Initial Results from Beacon, a Phase 1b/2a Dose Escalation Study of the anti-c-Kit Briquilimab Antibody in Adults with Chronic Spontaneous Urticaria

Poster #L24

Thomas Casale[1], Edwin Tucker[2], Jinwei Yuan[2], Daniel Adelman[2], David Ku[2], Annette Marcantonio[2], Patricia Carlos[2], Sophia R. Majeed[2], Wendy W. Pang[2], Martin Metz[3]

[1]Internal Medicine, Morsani College of Medicine, University of South Florida, Tampa, FL, USA; [2]Jasper Therapeutics, Redwood City, CA, USA; [3]Institute of Allergology, Charité-Universitätsmedizin Berlin, Germany

Background

- Chronic spontaneous urticaria (CSU) is a mast-cell driven, recurring inflammatory skin condition lasting ≥6 weeks, characterized by itchy wheals (hives), angioedema, or both
- The interaction of the c-Kit (CD117) receptor with its ligand stem cell factor (SCF) is an important regulator of mast cell function and survival, making it a potential therapeutic target to remove the underlying source of the inflammatory response in CSU
- Briquilimab is a humanized, aglycosylated, anti-c-Kit monoclonal antibody that directly blocks the SCF binding site on the c-Kit receptor, leading to c-Kit/SCF signal inhibition and mast cell apoptosis
- We report the preliminary results from the Phase 1b/2a randomized, double blind, placebo-controlled multiple ascending dose clinical study of subcutaneous briquilimab in participants with CSU who are symptomatic despite H1 antihistamines and omalizumab

Methods

Phase 1b/2a BEACON Study Design

- Randomized, double-blind, placebo-controlled, multiple ascending dose study (NCT 06162728)

Key eligibility criteria

- CSU diagnosis ≥ 6 mos.
- UAS7 ≥ 16
- 18+ years
- H1-antihistamine-failed
- Inadequate response to omalizumab**

Key assessments

- *Disease scores*: UAS7, UCT
- *Safety*: TEAEs, SAEs
- Pharmacokinetics
- *Mast cell depletion & recovery*: Serum tryptase, Skin biopsies

	Dose	Participants (randomization)	Schedule
Open label (n = 6)	10 mg 40 mg	n = 3+3 n = 3+3	Weeks 0, 4, 12, 20
Double-blind placebo-controlled (n = 71)	80 mg	n = 8 (3:1)	Q8W
	120 mg	n = 6 (2:1)	Q8W
		n = 6 (2:1)	Q12W
	180 mg	n = 10 (3:1)	Q8W
		n = 9 (3:1)	Q12W
	240 mg	n = 8* (3:1)	Single dose
	240 mg → 180 mg**	n = 8 (3:1)	Q8W
	240 mg**	n = 8 (3:1)	Q8W
	360 mg	n = 8* (3:1)	Single dose

Note: *Expanding 240 mg and 360 mg SD cohorts to 8 participants; **Enrolling omalizumab-naive participants with CSU; **UAS7** – urticaria activity score over 7 days; **UCT** – urticaria control test.

Results

Table 1. Baseline demographics and disease characteristics.

	10 mg / 40 mg (N = 6)	80 mg Q8W (N = 6)	120 mg pooled (N = 8)	180 mg pooled (N = 14)	240 mg (N = 3)	Pooled placebo (N = 12)
Age (years), median (range)	55 (31-63)	63 (22-77)	43 (23-82)	38 (18-73)	44 (29-64)	39 (26-60)
Female sex, n (%)	6 (100%)	3 (50%)	5 (63%)	7 (50%)	3 (100%)	10 (83%)
Weight (kg), median (range)	66 (55-93)	98 (77-129)	88 (63-122)	84 (64-131)	76 (67-84)	78 (66-110)
BMI, median (range)	25 (22-30)	34 (24-50)	29 (22-43)	31 (22-41)	27 (27-31)	27 (24-42)
UAS7 (0-42), mean (SD)	26.1 (9.5)	31.0 (7.9)	27.9 (8.6)	25.9 (7.8)	26.6 (10.9)	28.6 (9.4)
UCT (0-16), mean (SD)	3.6 (2.8)	3.3 (2.4)	3.7 (1.5)	4.4 (2.9)	3.7 (1.5)	3.7 (3.6)
Serum tryptase (ng/mL), mean (SD)	6.6 (1.4)	8.4 (2.6)	7.8 (5.1)	6.0 (3.2)	4.5 (1.0)	8.1 (4.7)

