Briquilimab demonstrates rapid, clinically meaningful reduction in disease activity in adults with chronic spontaneous urticaria (CSU): Results from a Phase 1b/2a study

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Conflict of Interest Statement

Dr. Martin Metz has received honoraria as a speaker and/or advisor for AbbVie, Advanz, ALK-Abello, Allegria, Almirall, Amgen, Argenx, AstraZeneca, Astria, Attovia, Berlin-Chemie, Blueprint, Celldex, Celltrion, DeepApple, Escient, Galderma, GSK, Incyte, Jasper Therapeutics, Lilly, Novartis, Pfizer, Pharvaris, Regeneron, Sanofi, Santa Ana Bio, Septerna, Teva, Third Harmonic Bio and Vifor.

Background

- Chronic spontaneous urticaria (CSU) is a mast-cell driven, recurring inflammatory skin condition lasting ≥ 6 weeks, with itchy wheals (hives), angioedema, or both.
- c-Kit receptor signaling, driven stem cell factor (SCF), is an important regulator of mast cell survival, making it a potential therapeutic target for CSU.
- Briquilimab is a humanized, aglycosylated, anti-c-Kit antibody that directly blocks the SCF binding site on c-Kit, 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 moderate to severe CSU who are symptomatic despite H1 antihistamines and omalizumab.

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

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

Screening/Eligibility

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

Study Operations

- **US Lead: Tom Casale, MD**
- **EU Lead: Martin Metz, MD**
- ~30 sites in the US & EU

Key Assessments

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

	Dose	Patients (Randomization)	Schedule
Open Label (n=6)	10mg	n=3+3	Weeks 0, 4, 12, 20
	40mg	n=3+3	
Double-Blind Placebo-Controlled (n=71)	80mg	n=8 (3:1)	Q8W
	120mg	n=6 (2:1)	Q8W
		n=6 (2:1)	Q12W
	180mg	n=10 (3:1)	Q8W
		n=9 (3:1)	Q12W
	240mg	n=4* (3:1)	Single Dose
	240mg → 180mg**	n=8** (3:1)	Q8W
	240mg**	n=8** (3:1)	Q8W
	360mg	n=8* (3:1)	Single Dose

Note: *Expanding 240 mg and 360 mg SD cohorts to 8 participants each; **Enrolling omalizumab-naïve participants with CSU.

Briquilimab is an investigative drug and is not approved for any indication.

Baseline Demographics and Disease Characteristics

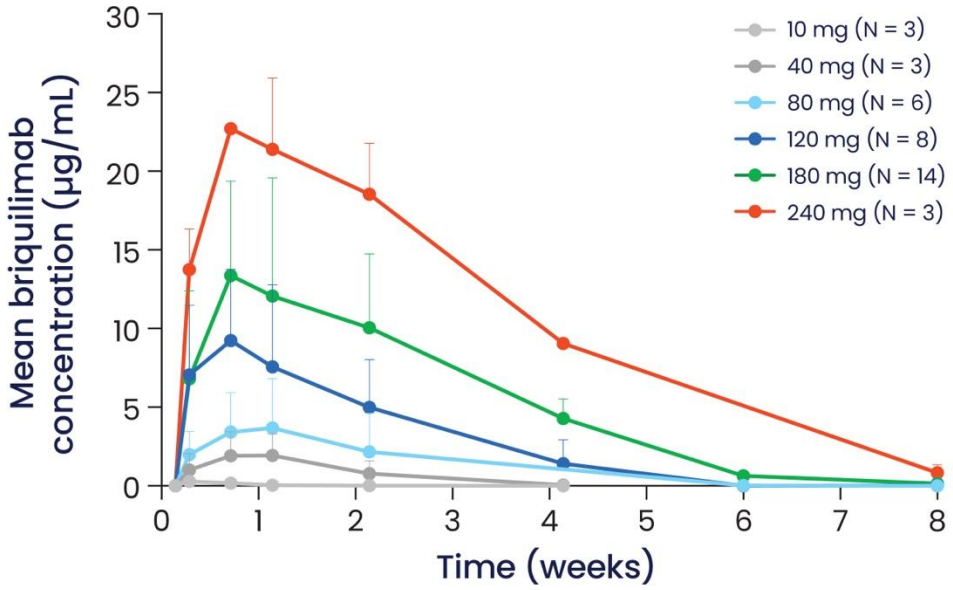
	Pooled Briquilimab (N=37)	Pooled placebo (N=12)
Age (years), median (range)	41 (18-82)	39 (26-60)
Female Sex, n (%)	24 (65%)	10 (83%)
BMI, median (range)	28 (22-50)	27 (24-42)
UAS7 (0-42), mean (SD)	27.3 (8.2)	28.6 (9.4)
ISS7 (0-21), mean (SD)	14.1 (3.8)	14.6 (4.7)
HSS7 (0-21), mean (SD)	13.2 (5.2)	14.0 (5.4)
UCT (0-16), mean (SD)	3.8 (2.3)	3.7 (3.6)
Serum tryptase (ng/mL), mean (SD)	6.7 (3.4)	8.1 (4.7)

