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Phase 1b/2a BEACON Study in Chronic Spontaneous Urticaria

Randomized, Double-Blind, Placebo-Controlled, Multiple Ascending Dose Study of Briquilimab Subcutaneously Administered

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1 June 2024

Disclosure of Conflict of Interest

Marcus Maurer is or recently was a speaker and/or advisor for and/or has received research funding from Allakos, Alexion, Alvotech, Almirall, Amgen, Aquestive, argenX, AstraZeneca, Celldex, Celltrion, Clinuvel, Escient, Evommune, Excellergy, GSK, Incyte, Jasper, Kashiv, Kyowa Kirin, Leo Pharma, Lilly, Menarini, Mitsubishi Tanabe Pharma, Moxie, Noucor, Novartis, Orion Biotechnology, Resoncance Medicine, Sanofi/Regeneron, Santa Ana Bio, Septerna, Servier, Third HarmonicBio, ValenzaBio, Vitalli Bio, Yuhan Corporation, Zurabio.

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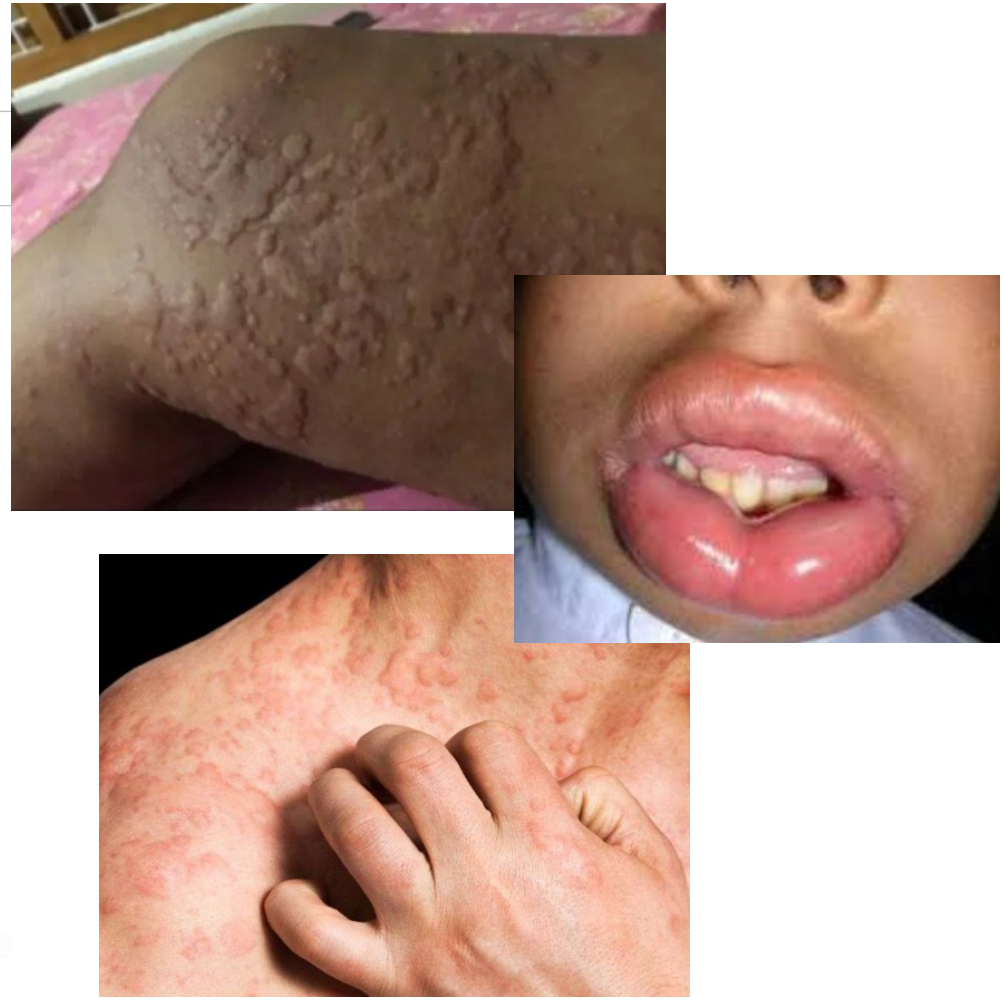
1 Mast Cells

