Poster 022

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Remibrutinib treatment did not impact mean total serum immunoglobulin levels or infection rates in patients with chronic spontaneous urticaria: Phase 2b study results

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CONCLUSIONS

- Remibrutinib treatment did not have any relevant impact on the total serum IgA, IgE, IgG, and IgM levels in patients with CSU in the Phase 2b core study and long-term extension study with 100 mg b.i.d. up to 52 weeks
- Remibrutinib has demonstrated safety and efficacy for up to 52 weeks in patients with CSU[4]
  - Exposure-adjusted infections rates did not increase with long-term remibrutinib treatment and remained comparable to any remibrutinib/placebo arm in the core study

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INTRODUCTION

- Chronic spontaneous urticaria (CSU) is characterized by the occurrence of wheals (hives) and/or angioedema for >6 weeks and has a major detrimental impact on patients' well-being[1]
- Remibrutinib is a novel, oral, highly selective Bruton's tyrosine kinase (BTK) inhibitor that has 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-antihistamine[2–5]
- Histamine release triggered by activation of Fc epsilon receptor I (FcεRI) receptors on the mast cell membrane plays a critical role in CSU pathophysiology and BTK enzyme is central to this process.[3] BTK signaling also plays an important role in B-cell development, and BTK mutation linked to X-linked agammaglobulinemia have been shown to affect serum immunoglobulin (Ig) levels[6]

OBJECTIVE

- To evaluate the impact of remibrutinib treatment on total serum Ig levels and on the infection rate in the Phase 2b core and extension studies

METHODS

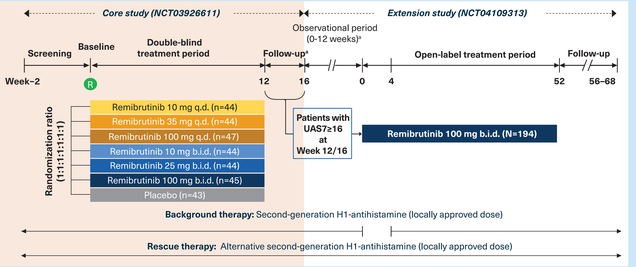
Study design and patients

- Phase 2b core study was a dose-finding, multicenter, randomized, double-blind, placebo-controlled study conducted across 17 countries in patients with CSU[3] (**Figure 1**)
- Eligible patients (having weekly Urticaria Activity Score [UAS7] ≥16 at the end of the treatment period or by the end of the follow-up period of the Phase 2b core study, or by the end of a 12-week observational period of the extension study) were enrolled in the treatment period of the extension study[4] (**Figure 1**)

Study assessments and statistical analysis

- Total serum Ig levels were assessed at baseline, Week 4 (only IgE), and Week 12 during the core study and at baseline, Week 12 (only IgE), Week 28, and Week 52 during the extension study.
- Exposure-adjusted incident rate (EAIR) for infection (per 100 patient-years) and Ig levels were analyzed using summary statistics based on safety population

Figure 1. Study design



[a]Patients with UAS7<16: 1) At Week 12, entered follow-up period of the core study; 2) At Week 16, entered the observational period of the extension study for up to 12 weeks, and on relapse during this period entered the treatment period of the extension study.
b.i.d., twice a day; N, total number of patients; n, number of patients included in each group; q.d., once daily; R, randomization; UAS7, weekly Urticaria Activity Score.

RESULTS

- Of 309 patients included in the Phase 2b core analysis, 194 rolled-over to the 52-week extension study and were included in the analysis
- Patient demographics, baseline disease characteristics, and serum Ig levels were comparable between the core and extension studies (**Table 1**)

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

Characteristics (mean±SD)	Core study		Extension study
	Any remibrutinib arm (N=267)	Placebo (N=42)	Remibrutinib 100 mg b.i.d. (N=194)
Age (years)	45.1±14.8	44.8±15.3	45.5±14.1
Female, n (%)	197 (73.8)	24 (57.1)	139 (71.6)
BMI (kg/m²)	28.1±6.1	27.2±6.4	28.1±6.2
Duration of CSU (years)	5.1±6.4	3.5±4.8	5.8±6.7
UAS7 score	29.9±7.0	27.7±7.7	27.9±8.2
Baseline serum Ig levels			
IgA (g/L)	2.2±0.97	2.4±1.3	2.3±1.0
IgE (µg/L)	655.6±1754.7	971.6±2740.6	817.5±2492.8
IgG (g/L)	10.9±2.4	10.8±2.6	11.0±2.4
IgM (g/L)	1.2±0.9	1.1±0.7	1.0±0.8

b.i.d., twice a day; BMI, body mass index; CSU, chronic spontaneous urticaria; Ig, immunoglobulin; N, total number of patients in each arm; SD, standard deviation; UAS7, weekly Urticaria Activity Score.