- As of the 31 January 2025 data cutoff date, 49 participants with moderate to severe CSU were enrolled across the 10 to 240 mg cohorts
- All participants were refractory or intolerant to omalizumab, representing a CSU population of highest unmet medical need

Results

Primary Efficacy Analysis

Table 2. Primary efficacy analysis of 80, 120 and 180 mg Q8W

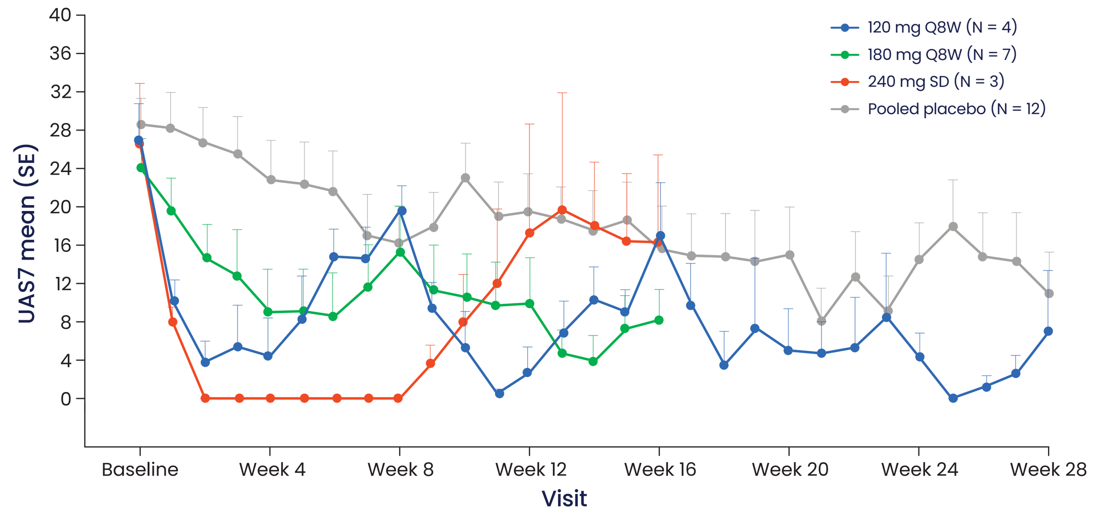
Week 12	80 mg Q8W (N = 6)	120 mg Q8W (N = 4)	180 mg Q8W (N = 7)	Pooled placebo (N = 12)
Mean (SE) UAS7	21.7 (7.2)	2.7 (2.7)	9.9 (4.8)	19.5 (4.0)
Mean (SE) UAS7 change from baseline	-9.3 (5.8)	-27.2 (3.9)	-15.1 (4.7)	-9.2 (3.6)
Complete response (CR) rate (UAS7 = 0)	17%	50%	43%	8%
Well controlled rate (UAS7 ≤ 6)	33%	75%	43%	8%

Note: 50% of participants in the pooled placebo group utilized rescue medications, including steroids, during the study; Last observation carried forward method (LOCF) was used for data imputation.

