Remibrutinib (LOU064) reduces the use of rescue medication in patients with chronic spontaneous urticaria: Findings from a Phase 2b study

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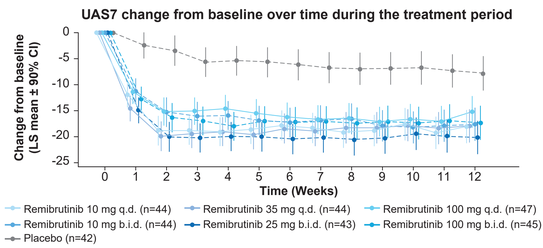
INTRODUCTION

- Chronic spontaneous urticaria (CSU) is characterised by the spontaneous 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 novel, highly selective and potent covalent oral Bruton's tyrosine kinase inhibitor (BTKi), that has demonstrated clinical efficacy and a favorable safety profile in a Phase 2b dose-finding study (NCT03926611) of patients with moderate to severe CSU inadequately controlled by H_1-AH[2–4]

OBJECTIVE

- To report the use of second-generation H_1-AH as rescue medication in patients with moderate to severe CSU from a Phase 2b study

Figure 1. Remibrutinib dose showed rapid and significant improvement in UAS7 score over 12 weeks versus placebo[4]



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)

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

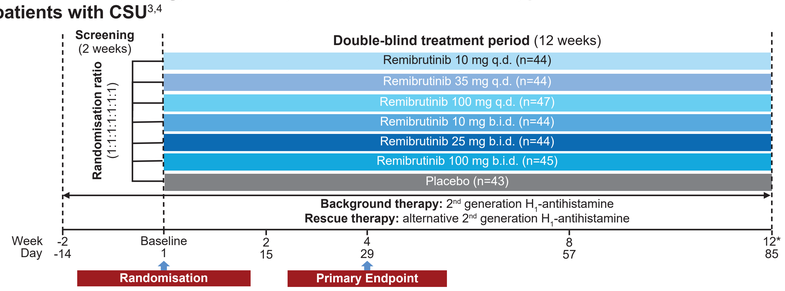
- Weekly Urticaria Activity Score (UAS7) scores improved from baseline up to Week 12 in all remibrutinib doses compared with placebo
- A rapid improvement in UAS7 was observed as early as at Week 1, which was maintained up to Week 12

METHODS

Study design

- Patients received second generation H_1-AH at a locally approved licensed dose and posology as background therapy throughout the study[3,4]

Figure 2. A dose-finding, multicenter, randomised, double-blind, placebo-controlled Phase 2b study in patients with CSU[3,4]



*Eligible patients rolled over into an extension study at Week 12 or at Week 16, following roll-over criteria defined in the extension study protocol and dependent on HAs/EC approval from participating countries. Background therapy was a second-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 second-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; HAs, health authorities; n, number of patients randomised in each group; q.d, once daily

Study outcomes

- Number of rescue H_1-AH tablets used over the preceding 24 hours to control itch or hives was evaluated from baseline to Week 12
- Rescue medication allowed was second generation H_1-AH eliminated primarily via renal excretion. The rescue medication had to be different from the background H_1-AH and was given as needed for the treatment of unbearable symptoms during screening, treatment and follow-up periods

Data analysis

- The weekly use of rescue medication was calculated as the sum of the doses per day, over 7 days described using summary statistics

RESULTS

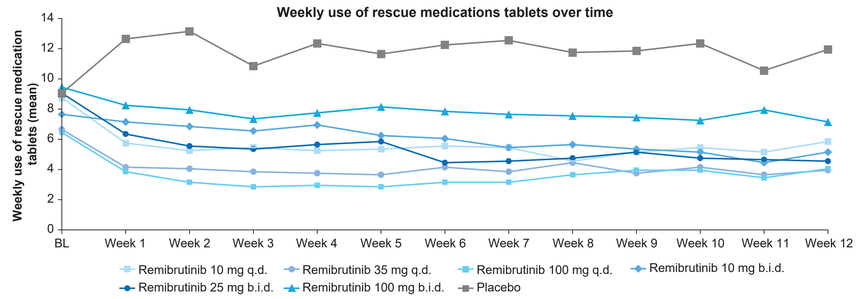
Table 1. Baseline demographics and disease characteristics (randomised set) were generally balanced between treatment arms

Baseline characteristics	Phase 2b Core Study							
	Remibrutinib						Placebo n=43	Total Randomised N=311
	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	45.0±14.90
Female, n (%)	35 (79.5)	30 (68.2)	39 (83.0)	32 (72.7)	32 (72.7)	29 (64.4)	25 (58.1)	222 (71.4)
Weight (kg)	78.4±19.43	79.0±20.20	76.6±14.66	78.3±16.77	77.0±19.90	78.9±19.30	78.3±16.48	78.1±18.02
Baseline DLQI score	14.9±7.1	12.6±6.5	12.7±7.1	12.7±6.2	12.9±6.6	10.8±6.7	13.4±7.9	12.8±6.9
Baseline UAS7 score	31.4±7.1	31.2±7.2	28.5±7.0	29.8±6.7	29.3±7.9	29.3±6.0	27.6±7.6	29.6±7.1
Duration of CSU (years)	6.2±7.7	5.9±8.8	5.3±5.8	4.9±5.5	3.8±4.5	4.5±5.2	3.6±4.8	4.9±6.2
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)	84 (27.0)