- All participants were refractory or intolerant to omalizumab, representing a CSU population of highest unmet medical need.

Briquilimab Demonstrates Rapid T_{max} and High C_{max} and Rapid, Dose-dependent Reductions in Serum Tryptase

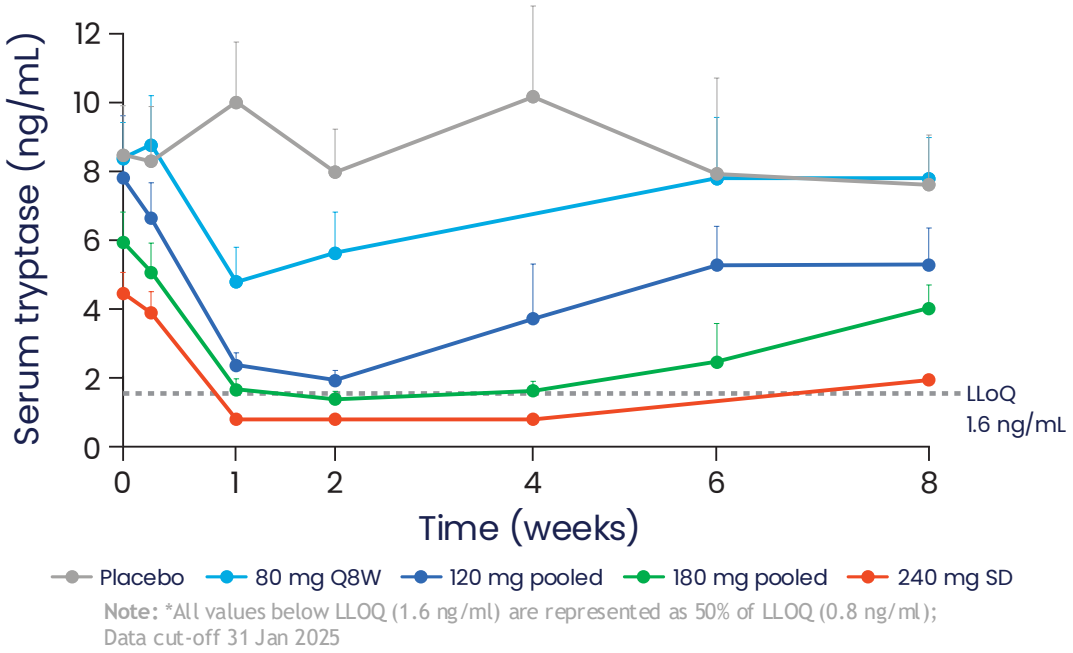
Consistent with Early Onset of Clinical Responses in CSU Patients