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 suffer numerous physical/psychological symptoms that significantly impair quality of life (sleep/work disturbances, depression)
- One of most prevalent dermatologic conditions affecting ~1% of global population, that commonly persists for 5+ years[1,2]

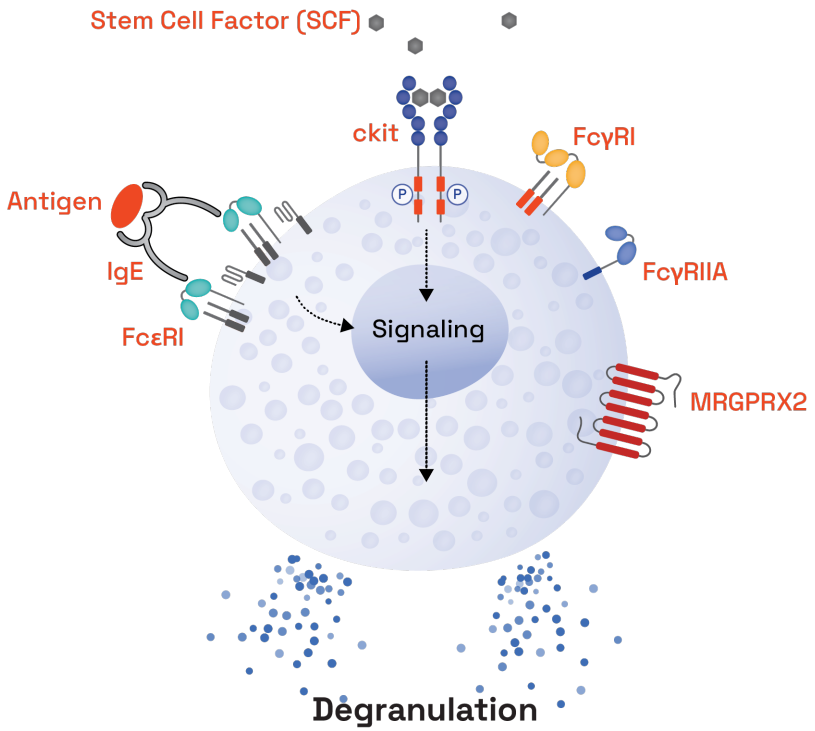


1 Kolkhir P, et al. Nature Reviews. 2022; 2 Saini S, Kaplan A. JACI Practice. 2018.

1 Mast Cells

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

- 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

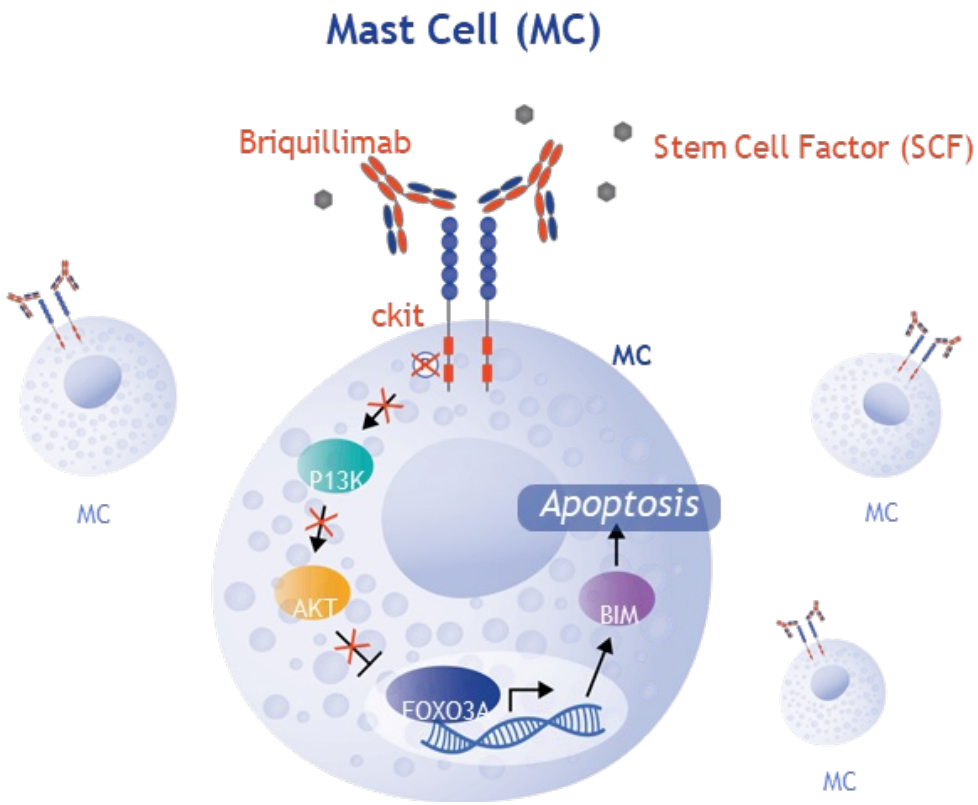


Theoharides et al. N Engl J Med. (2015)

1 Mast Cells

Depletion of mast cells by anti-c-Kit monoclonal antibody blockade is a novel approach to treat urticarias

- 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]
