EAACI
HYBRID CONGRESS
2023

9-11 JUNE - HAMBURG
GERMANY

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Remibrutinib (LOU064) treatment improves hive severity in patients with chronic spontaneous urticaria: Findings from a Phase 2b study

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ORAL Session (OAS) 20
Novel treatment approaches in urticaria
Saturday, 10 June 2023

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1 Disclosures and acknowledgements

- In relation to this presentation, the following real or perceived conflicts of interest declared:
  - Ana Giménez-Arnau reports roles as a medical advisor for Uriach Pharma, Sanofi and Genentech, Novartis, FAES, GSK, AMGEN, Celldex, Escient, Thermo Fisher and has research grants supported by Uriach Pharma, Novartis, and Instituto Carlos III- FEDER; she also participates in educational activities for Uriach Pharma, Novartis, Genentech, Menarini, LEO- PHARMA, GSK, MSD, Almirall, AVENE, and Sanofi

The authors wish to thank all investigators and patients involved in the trial

- The authors also thank Sushant Thakur and Anuja Shah of Novartis Healthcare Pvt. Ltd., Hyderabad, for providing medical writing assistance in accordance with Good Publication Practice guidelines (www.ismpp.org/gpp). The final responsibility for the content lies with the authors
- This study is funded by Novartis Pharma AG, Basel, Switzerland

2 Introduction and study objective

- **Chronic spontaneous urticaria (CSU)** is characterised by the occurrence of **wheals (hives) and/or angioedema** for ≥6 weeks and has a major **impact on patients' well-being**[1]
- Second-generation H_1-antihistamines (H_1-AH) are recommended as first-line treatment for CSU[1]
- **Remibrutinib (LOU064)** is a highly selective, oral BTK inhibitor that offers fast disease control in CSU patients who remain symptomatic despite H_1-AH.[2] It is currently in Phase 3 development for the treatment of CSU (REMIX-1: NCT05030311[3], REMIX-2: NCT05032157[4])
- Remibrutinib showed **clinical efficacy** and a **favorable safety profile** for up to **12 weeks** in the Phase 2b study and up to **52 weeks** in the open-label Phase 2b extension study in patients with CSU inadequately controlled by H_1-AH[5,6]

Objective

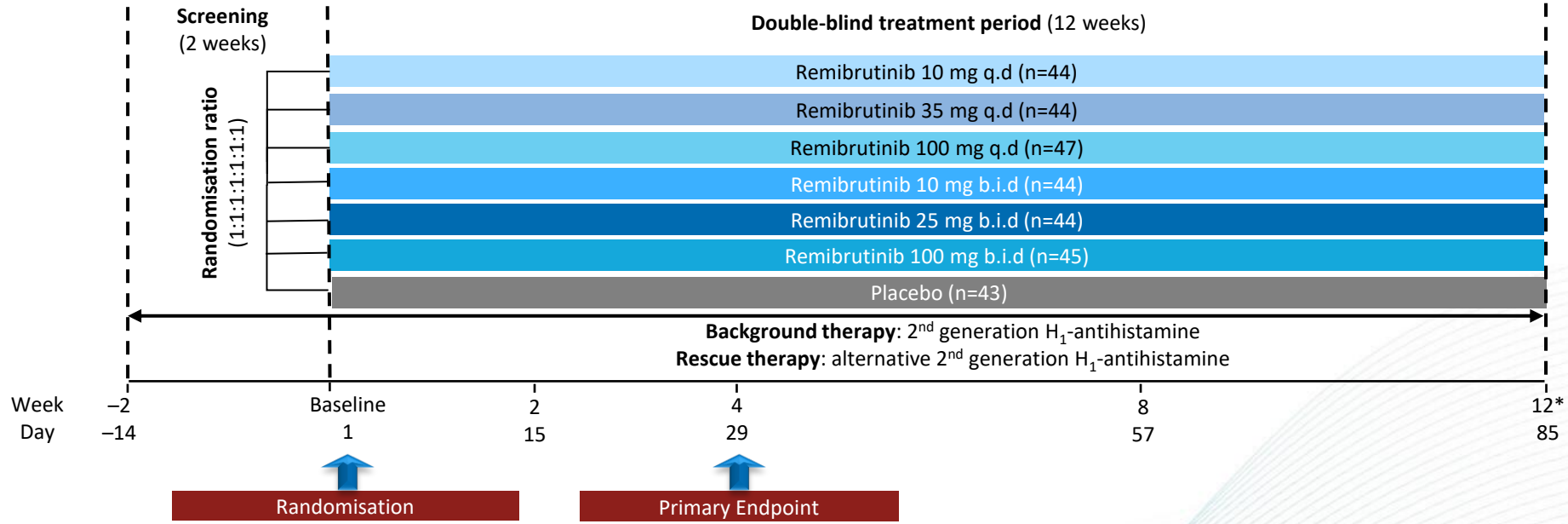
To explore the effect of remibrutinib on hive severity in patients with CSU from the Phase 2b study