Briquilimab serum concentration over time in CSU patients following subcutaneous (SC) administration



- 240 mg briquilimab SC T_{max} is 4-7 days with a half-life of approximately 9 days

Serum Tryptase over time in CSU patients



Note: *All values below LLOQ (1.6 ng/ml) are represented as 50% of LLOQ (0.8 ng/ml); Data cut-off 31 Jan 2025

- Reduction below LLOQ in all 240 mg participants and in 57% of 180 mg participants by Week 2

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Primary Efficacy Analysis of 80, 120 and 180 mg Q8W Cohorts

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

Resolution of hives and itch, consistent with briquilimab-mediated mast cell depletion

Week 12	80 mg Q8W (N=6)	120 mg Q8W (N=4)	180 mg Q8W (N=7)	Pooled placebo (N=12)[1]
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)
Mean (SE) ISS7 change from baseline	-4.8 (2.7)	-13.3 (0.9)	-8.1 (2.4)	-4.8 (1.8)
Mean (SE) HSS7 change from baseline	-4.5 (3.1)	-13.8 (3.1)	-7.0 (2.4)	-4.4 (1.9)
Complete response (CR) rate[2, 3]	17%	50%	43%	8%
Well controlled rate[3]	33%	75%	43%	8%

1. 50% of participants in the pooled placebo group utilized rescue medications, including steroids during the study.
2. Median time to first dose CR <3 weeks (pooled 120mg, 180mg)
3. Last observation carried forward (LOCF) method was applied for missing data.

Primary Efficacy Analysis of 120 and 180 mg Q12W Cohorts

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

Resolution of hives and itch, consistent with briquilimab-mediated mast cell depletion