- 75% WC disease observed at 12 Weeks - 4 weeks post second dose

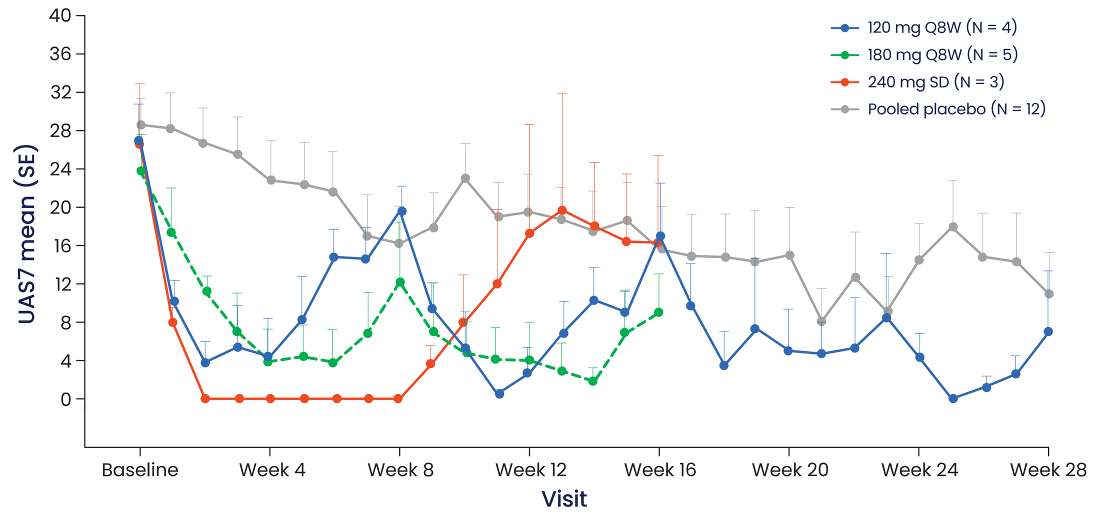
Figure 1. Dose dependent UAS7 reductions observed over 28-week treatment period.

A. Mean UAS7 score over time.



- Deeper UAS7 reductions observed in subsequent doses

B. Sensitivity analysis.



Note: 50% of participants in the pooled placebo group utilized rescue medications, including steroids, during the study; **SE** – standard error.

- A sensitivity analysis was conducted to evaluate dose-dependent responses excluding participants with potentially non-mast-cell-mediated chronic urticaria
- 2 participants in the 180 mg Q8W cohort with typical PK and tryptase reductions below LLOQ by 1-week post dose, did not have an appreciable change in UAS7 score, suggestive of non-mast cell mediated urticarial disease

Table 3. Primary efficacy analysis of 120 and 180 mg Q12W

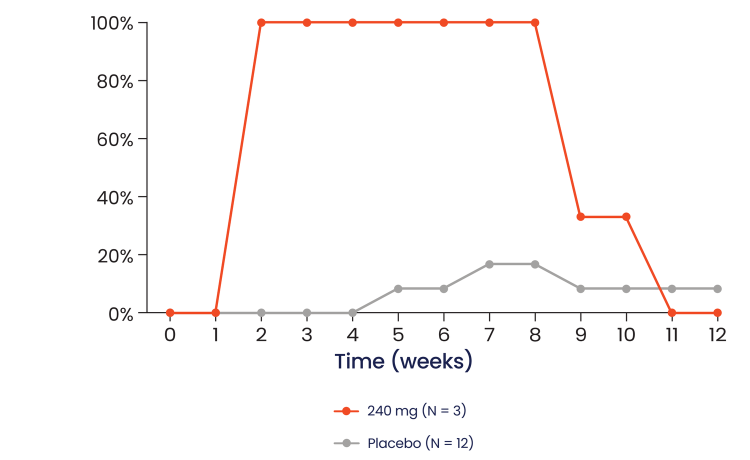
Week 16	120 mg Q12W (N = 4)	180 mg Q12W (N = 7)	Pooled placebo (N = 12)
Mean (SE) UAS7 score	0.5 (0.5)	7.2 (4.9)	15.6 (4.5)
Mean (SE) UAS7 change from baseline	-29.8 (6.9)	-21.7 (6.5)	-13 (3.2)
Complete response rate (UAS7 = 0)	50%	57%	17%
Well controlled rate (UAS7 ≤ 6)	75%	57%	33%

Note: 50% of participants in the pooled placebo group utilized rescue medications, including steroids, during the study; Last observation carried forward method (LOCF) was applied for missing data; Median time to first dose CR < 3 weeks (pooled 120 mg, 180 mg).

