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Initial Results from SPOTLIGHT, a Phase 1b/2a Study of Briquilimab in Adults with Chronic Inducible Urticaria (CIndU) who Remain Symptomatic Despite H1-Antihistamine Treatment

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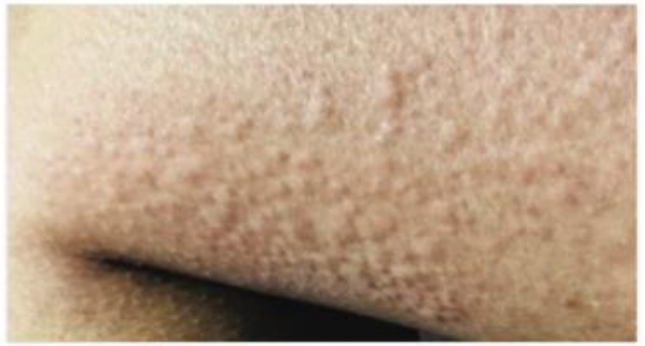
Conflict of Interest Statement

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

Background

- **Chronic inducible urticaria (CIndU)** is a debilitating inflammatory condition of the skin with a specific trigger such as heat, cold, sunlight, rubbing or friction[1,2]
- Mast cell degranulation, leading to the release of inflammatory mediators, is the key driver of severe itching, hives and angioedema in CIndU patients[3]
- CIndU patients **suffer both physically and psychologically**. Severe disease has a **negative impact on QoL** similar to other dermatologic diseases like plaque psoriasis
- Briquilimab, a humanized, aglycosylated, monoclonal antibody, directly blocks SCF binding to KIT, leading to inhibition of SCF/KIT signaling and mast cell apoptosis[4,5]
- Briquilimab (subcutaneous) was evaluated for safety, tolerability, and preliminary efficacy in a Phase 1b/2a open-label, dose escalation trial (NCT06353971, SPOTLIGHT) in adult participants with CIndU who are symptomatic despite treatment with H1 antihistamines
- We report initial results from the SPOTLIGHT study

Cold Urticaria



Symptomatic Dermographism

1. Munoz M, et al. Current Allergy and Asthma Reports June 2024
2. Ozdemir SO, et al. JEADV Mar 2024
3. Kulthanan K. et al. Front Immunol. Jul 2022
4. Bouzid H, et al EMBRN Hybrid Congress, May 29-31, 2024
5. Tucker E, et al. EAACI Hybrid Congress, May 31- June 3 2024

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

Phase 1b/2a SPOTLIGHT study of subcutaneous briquilimab in CIndU

Open-label, cold urticaria & symptomatic dermographism, single ascending dose study

Screening/Eligibility

- Diagnosis of Cold Urticaria (ColdU) or Symptomatic Dermographism (SD) for ≥ 3 mos.
- H1-antihistamine-failed
- 18+ years

Study Operations

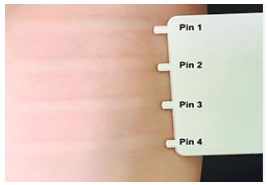
- **Lead PI: Martin Metz, MD**
- 7 sites in the EU
- N = 27

Key Assessments

- **Provocation Test:** TempTest (ColdU), FricTest (SD)
- **Disease Scores:** Urticaria control test (UCT)
- **Mast Cell Depletion & Recovery:** Serum Tryptase, Skin Biopsies
- **Safety:** TEAEs, SAEs

40 mg n=3
120 mg n=12
180 mg n=12

Single Subcutaneous Dose → 12 Week Efficacy Observation Period (6 Week Preliminary Analysis) + 24 Week Additional Safety Observation



FricTest™ – Symptomatic Dermographism

CR – Fric test negative (Total Fric score: 0 pins)

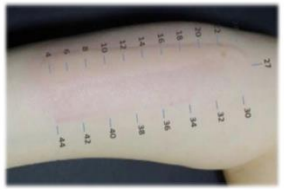
PR – Fric test (Total Fric score: ≤ 2 pins)

Provocation Tests Used for Clinical Evaluation

TempTest™ – Cold Induced Urticaria

CR – Negative test at ≤ 4°C

PR – Improvement by ≥ 4°C



Abbreviations: ColdU – cold urticaria; SD – symptomatic dermographism; UCT – Urticaria Control Test; TEAEs- treatment emergent adverse events; SAEs – serious adverse events; CR – Complete response, PR – Partial Response

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SPOTLIGHT: Baseline Demographics