BTK, bruton tyrosine kinase; CSU, chronic spontaneous urticaria.

1. Zuberbier T, et al. *Allergy*. 2022;77(3):734-766; 2. Angst D, et al. *J Med Chem*. 2020;63:5102–5118; 3. ClinicalTrial.gov.in. NCT05030311. Accessed on 28th April 2023; 4. ClinicalTrial.gov.in. NCT05032157. Accessed on 28th April 2023; 5. Maurer M, et al. *J Allergy Clin Immunol.* 2022;150(6):1498-1506.e2; 6. Carr W, et al. *AAAAI* 2023 (Oral Presentation 3611 - Late-breaker).

3 Study design

A dose-finding, multicenter, randomised, double-blind, placebo-controlled Phase 2b study in patients with CSU (NCT03926611)



- Patients received second generation H_1-AH at a locally approved licensed dose and posology as background therapy throughout the study

*Eligible patients rolled over into an extension study (NCT04109313) at Week 12 or at Week 16, following roll-over criteria defined in the extension study protocol and dependent on HA/EC approval from participating countries. Background therapy was a 2nd generation H_1-AH at a locally approved licensed posology that had to be administered daily with a stable treatment regimen throughout the study. Rescue therapy was a 2nd generation H_1-AH at a locally approved licensed posology that differed from the background H_1-AH, was eliminated primarily via renal excretion, and could only be given to treat unbearable symptoms (itch) of CSU on a day-to-day basis.
b.i.d., twice daily; AH, antihistamines; CSU, chronic spontaneous urticaria; EC, ethical committee; HA, health authority; n, number of patients randomized in each group; q.d, once daily.
Maurer M, et al. *J Allergy Clin Immunol.* 2022;150(6):1498-1506.e2.

3 Study outcomes and data analysis

Study outcomes

- Change from baseline in HSS7 at Weeks 2, 4, and 12
- Proportion of patients with HSS7=0 (no hives) at Weeks 2, 4, and 12

The hives (wheals) severity score, defined by number of hives, was recorded by the subject twice daily in their eDiary on a scale of 0 (none) to 3 (>12 hives/12 hours)

Data analysis

- A weekly score (HSS7) was derived by adding up the average daily scores of the 7 days preceding the visit. The possible range of the weekly score was therefore 0 – 21

AH, antihistamines; HSS7, weekly Hives Severity Score.

4 Patient demographics and baseline disease characteristics were generally balanced between treatment arms (randomized set)

