaria (CSU)

NCT06162728

Authors: Marcus Maurer[1,2], Ed Tucker[3], Jinwei Yuan[3], Daniel Adelman[3], David Ku[3], Annette Marcantonio[3], Patricia Carlos[3], Wendy Pang[3], Thomas Casale[4]

1 Institute of Allergology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany

2 Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany

3 Jasper Therapeutics

4 Division of Allergy and Immunology, University of South Florida Health Morsani College of Medicine, Tampa, Fla

Background: Chronic spontaneous urticaria (CSU) is defined by pruritic wheals (hives) and/or angioedema for more than six weeks without an identified trigger.

Oral H1-antihistamines are the first-line recommended treatment for CSU, but about 40-50% of patients do not respond. Omalizumab is an add-on therapy, but less than 50% of patients have complete symptom resolution. Thus, there is clearly a significant need for new treatment options for CSU patients.

Given the significant role of MCs in CSU, the development of novel therapies that deplete skin MCs offers a potential new treatment modality.

Briquilimab is an aglycosylated monoclonal antibody that binds to the cell-surface receptor c-Kit, also known as CD117, thereby inhibiting binding of stem cell factor and signaling through the receptor, initiating MC apoptosis. Therefore, briquilimab (administered subcutaneously) with a half-life of approximately 9 days, when dosed at intervals of 8 weeks or 12 weeks, has therapeutic potential for treatment-refractory CSU patients while avoiding unnecessary exposure to other C-Kit expressing tissues. We postulate that once MCs are depleted, the perpetrators of CSU are removed and subsequent dosing can be aligned to skin MC recovery which generally takes 12-18 weeks.

Trial Design:

The BEACON study is a randomized phase 1b/2a, multiple ascending dose trial divided into 3 parts to assess the safety, tolerability, and preliminary efficacy of different dose levels of briquilimab administered subcutaneously in adult participants with CSU, who remain symptomatic despite treatment with antihistamines and omalizumab or who cannot tolerate omalizumab. The trial will explore up to 6 ascending dose levels (Cohorts 1, 2, 3, 4, 5 and 6) as shown in Figure 1. The trial will enroll approximately 40 patients from US and Germany.

Endpoints:

Safety and tolerability: Review of laboratory date (hematology, clinical chemistry, urinalysis), physical examinations, vital signs, ECG, reports of treatment emergent adverse events (TEAEs)

Pharmacokinetics: Cmax, tmax and AUClast

Preliminary Efficacy: Change from baseline to Week 12 in Urticaria Activity Score (UAS7), Hives Severity Score (HSS7), Itch Severity Score (ISS7) and Urticaria Control Test (UCT)

Pharmacodynamics: Serum tryptase, anti-drug antibody assessments

Conclusions: This controlled multi-ascending dose trial will provide important assessments into the safety, tolerability and initial evidence of efficacy in patients administered briquilimab with treatment-refractory CSU and inform potential future clinical trials on optimal dosing and dosing schedules.

Figure 1: Trial Design