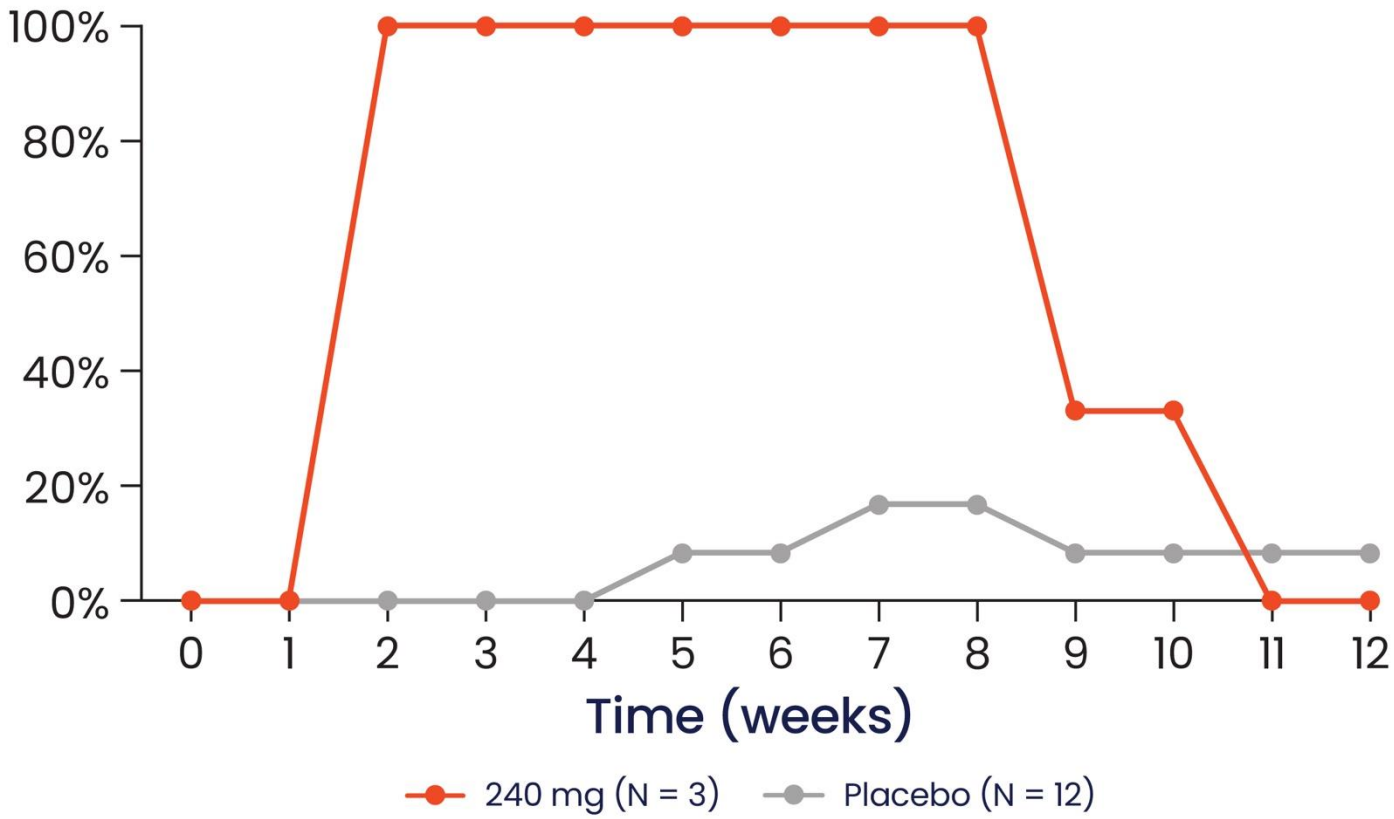
Week 16	120 mg Q12W (N=4)	180 mg Q12W (N=7)	Pooled placebo (N=12)[1]
Mean (SE) UAS7	0.5 (0.5)	7.2 (4.9)	15.6 (4.5)
Mean (SE) UAS7 change from baseline	-29.8 (6.9)	-21.7 (6.5)	-13 (3.2)
Mean (SE) ISS7 change from baseline	-14.2 (3.6)	-11.3 (3.1)	-6.8 (1.6)
Mean (SE) HSS7 change from baseline	-15.5 (3.3)	-10.4 (3.4)	-6.2 (1.8)
Complete response (CR) rate[2,3]	50%	57%	17%
Well controlled rate[3]	75%	57%	33%

1. 50% of participants in the pooled placebo group utilized rescue medications, including steroids during the study.
2. Median time to first dose CR <3 weeks (pooled 120mg, 180mg)
3. Last observation carried forward (LOCF) method was applied for missing data

Primary Efficacy Analysis of 240mg Single Dose Cohort

Mean baseline UAS7=26.6; Mean week 2 UAS7=0

Complete response
Weeks 1-12 (UAS7 = 0)