- Partial c-Kit inhibition blunts mast cell activation
- Depletion of cutaneous MCs are Cmax dependent, whereas unwanted effects appear AUC driven.
- Once MC are depleted, unwanted effects minimized by intermittent dosing.



Briquilimab-Mediated Mast Cell Apoptosis

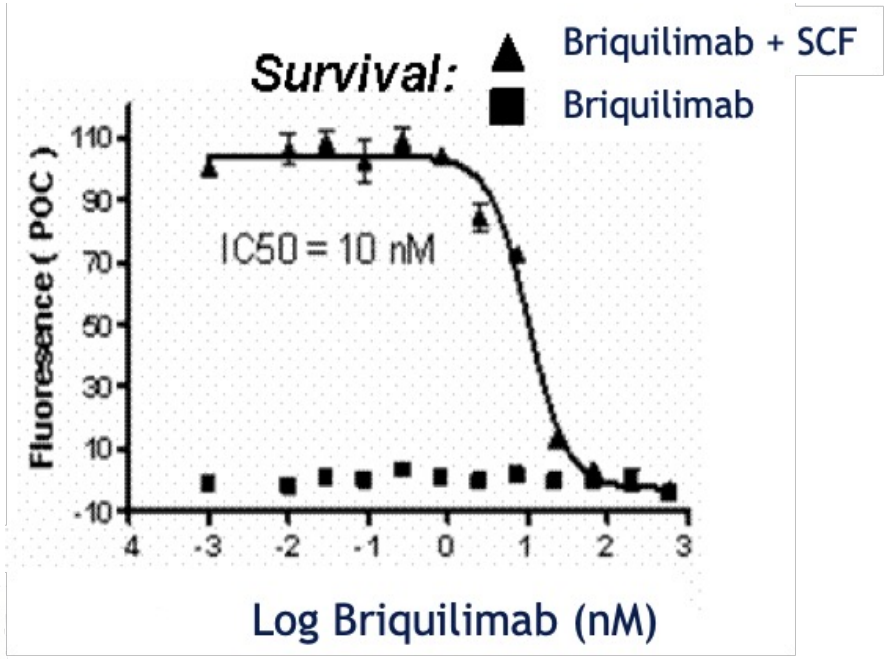
1 Moller C et al. Blood (2005); 2 Hundley TR et al. Blood (2004); . Arnold JN et al. Annu Rev Immunol (2007)

2 Briquilimab

Briquilimab blocks c-Kit signaling leading to durable mast cell depletion

- Briquilimab is an aglycosylated IgG1 anti c-Kit antibody with high affinity to c-Kit (Kd <5pm)
- Briquilimab blocks c-Kit signaling by blocking the SCF ligand binding site on the receptor and triggering apoptosis
- Mast cell depletion occurs within hours to days