	Briquilimab 40mg (n=3)	Briquilimab 120mg (n=12)	Briquilimab 180mg (n=12)	Total (n=27)
Age (years), mean (SD)	35.3 (8)	46.4 (13.8)	39.9 (16)	42.3 (14.5)
Female, n (%)	1 (33%)	8 (67%)	7 (58.3%)	16 (59.3%)
Weight (kg), median (range)	86 (69-94)	99 (57-115)	86.5 (54-104)	89 (54-115)
Cold Urticaria, n(%)	1 (33.3%)	4 (33.3%)	3 (25%)	8 (29.6%)
Symptomatic Dermographism, n(%)	2 (66.7%)	8 (66.7%)	9 (75%)	19 (70.4%)
Baseline Provocation Threshold				
TempTestTM - Critical temperature threshold (°C), mean (range)	16 (16-16)	20.8 (15-27)	18.7 (10-26)	19.4 (10-27)
FricTestTM –Total Fric score , mean (range)	3.5 (3-4)	3.9 (3-4)	3.7 (3-4)	3.7 (3-4)
Urticaria Control Test (UCT) score, mean (SD)	3.7 (2.5)	6.3 (3.3)	6.5 (2.7)	6.1 (3)
Tryptase (ng/ml), mean (SD)	4.7 (0.6)	7.6 (6.4)	5.1 (2.3)	6.5 (4.6)

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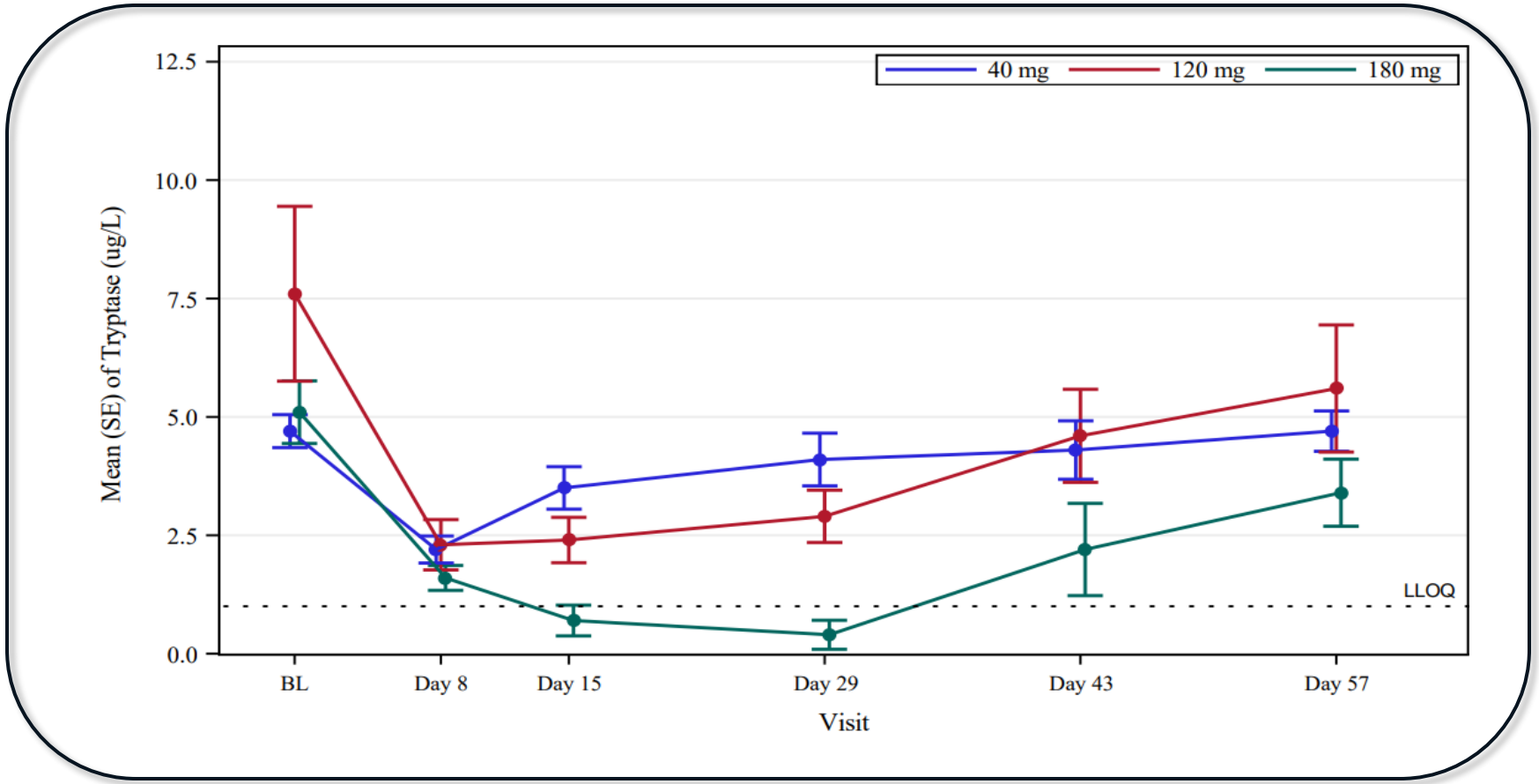
SPOTLIGHT: Dose dependent reductions in serum tryptase

