Poster 017

Lee Clore | stant@cloremd.com

Remibrutinib monotherapy reduced rescue medication in chronic spontaneous urticaria patients: Findings from a Phase 2b extension study

Lee Clore,[1] Warner Carr,[2] Jeffrey Tillinghast,[3] Vipul Jain,[4] John Reed,[5] Petra Staubach,[6] Karine Lheritier,[7] Pauline Walsh,[8] Ivan Nikolaev,[7] Sibylle Haemmerle,[7] Ana M Giménez-Arnau[9]

[1]Allergy and Asthma Specialists, PSC, Owensboro, Kentucky, USA; [2]Allergy and Asthma Associates of Southern California, and Southern California Research, Mission Viejo, California, USA; [3]The Clinical Research Center, St. Louis, Missouri, USA; [4]Division of Clinical Immunology and Allergy, Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [5]Department of Dermatology, Churchill Hospital, University of Oxford, United Kingdom; [6]Department of Dermatology, University Medical Center, Mainz, Germany; [7]Novartis Pharma AG, Basel, Switzerland; [8]Novartis Ireland Limited, Dublin, Ireland; [9]Department of Dermatology, Hospital del Mar Research Institute, Universitat Pompeu Fabra, Barcelona Spain

Scan to obtain:
• Poster

To download a copy of this poster, visit the web at: https://bit.ly/UKCAAAAI

INTRODUCTION

- Chronic spontaneous urticaria (CSU) is characterized by recurrent wheals (hives) and/or angioedema for more than 6 weeks and can have a major impact on patients' well-being[1]
- Remibrutinib is a novel, oral, highly selective Bruton's tyrosine kinase (BTK) inhibitor that demonstrated safety and efficacy for up to 52 weeks in the Phase 2b core and extension studies (NCT03926611 and NCT04109313) and in the 24-week primary analysis of the Phase 3 studies (REMIX-1: NCT05030311, REMIX-2: NCT05032157) in patients with CSU inadequately controlled by H1-antihistamines (H1-AH)[2–5]
- In the Phase 2b core study, remibrutinib reduced rescue H1-AH use in patients with CSU who also took concomitant background H1-AH at label dose.[3]
- Here we report the effect on rescue medication use by remibrutinib as monotherapy (first 4 weeks) as well as with background H1-AH medication during the Weeks 5 to 52 of the Phase 2b extension study

OBJECTIVE

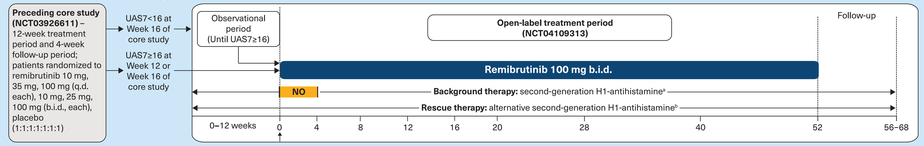
- To evaluate rescue medication use in absence of background medication in first 4 weeks of the Phase 2b extension study

METHODS

Study design

- Eligible patients (having weekly Urticaria Activity Score [UAS7] ≥16 at the end of the treatment or follow-up period of the Phase 2b core study, or by the end of the observational period of the extension study) were enrolled in the extension study and received remibrutinib 100 mg twice daily for 52 weeks[4] (**Figure 1**)
- No background H1-AH was allowed from baseline to Week 4 of the treatment phase of the extension study
- Second-generation H1-AH (different from background H1-AH) were allowed as rescue medication as needed

Figure 1. Study design[4]



[a]Background therapy (given with a stable treatment regimen) was not permitted for the first 4 weeks of the treatment period and was administered at the discretion of the investigator thereafter; [b]Rescue therapy differed from the background H1-antihistamine, eliminated primarily via renal excretion, and was only given to treat unbearable symptoms (itch) of CSU on a day-to-day basis.
b.i.d., twice daily; CSU, chronic spontaneous urticaria; N, total number of patients; q.d., once daily; UAS7, weekly Urticaria Activity Score.