- 75% WC disease observed at 16 Weeks - 4 weeks post second dose

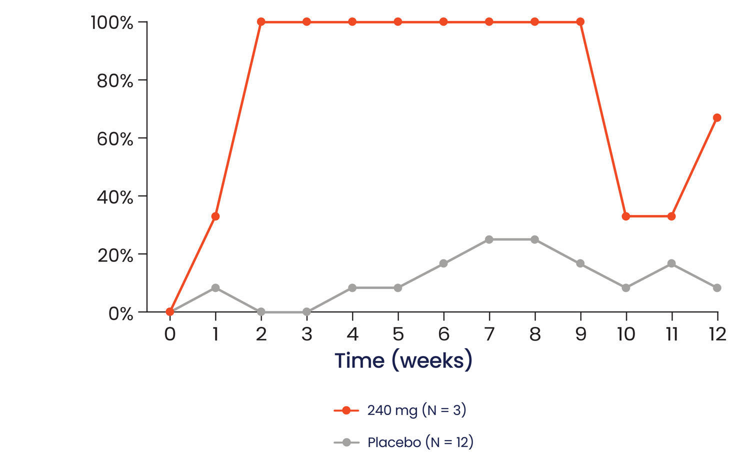
Figure 2. 240 mg single dose complete response and well controlled.

A. 240 mg complete response weeks 1-12 (UAS7 = 0).



- Mean baseline UAS7 = 26.6, mean Week 2 UAS7 = 0

B. 240 mg well controlled weeks 1-12 (UAS7 ≤ 6).

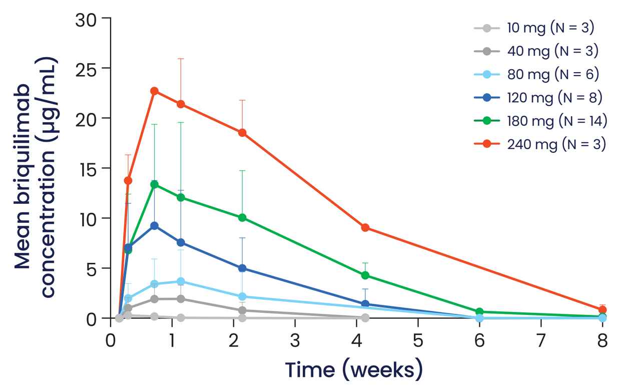


Acknowledgments

We thank all the participating investigators, study participants and their families.

Briquilimab Pharmacokinetics and Pharmacodynamics

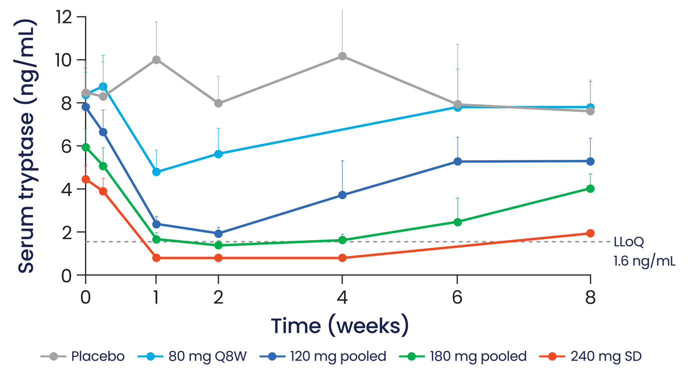
Figure 3. Briquilimab demonstrates rapid T_{max} and high C_{max} consistent with early onset of clinical response in participants with CSU.



- Preliminary PK data in participants with CSU indicates briquilimab PK is comparable to historical data in healthy volunteers
- 240 mg briquilimab SC T_{max} is 4-7 days with a half-life of approximately 9 days

Note: Plot depicts mean (standard deviation) briquilimab concentration over time; Briquilimab exhibits predictable clearance with no meaningful drug accumulation anticipated at doses up to 240 mg every 8 weeks.

Figure 4. Briquilimab demonstrated dose dependent reductions in serum tryptase.



- Reduction below lower limit of quantification (LLOQ) in all 240 mg dose participants and in 57% of participants at 180 mg dose by Week 2

Note: Plot depicts mean (standard deviation) serum tryptase concentration over time; *All values below LLOQ (1.6 ng/ml) are represented as 50% of LLOQ (0.8 ng/ml).

Summary of Adverse Events

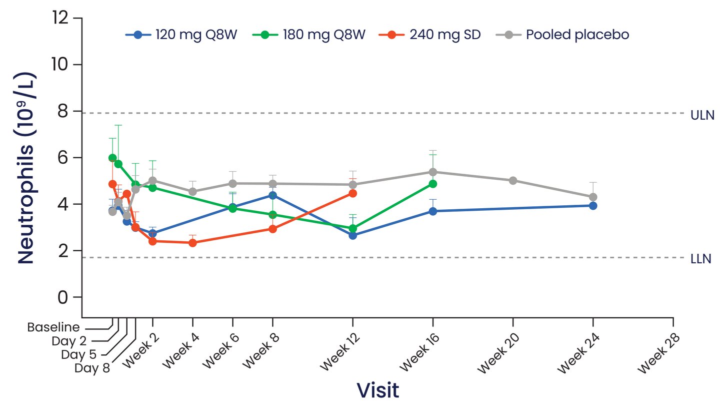
Table 4. Briquilimab demonstrated a favorable safety profile.