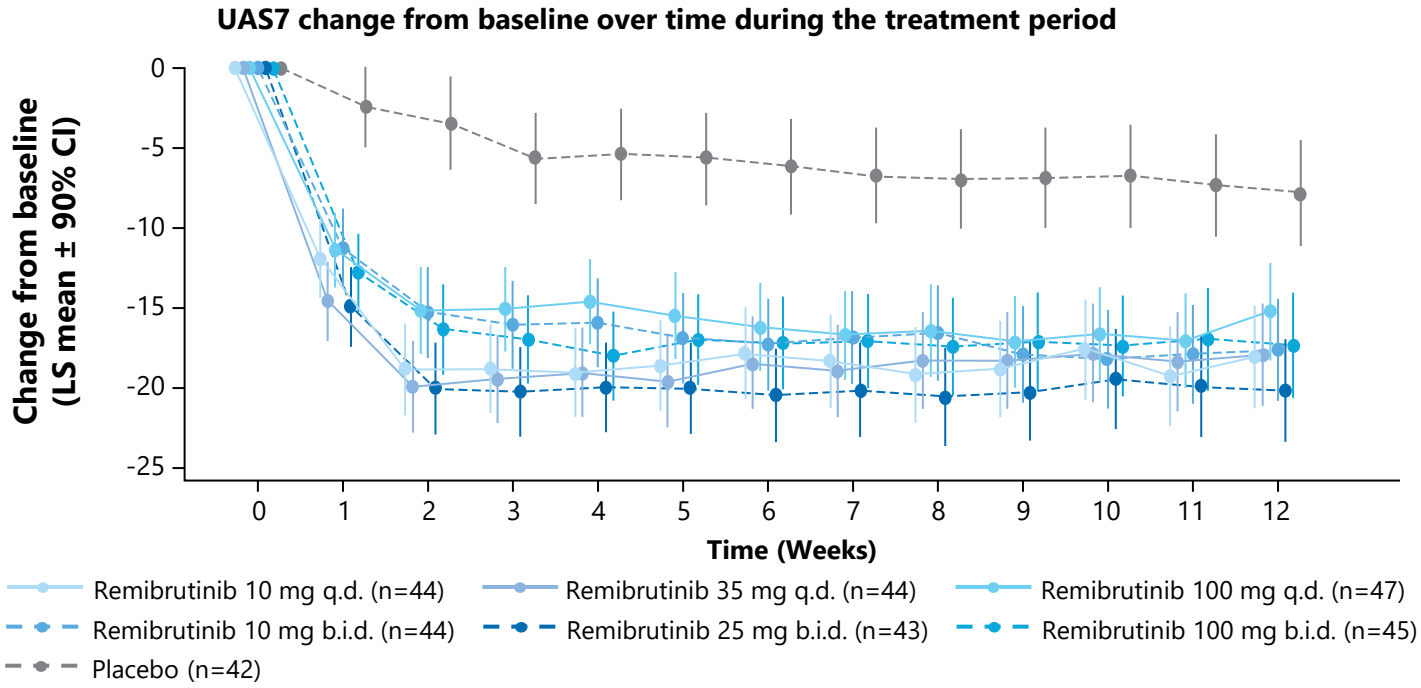
Baseline characteristics	Phase 2b Core Study						
	Remibrutinib						Placebo N=43
	10 mg q.d. n=44	35 mg q.d. n=44	100 mg q.d. n=47	10 mg b.i.d. n=44	25 mg b.i.d. n=44	100 mg b.i.d. n=45	
Age (years)	42.5±16.04	44.0±16.47	45.2±13.40	46.1±15.21	47.4±14.62	44.9±13.76	45.1±15.24
Female, n (%)	35 (79.5)	30 (68.2)	39 (83.0)	32 (72.7)	32 (72.7)	29 (64.4)	25 (58.1)
Baseline UAS7 score	31.4±7.06	31.2±7.22	28.5±7.00	29.8±6.69	29.3±7.92	29.3±5.96	27.6±7.62
Duration of CSU (years)	6.2±7.71	5.9±8.82	5.3±5.82	4.9±5.46	3.8±4.54	4.5±5.21	3.6±4.78
Baseline HSS7 score*	16.9±4.35	17.6±3.92	15.9±4.22	16.3±4.26	15.6±4.59	16.6±3.75	15.9±4.67
Previous exposure to anti-IgE therapy, n (%)	13 (29.5)	13 (29.5)	13 (27.7)	11 (25.0)	10 (22.7)	12 (26.7)	12 (27.9)

- The mean baseline HSS7 was similar between any remibrutinib dose (15.6–17.6) and placebo (15.9)

*based on Full analysis set.
Data are presented as mean±SD, unless stated otherwise. b.i.d., twice a day; CSU, chronic spontaneous urticaria; HSS7, weekly Hive Severity Score; n, number of patients; N, total number of patients; q.d., once a day; SD, standard deviation; UAS7, weekly Urticaria Activity Score.
Maurer M, et al. *J Allergy Clin Immunol.* 2022;150(6):1498-1506.e2.