Study assessments

- Efficacy was assessed as change from baseline (CFB) in UAS7 up to Week 52
- The number of rescue H1-AH tablets used was recorded once daily in an eDiary by the patients
- The weekly use of rescue medication was calculated as the sum of tablets per day over 7 days, described using summary statistics
- Rescue medication use was assessed in the first 4 weeks of the treatment period (background medication prohibited) and between Weeks 5 and 52 (background medication permitted)

RESULTS

- Overall, 194 patients received remibrutinib 100 mg b.i.d. in the extension study
- Patient demographics and disease characteristics from the baseline of the Phase 2b extension study are presented in **Table 1**

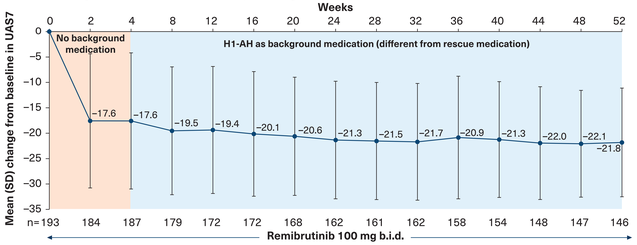
Table 1. Patient demographics and baseline disease characteristics (safety set)

Characteristics	Remibrutinib 100 mg b.i.d. (N=194)
Age (years)	45.5±14.12
Female, n (%)	139 (71.6)
Duration of CSU (years)	5.8±6.68
Baseline UAS7	27.9±8.23
Baseline UAS7 disease status, n (%)	
Mild disease (6 to <16)	5 (2.6)
Moderate disease (16 to <28)	94 (48.5)
Severe disease (28 to 42)	93 (47.9)
Previous exposure to anti-IgE therapy[a], n (%)	54 (27.8)

Data are expressed as mean±SD unless stated otherwise. [a]Recorded at the time of enrollment in the core study.
b.i.d., twice daily; CSU, chronic spontaneous urticaria; IgE, immunoglobulin E; n, number of patients in each category; N, total number of patients; SD, standard deviation; UAS7, weekly Urticaria Activity Score.

- Remibrutinib 100 mg b.i.d. showed improvement in terms of change from baseline (CFB) in UAS7 as early as Week 2 (mean±standard deviation [SD], −17.6±13.2), which was sustained up to Week 52 (−21.8±10.7; **Figure 2**)

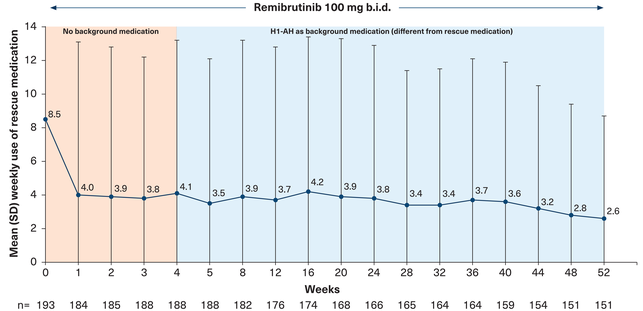
Figure 2. Change from baseline in UAS7 over time during the 52-week treatment period (as observed; safety set)



b.i.d., twice daily; H1-AH, H1-antihistamines; n, number of patients at each time point; UAS7, weekly Urticaria Activity Score.

- A total of 45.9% (89/194) of patients received background medication (second-generation H1-antihistamines) from Week 5 to 52 and 91.2% (177/194) of patients received rescue medication (alternative second-generation H1-antihistamines) throughout the 52-week treatment period
- A reduction in weekly rescue medication use was observed as early as Week 1 compared with baseline and remained consistently low through Week 4 with remibrutinib monotherapy; the weekly rescue medication use (number of tablets), mean±SD was 4.0±9.1, 3.9±8.9, 3.8±8.4, and 4.1±9.0 for Weeks 1, 2, 3, and 4, respectively vs 8.5±10.9 at baseline (**Figure 3**)
- The rescue medication use in the first 4 weeks in the absence of background medication was consistent with that in the presence of concomitant background medication between Weeks 5 and 52 (weekly mean±SD range: 2.6±6.1 to 4.4±9.9 [at Weeks 14 and 15]; **Figure 3**)

Figure 3. Weekly use of rescue medication tablets in patients with CSU on remibrutinib 100 mg b.i.d. (safety set)



b.i.d., twice daily; CSU, chronic spontaneous urticaria; H1-AH, H1-antihistamines; n, number of patients at each time point; SD, standard deviation.