Data are presented as mean±SD, unless stated otherwise.
b.i.d., twice daily; CSU, chronic spontaneous urticaria; DLQI, Dermatology Life Quality Index; n, number of patients; N, total number of patients; q.d., once daily; SD, standard deviation; UAS7, weekly Urticaria Activity Score

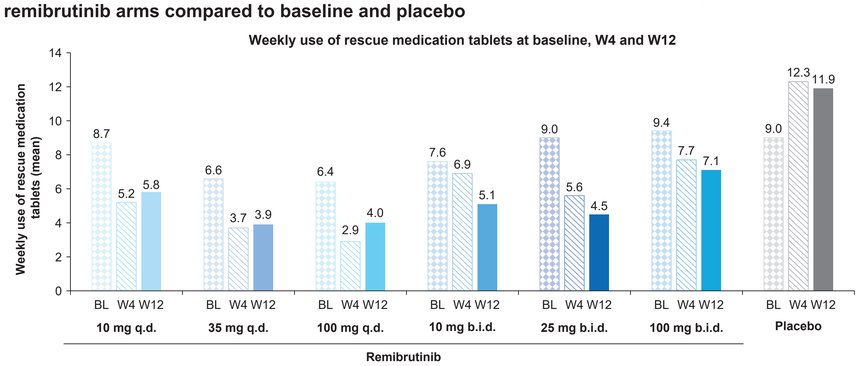
- Compared to baseline, there was decreased use of rescue medication as early as Week 1 across all remibrutinib arms which remained low during the study whereas the placebo arm showed an increased use of rescue medication

Figure 3. Reduction in weekly use of rescue medication tablets was observed early in all remibrutinib arms and remained low throughout the study



Full analysis set.
BL, baseline; b.i.d., twice daily; q.d., once daily

Figure 4. At Week 12, the mean weekly use of rescue medication was numerically lower across remibrutinib arms compared to baseline and placebo



Full analysis set.
BL, baseline; b.i.d., twice daily; q.d., once daily; W, week

CONCLUSIONS

- The present analysis from a first-in-patient, Phase 2b dose-finding remibrutinib trial demonstrated:
  - Remibrutinib reduced the need for rescue medication as early as Week 1, compared to baseline and placebo across all doses over 12 weeks in patients with CSU
  - Despite reduced use of H_1-AH, an improvement in CSU symptoms was observed in all treatment arms, as reported previously[4]
- Remibrutinib showed a favorable safety profile across all doses[5]

References

1. Zuberbier T, et al. *Allergy*. 2022;77(3):734–766
2. Angst D, et al. *J Med Chem*. 2020;63:5102–5118
3. Maurer M, et al. *AAD*. 25–29 March 2022
4. Maurer M, et al. *EADV*. 29 September –2 October 2021
5. Maurer M, et al. *EADV*. 29–31 October 2020. (Presentation # D3T01.3)

Conflicts of Interest

Marcus Maurer is or recently was a speaker and/or advisor for and/or has received research funding from Amgen, Allakos, Aralez, AstraZeneca, Celldex, FAES, Genentech, GI Innovation, Kyowa Kirin, Leo Pharma, Menarini, Novartis, Moxie, MSD, Roche, Sanofi, Third Harmonic, UCB and Uriach; **John Reed** reports roles as a medical advisor and has participated in educational activities for Novartis; **Petra Staubach** has received research funding and/or fees for consulting and/or lectures from Novartis, CSL Behring, Shire, MSD, Schering-Plough, Abbvie, Viro Pharma, Leo Pharma, Leti Pharma, Pohl-Boskamp GmbH, Astella, Allergika, Karrer, Allmirall, Sanofi, Octapharma, Pfleger GmbH, Beiersdorf, L´Oreal, Lilly, Janssen, Celgene, Hermal, UCB, Allmirall, Astelas, Sobi and Pfizer; **Karine Lheritier**, **Ivan Nikolaev**, and **Sibylle Haemmerle** are employees of Novartis Pharma AG, Basel, Switzerland; **Pauline Walsh** is an employee of Novartis Ireland Limited, Dublin, Ireland; **Vinayak Meti** is an employee of Novartis Healthcare Private Limited, Hyderabad, India; **Ana Giménez-Arnau** reports roles as a Medical Advisor for Uriach Pharma, Sanofi and Genentech, Novartis, FAES, GSK, AMGEN, 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.

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