Note: Data cut-off 31 Jan 2025

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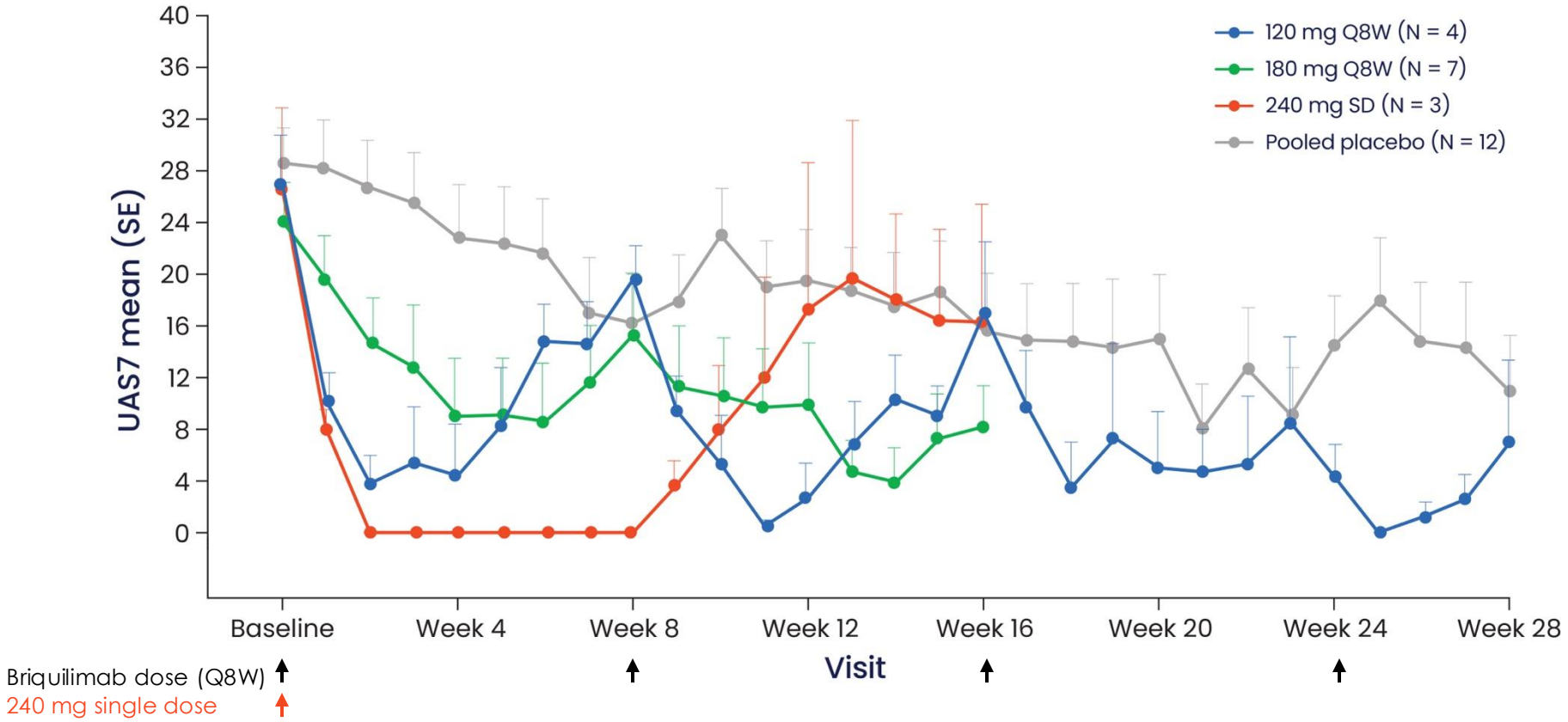
Dose Dependent UAS7 Reductions Observed Over 28-Week Treatment Period

Deeper UAS7 reductions observed in subsequent doses



Note: 1. 50% of participants in the pooled placebo group utilized rescue medications, including steroids during the study; Data cut-off 31 Jan 2025.

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Briquilimab Demonstrated a Favorable Safety Profile

28-week exposure for 10 mg – 180 mg doses, as of 31Jan25

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: Most commonly reported AEs (≥5 participants): nasopharyngitis, fatigue, hair color change, taste changes; **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

Safety Observations Possibly Related to c-Kit Blockade were Infrequent and Generally Limited to Grade 1 Events

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

Adverse event	Pooled briquilimab N = 37 (n, %)	Pooled placebo N = 12 (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 on treatment. • 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.

Note: Data cut-off 31Jan2025.