Mast cell survival assay



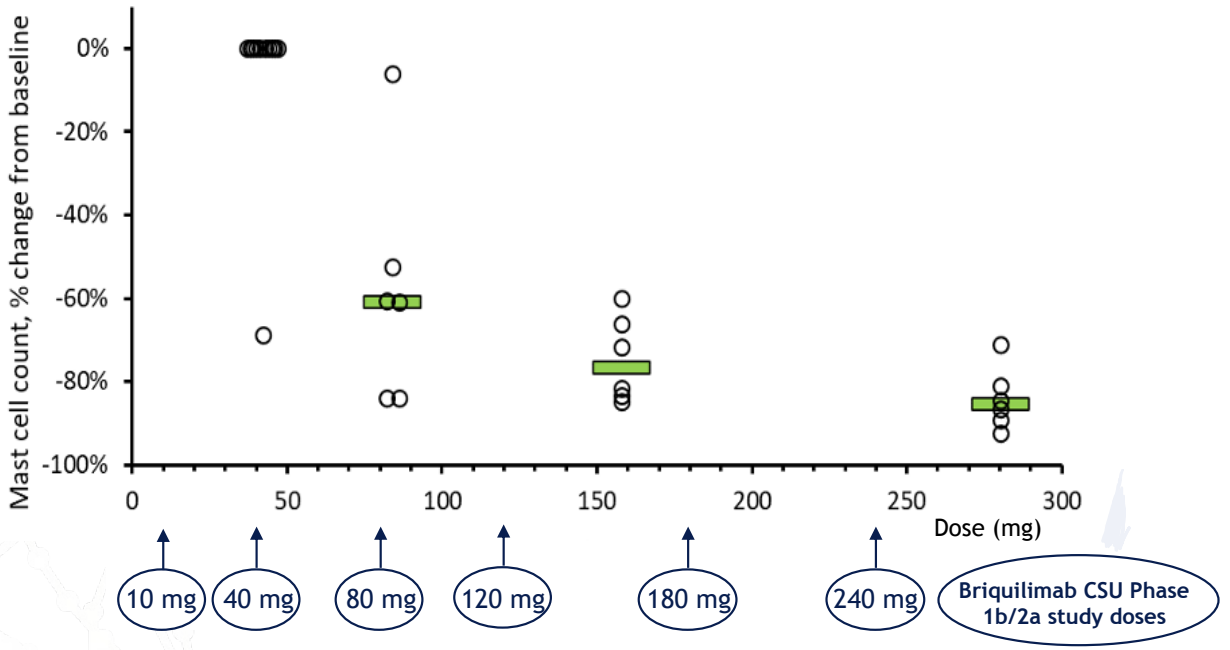
Jasper internal data

2 Briquilimab

Single subcutaneous injection of briquilimab significantly depletes human skin MCs

- 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
- MC take at least 3 months to recover, potentially leading to durable disease control[2]

Skin mast cell depletion 4 weeks after single dose (≥42 mg)[1]
Briquilimab Healthy Volunteer Phase 1 Subcutaneous Study



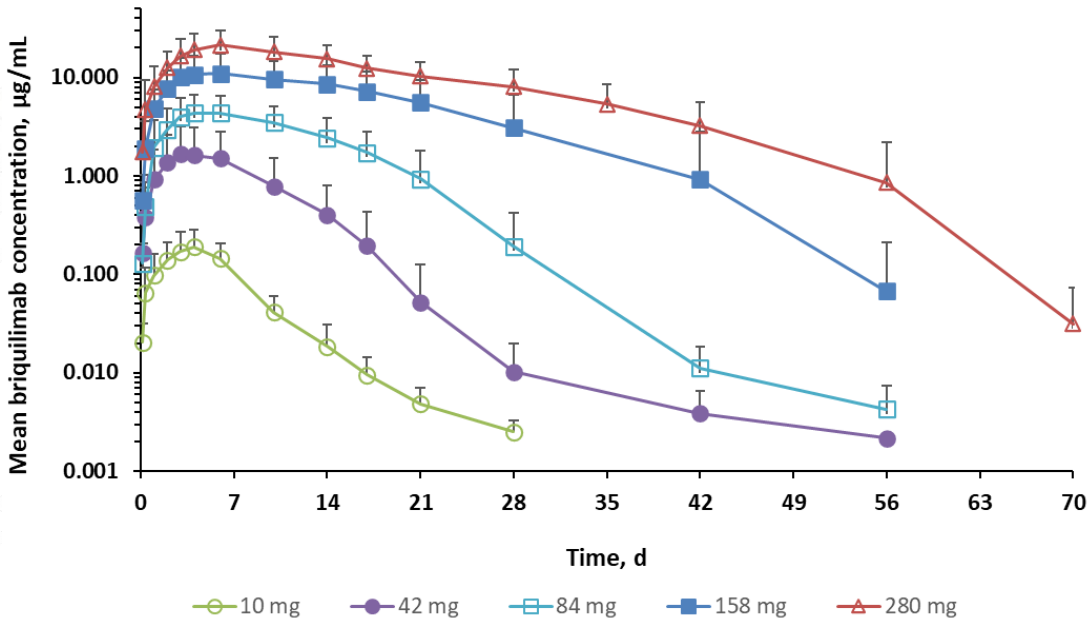
1 Jasper internal data (Phase 1a, healthy volunteer study). Skin biopsies were used to count mast cells; 2 Maurer et al, GA²LEN Global Urticaria Forum – Berlin, December 6, 2022