4

Remibrutinib (all doses) showed rapid and significant improvement in UAS7 score over 12 weeks versus placebo



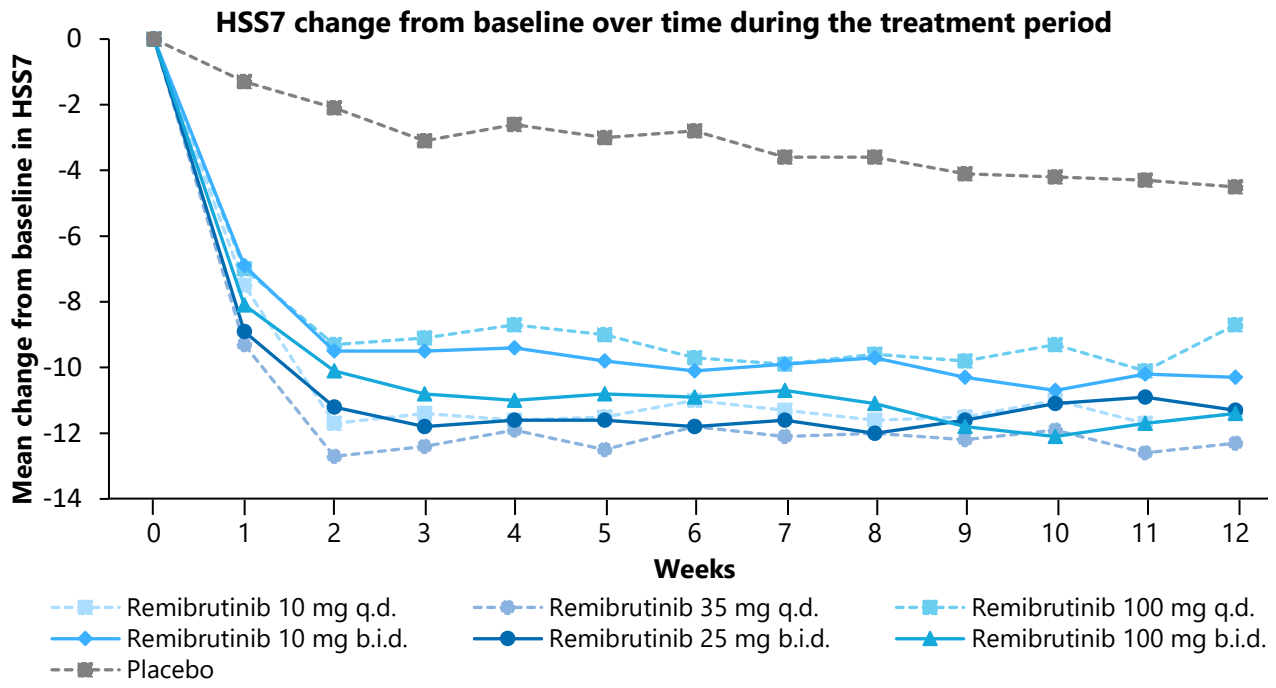
Change from baseline in UAS7 at Week 12 for each remibrutinib dose	
Treatment arm	**LS mean change (SE)**
Remibrutinib 10 mg q.d. (N=44)	-18.1 (1.9)
Remibrutinib 35 mg q.d. (N=44)	-18.0 (1.9)
Remibrutinib 100 mg q.d. (N=47)	-15.3 (1.9)
Remibrutinib 10 mg b.i.d. (N=44)	-17.7 (1.9)
Remibrutinib 25 mg b.i.d. (N=43)	-20.2 (2.0)
Remibrutinib 100 mg b.i.d. (N=45)	-17.4 (2.0)
Placebo (N=42)	-7.9 (2.0)

- UAS7 scores improved from baseline up to Week 12 in all remibrutinib doses compared with placebo
- A rapid improvement in UAS7 was observed as early as at Week 1, which was maintained up to Week 12

Full analysis set.
b.i.d., twice daily; CI, confidence interval; LS, least square; N, number of patients; q.d., once daily; SE, standard error; UAS7, weekly Urticaria Activity Score.
Maurer M, et al. *J Allergy Clin Immunol.* 2022;150(6):1498-1506.e2.