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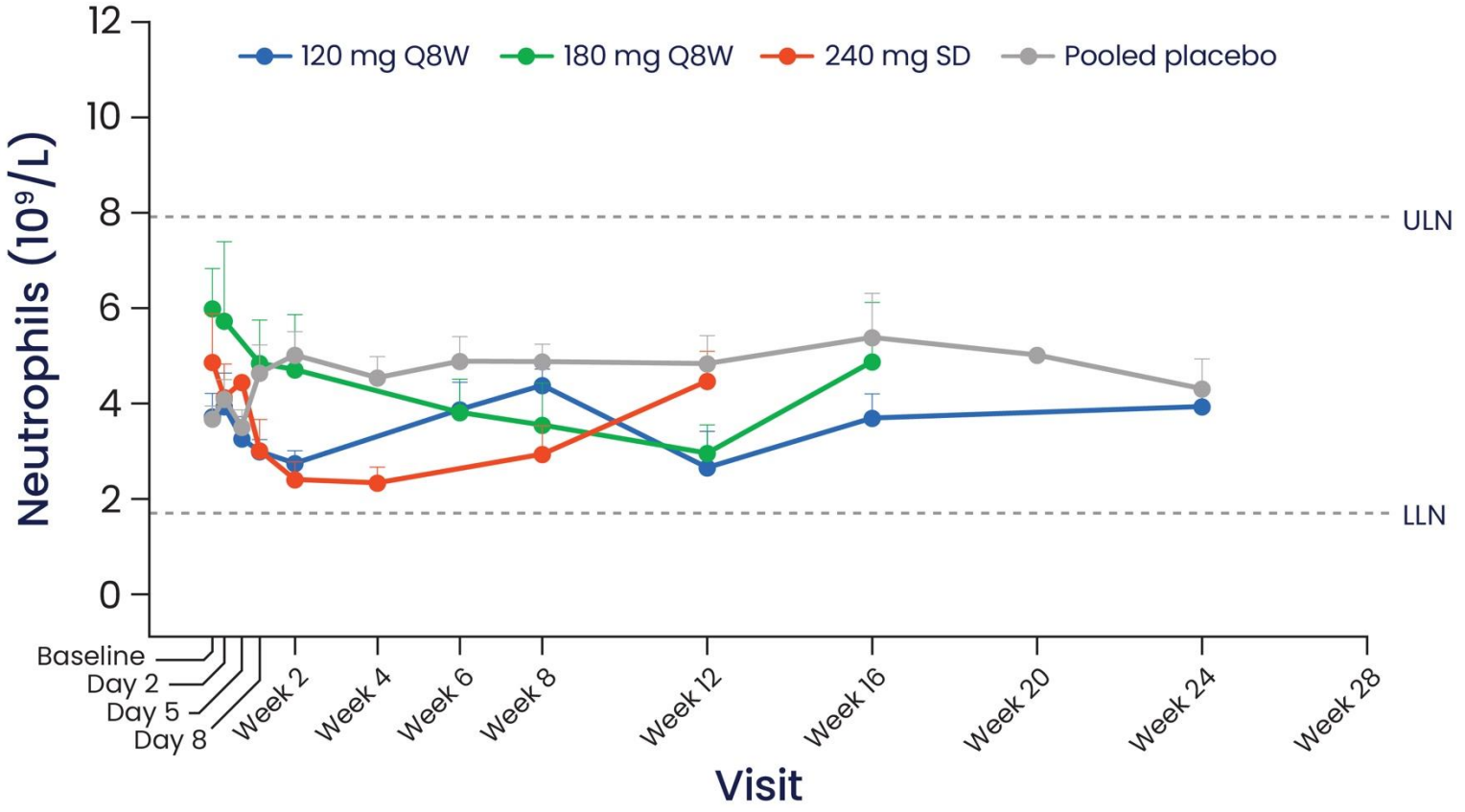
Neutrophil Counts Generally Remained Stable, with Predictable Reduction Which Subsequently Resolved

No discontinuations or dose delays due to reductions in neutrophil counts



Note: ULN = upper limit of normal; LLN = lower limit of normal; Data cut-off 31Jan2025; Source – Figure 14.3.4.1.

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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 cohorts)
- Dose dependent durability observed in complete responses and well-controlled disease
  - High CR rate observed, durable to 8 weeks, following single 240 mg dose
- 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

Acknowledgements

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Thank You.

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