Number of participants with:	Pooled Briquilimab N = 37, n (%)	Pooled placebo N = 12, n (%)
Any DLT	0 (0)	0 (0)
Any TEAE	27 (73.0)	8 (66.7)
Any treatment-related serious TEAE	1 (2.7)[1]	0 (0)
Any hypersensitivity	1 (2.7)[1]	0 (0)
Any anaphylaxis	0 (0)	0 (0)
Any TEAE leading to discontinuation of IP	1 (2.7)[1]	0 (0)
Adverse event ≥ Grade 3	1 (2.7)[2]	1 (8.3)[3]

Note: **1.** Single participant, 180 mg Q8W, CoFAR grade 2 hypersensitivity reaction; **2.** Single participant, 180 mg Q12W, CTCAE grade 3 AE: neutropenia, unrelated – prior history of idiopathic neutropenia, thrombocytopenia; **3.** Single participant, placebo, CTCAE grade 3 bronchitis.

- Most commonly reported AEs (≥5 participants): nasopharyngitis, fatigue, hair color change, taste changes
- 28-week exposure for 10 mg - 180 mg doses, 16-weeks for 240 mg dose as of 31Jan25 data cut

Figure 5. Neutrophil counts generally remained stable, with predictable reduction which subsequently resolved.



Note: **LLN** – lower limit of normal; **ULN** – upper limit of normal.

- No discontinuations or dose delays due to reductions in neutrophil counts

Table 5. Safety observations possibly related to c-Kit blockade were infrequent and generally limited to Grade 1 events.

Adverse event	Pooled briquilimab N = 37, n (%)	Pooled placebo N = 37, n (%)	CTCAE grade/comments
Hair color changes	4 (10.8)	1 (8.3)	• All reported as Grade 1 • 2 cases reported to be resolved/resolving • 1 at 80 mg, 1 at 120 mg, 2 at 180 mg and 0 at 240 mg
Skin discoloration	0 (0)	1 (8.3)	• No skin discoloration observed with patient exposure up to 28 weeks
Taste change / hypogeusia	6 (16.2)	0 (0.0)	• All mild, Grade 1 occurring on first dose, 2 recurrences (resolved) • Taste reductions: bitter, salt, umami • Resolved in 5 participants: median time to resolution of 31 days • 1 at 80 mg, 1 at 120 mg, 1 at 180 mg and 3 at 240 mg
Neutropenia / neutrophil count decreased	5 (13.5)	1 (8.3)	• All resolved while on therapy prior to subsequent dose • Grade 3 neutropenia in a single participant with prior history of idiopathic neutropenia and thrombocytopenia, resolved on therapy • Grade 1 neutropenia/neutrophil count decrease in 5 participants, all resolved on therapy • No associated fevers or infections • 0 at 80 mg, 2 at 120 mg, 2 at 180 mg and 1 at 240 mg

- Majority resolved during repeat dosing and none resulted in discontinuations or dose delays

Conclusions

- Subcutaneous briquilimab demonstrated an early T_{max} consistent with rapid onset of clinical response
  - Rapid decline in UAS7 as early as Week 1
  - Median time to first dose CR <3 weeks (pooled 120 mg, 180 mg)
- Dose dependent durability observed in complete responses and well-controlled disease
  - High CR rate observed, durable to 8 weeks, following single 240 mg administration
- Briquilimab was well tolerated and demonstrated a favorable safety profile
  - Predictable clearance may allow for restoration of signaling on other c-Kit expressing cells
- Dose optimization, based on PK/PD variables, may enhance efficacy and mitigate potential safety events
- Mast cell depletion, occurring after briquilimab administration, appears to be a promising therapeutic approach for mast cell mediated diseases, including CSU
- The data support advancing into a late-stage clinical development program for CSU

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