Reduction to below Lower Limit of Quantification (LLOQ) (1 µg/L) seen in 83.3% (10/12) participants at 180mg



All values below LLOQ (**1.0 µg/L) are represented as 0 µg/L**

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SPOTLIGHT: Week 8 Efficacy Evaluation

Single dose of 180 mg briquilimab resulted in all participants **(100%)** showing a complete or partial response by Week 8

	Briquilimab 40mg (n=3)	Briquilimab 120mg (n=12)	Briquilimab 180mg (n=12)	Briquilimab All doses (n=27)
Complete Response, n (%)	1 (33.3%)	10 (83.3%)	11 (91.6%)	22 (81.5%)
ColdU, n	0	3	3	6
Symptomatic Dermographism, n	1	7	8	16
Partial Response, n (%)	2 (66.7%)	1 (8.3%)	1 (8.4%)	4 (14.8%)
ColdU, n	1	0	0	1
Symptomatic Dermographism, n	1	1	1	3
Complete or Partial Response at any time, n (%)	**3 (100%)**	**11 (91.6%)**	**12 (100%)**	**26 (96.3%)**

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SPOTLIGHT: 180 mg Week 8 Efficacy Evaluation

Depth of Response

- 100% (12/12) of participants achieved a CR or PR by week 8
- 83.3 % (10/12) of participants had a reduction in serum tryptase below LLOQ (1 µg/L)

Rapid Onset of Effect

- 66.6% (8/12) of participants had a CR or PR by week 2

Durability of Effect

- There were 5 CRs and 2 PRs at week 8 (58.3%, 7/12), durability assessment ongoing

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SPOTLIGHT: Safety and Tolerability

	Briquilimab 40mg (n=3)	Briquilimab 120mg (n=12)	Briquilimab 180mg (n=12)
Any adverse event	2	12	10
Any serious adverse event	0	2*	0
Any adverse event leading to discontinuation	0	0	0
Adverse event leading to death	0	0	0
Adverse event ≥ grade 3	0	1*	0

*SAE: Biliary colic leading to cholecystectomy, Grade 3 Fracture of the right shoulder (both unrelated)

AEs occurring in ≥3 participants: Nasopharyngitis, neutrophil count decrease, fatigue, headache, abdominal pain, COVID-19, diarrhea, dizziness, nausea

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SPOTLIGHT Safety/tolerability observations possibly related to KIT blockade were generally limited to low grade events

All events were Grade 1 or 2 and none resulted in discontinuations

Adverse Event as reported term	Briquilimab 40 mg (N=3) n (%)	Briquilimab 120 mg (N=12) n (%)	Briquilimab 180 mg (N=12) n (%)	Total Pooled (N=27) n (%)
Hair color changes	0 (0)	0 (0)	0 (0)	0 (0)
Skin discoloration	0 (0)	0 (0)	0 (0)	0 (0)
Taste change/Hypogeusia	0 (0)	1 (8.3)	2 (16.7)	3 (11.1)
Neutrophil count decreased	1 (33.3)	1 (8.3)	6* (50)	8 (29.6)

* Four events were Grade 1, two were Grade 2; five of six events occurred at the time of viral infection, median time to resolution 16 days