2 Briquilimab

Briquilimab pharmacokinetics may enable optimal biologic dosing

- Briquilimab is designed to minimize unwanted c-Kit-related effects
- Half life = 9 days
- Low frequency of ADAs and do not appear to affect PK
- Drug elimination profile is favorable for minimizing off target effects

Pharmacokinetics (≥10 mg)[1]
Briquilimab Healthy Volunteer Phase 1 Subcutaneous Study



1 Jasper internal data (Phase 1a, healthy volunteer study)

3 Trial Design

Briquilimab Phase 1b/2a BEACON study in patients with Chronic Spontaneous Urticaria (CSU)

- Study Goal:
  - Identify the optimal therapeutic doses & dosing frequency of SC briquilimab to inform future registrational trials
- Key Objectives:
  - Multiple briquilimab dose levels, and intervals ranging from 4 to 12 weeks 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

Status: Patient enrollment ongoing at sites in US and EU

3 Trial Design

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Screening/Eligibility

- CSU diagnosis ≥ 6 mos.
- UAS7 ≥ 16
- 18+ years

- H1-antihistamine-failed
- Inadequate response to omalizumab

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Study Operations

- **US Lead: Tom Casale, MD**
- **EU Lead: Marcus Maurer, MD**

Key Assessments

- ✓ **Disease Scores:** UAS7, UCT
- ✓ **Mast Cell Depletion & Recovery:** Serum Tryptase, Skin Biopsies
- ✓ **Safety:** TEAEs, SAEs

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	Patients (Randomization)	Dose (Frequency)	Cohorts	Key Assessments & Follow Up
Part 1 Open Label (n=6)	3+3	10 mg	Dose W0, 4, 12, 20	Day 8 - Safety Assessment Week 12 - UAS7 Efficacy Assessment 24 week - Follow Up
	3+3	40 mg	Dose W0, 4, 12, 20	

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	3+3	40 mg	Dose W0, 4, 12, 20	
Part 2 Double-Blind Placebo-Controlled (n=28)	n=8 (3:1)	80 mg (Q8W)	Dose W0, 8, 16, 24	Day 8 - Safety Assessment Week 12 - UAS7 Efficacy Assessment* 24 week - Follow Up
	n=6 (2:1)	120 mg (Q8W)	Dose W0, 8, 16, 24	
	n=6 (2:1)	120 mg (Q12W)	Dose W0, 12, 24	
	n=8 (3:1)	180 mg (Q12W)	Dose W0, 12, 24	

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Part 3 Double-Blind Placebo-Controlled (n=4)	n=4 (3:1)	240 mg	Single Dose	Day 8 - Safety Assessment Week 12 - UAS7 Efficacy Assessment* 36 week - Follow Up

4 Summary

- Briquilimab design and characteristics offers a new approach to treatment of MC diseases
- Beacon study is enrolling to assess an optimal biologic dosing schedule
  - Takes advantage of the MC recovery time (over 12 weeks)
  - Potential to deplete MCs, with durable efficacy and reduced undesirable effects
  - Beacon study results planned for 2H 2024
- CIndU study (Spotlight) recruiting – study design poster #D3.245 at EAACI 2024
- Broader therapeutic application in additional MC-mediated diseases

4 Summary

Thank you to the patients and our Beacon investigators in the US and Germany!

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