CONCLUSIONS

- Remibrutinib 100 mg b.i.d. showed early improvements in disease activity (reduction from baseline in UAS7) which were sustained up to 52 weeks in patients with CSU inadequately controlled by H1-AH
- Weekly use of H1-AH (rescue medication) was reduced with remibrutinib treatment to a similar degree when used as monotherapy vs when background H1-AH at standard dose was added

Poster presented at: The American Academy of Allergy, Asthma & Immunology Annual Meeting; February 23–26, 2024; Washington, DC.

Disclosures

Lee Clore is a speaker and/or advisor for Regeneron, Sanofi, GSK, Incyte, Pfizer and Eli Lilly and is conducting clinical trials for Allergy Therapeutics, AstraZeneca, Eli Lilly, GSK, Novartis, Celldex, Regeneron, Sanofi, and Teva. **Warner Carr** is either a speaker or consultant for Amgen, AstraZeneca, DBV, MERZ, Optinose, Regeneron, Sanofi, Teva and Aluna. **Jeffrey Tillinghast** reports performing clinical research for 3M, Amphastar, AstraZeneca, Cephalon, Genentech, GlaxoSmithKline, Janssen, Lupin, Mylan, Novartis, Roxane and Teva Pharmaceutical Industries. **Vipul Jain** has consulted as and/or advised and/or received research funding from Pediapharm, Medexus, Sanofi, Regeneron, Bausch, Novartis, AbbVie, Aralez, ALK, Celgene, Amgen, LEO Pharma, Mylan, Pfizer, Covis Pharma, Galderma, Eli Lilly and Company, GSK, Kymab, Arcutis Biotherapeutics, and AstraZeneca and also participated as a primary investigator in clinical trials sponsored by Probity medical research Inc and is a director of Allergy Research Canada Inc. **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, Viropharma, Leo Pharma, Leti Pharma, Pohl-Boskamp GmbH, Astella, Allergika, Karrer, Allmirall, Sanofi, Octapharma, Pfieger GmbH, Beiersdorf, L´Oreal, Lilly, Janssen, Celgene, Hermal, UCB, Allmirall, Asteles, Sobi, and Pfizer. **Sibylle Haemmerle, Karine Lheritier,** and **Ivan Nikolaev** are employees of Novartis Pharma AG, Basel, Switzerland. **Pauline Walsh** is an employee of Novartis Ireland Limited, Dublin, Ireland. **Ana M Giménez-Arnau** is or recently was a speaker and/or advisor for and/or has received research funding from Almirall, Amgen, AstraZeneca,Avene, Celldex, Escient Pharmaceutials, Genentech, GSK, Instituto Carlos III- FEDER, Leo Pharma, Menarini, Mitsubishi Tanabe Pharma, Novartis, Sanofi–Regeneron, Servier, Thermo Fisher Scientific, Uriach Pharma / Neucor.

Acknowledgments

All authors participated in the development of the poster for presentation. The authors wish to thank all investigators and patients involved in the trial. The authors thank **Suparna Mukherjee** and **Mohammad Fahad Haroon** for editorial and medical writing support, and **Hareesh Cheela** for the design support (all Novartis Healthcare Pvt. Ltd., Hyderabad, India), which was funded by Novartis Pharma AG, Basel, Switzerland, in accordance with the Good Publication Practice (GPP3) guidelines (http://www.ismpp.org/gpp3).

Funding

This study was sponsored by Novartis Pharma AG, Basel, Switzerland.

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. *J Allergy Clin Immunol*. 2022;150(6):1498–1506.e2.
4. Jain V, et al. *J Allergy Clin Immunol*. 2023;S0091-6749(23)01346-5.
5. Saini S, et al. *ACAAI 2023*. Oral Presentation LB001 – Late-breaker; November 12, 2023; Anaheim, CA.