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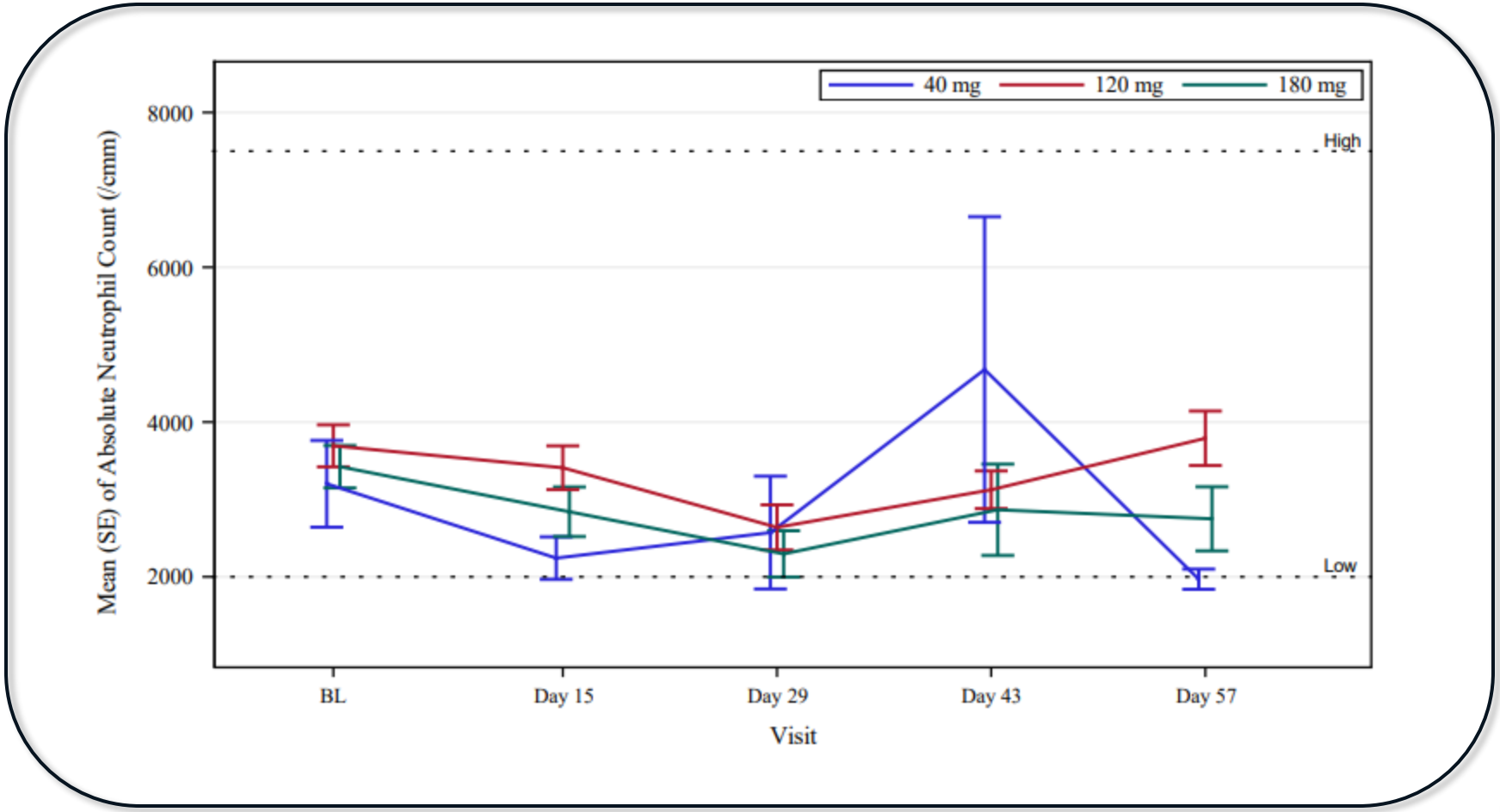
SPOTLIGHT: Absolute Neutrophil Count

Neutrophil counts generally remained stable, with predictable reductions which subsequently resolved



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Conclusions

- Single 180mg dose of briquilimab demonstrated 100% clinical response in participants with CIndU
  - 91.6% of participants in 180 mg cohort achieved complete response vs 83.3% in 120 mg cohort
  - Rapid onset of symptom control with 66.7% achieving clinical response by week 2
  - Deep reduction of tryptase observed with 83.3% of participants below LLOQ in 180 mg cohort
- Durability of the 180 mg dose demonstrated with 5 CRs and 2 PRs at 8 weeks (58.3% of participants)
- Briquilimab was well tolerated in participants with CIndU
- Participants from SPOTLIGHT may roll over to open label extension, briquilimab 180mg Q8W
- Briquilimab's robust efficacy and safety, supports continued evaluation in both CIndU and CSU
- Full SPOTLIGHT study results will be released in 2nd half of 2025

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Acknowledgements

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