4

Remibrutinib (all doses) showed higher reduction from baseline in HSS7 versus placebo over 12 weeks

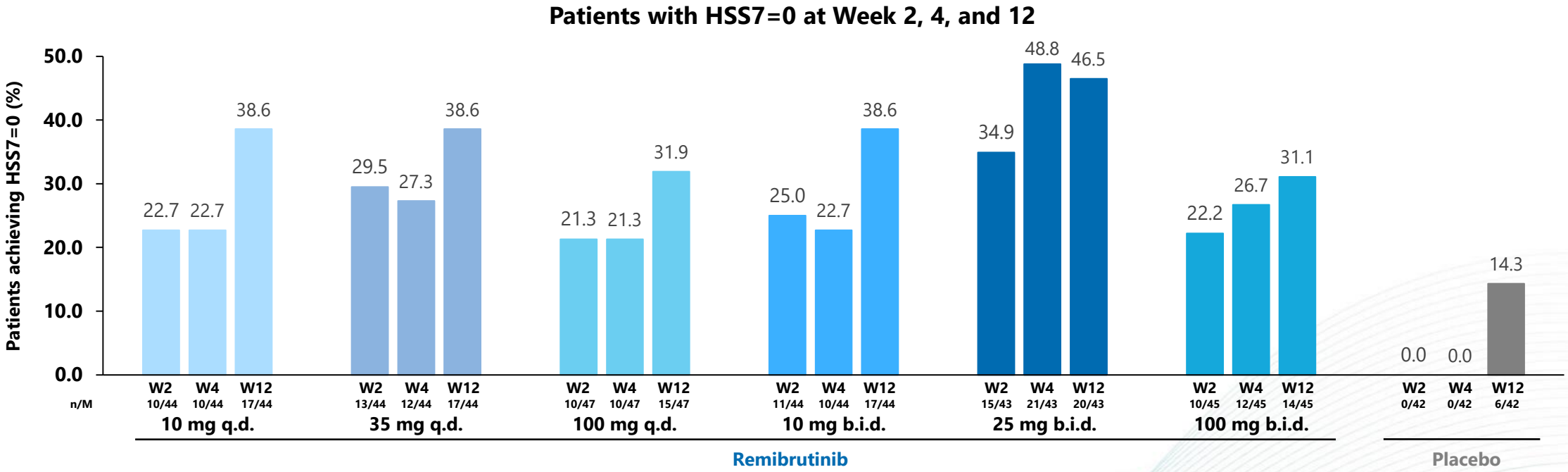


Change from baseline in HSS7 at Week 12	
Treatment arm	**Mean±SD**
Remibrutinib 10 mg q.d. (N=44)	-11.4±7.31
Remibrutinib 35 mg q.d. (N=44)	-12.3±7.12
Remibrutinib 100 mg q.d. (N=47)	-8.7±7.05
Remibrutinib 10 mg b.i.d. (N=44)	-10.3±7.96
Remibrutinib 25 mg b.i.d. (N=43)	-11.3±8.16
Remibrutinib 100 mg b.i.d. (N=45)	-11.4±6.64
Placebo (N=42)	-4.5±7.41

- The mean reduction in HSS7 from baseline was higher with remibrutinib (any dose) versus placebo at Week 2 (reduction: 9.3 to 12.7 vs 2.1), Week 4 (reduction: 8.7 to 11.9 vs 2.6), Week 8 (reduction: 9.6 to 12.0 vs 3.6), and Week 12 (reduction 8.7 to 12.3 vs 4.5)

Full analysis set.
BL, baseline; b.i.d., twice a day; HSS7, weekly Hive Severity Score; n, number of patients who responded; q.d., once a day; SD, standard deviation

4 Proportion of patients achieving HSS7=0 was higher with remibrutinib (all doses) than with placebo (non responder imputation)



- A higher proportion of patients achieved HSS7=0 with remibrutinib versus placebo at Week 2 (21.3% to 34.9% vs 0%), Week 4 (21.3% to 48.8% vs 0%), and Week 12 (31.1% to 46.5% vs 14.3%)

Full analysis set.
b.i.d., twice a day; HSS7, weekly Hive Severity Score; n, number of patients who responded; M, number of patients evaluated; q.d., once a day; W, week.

5 Conclusions

- The present analysis from the Phase 2b dose-finding trial in patients with CSU inadequately controlled by H_1-antihistamines showed:
  - **Rapid improvement** in HSS7 with remibrutinib (all doses) **as early as Week 2**, which was **sustained for up to 12 weeks** versus placebo
  - More patients on remibrutinib (all doses) achieved HSS7=0 versus placebo
- Larger studies are ongoing to confirm the findings of this Phase 2b study

CSU, chronic spontaneous urticaria; H_1-AH, H_1-antihistamines.

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