- Infections rates (EAIR) did not increase with long-term exposure to remibrutinib treatment (**Table 2**)

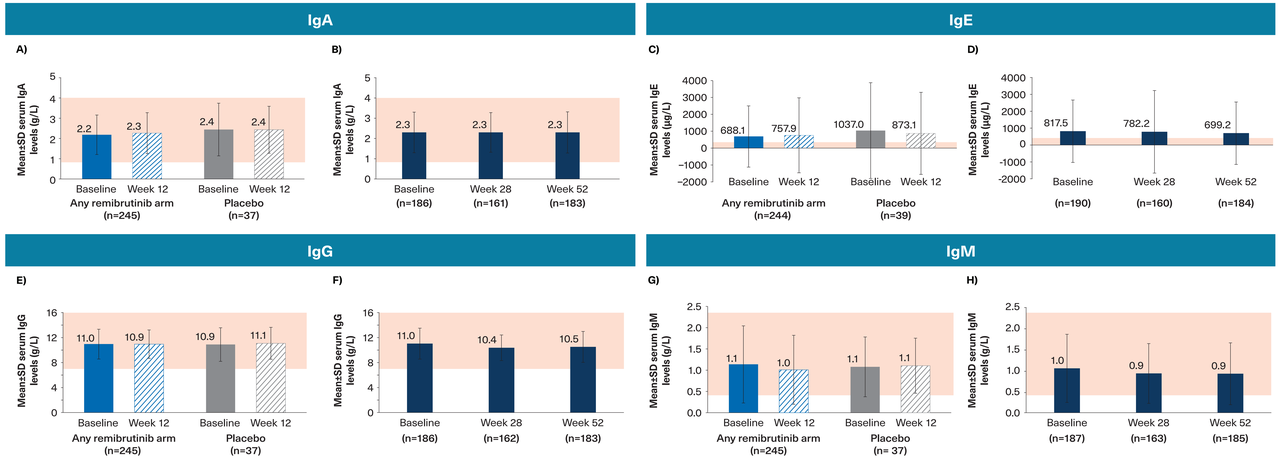
Table 2. Infection rates (EAIR) in the core and extension studies (safety set)

Characteristic	Core study		Extension study
	Any remibrutinib arm (N=267)	Placebo (N=42)	Remibrutinib 100 mg b.i.d. (N=194)
Infection rates (EAIR, 95% [CI])	107.7 (83.5, 136.8)	98.7 (45.1, 187.3)	40.3 (30.9, 51.8)

Infections were defined as MedDRA SOC infections and infestations.
b.i.d., twice daily; CI, confidence interval; EAIR, exposure-adjusted incidence rate; MedDRA, Medical Dictionary for Regulatory Activities; N, total number of patients; SOC, System Organ Class.

- No meaningful change from baseline in the total serum Ig levels in any remibrutinib arm was observed at Week 12 in the core study or Weeks 28 and 52 in the extension study (**Figure 2**)

Figure 2. Serum Ig levels in the core study (A, C, E, G) and the extension study (B, D, F, H; safety set)



Shaded area represent normal range of serum Ig levels.
Ig, immunoglobulin; n, number of patients evaluated in each arm; SD, standard deviation.

Disclosures

Warner Carr is either a speaker or consultant for Amgen, AstraZeneca, DBV, MERZ, Optinose, Regeneron, Sanofi, Teva, and Aluna. **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 Pharmaceuticals, Genentech, GSK, Instituto Carlos IIIFEDER, Leo Pharma, Menarini, Mitsubishi Tanabe Pharma, Novartis, Sanofi–Regeneron, Servier, Thermo Fisher Scientific, Uriach Pharma/Neucor. **Karine Lheritier, Sibylle Haemmerle,** and **Artem Zharkov** are employees of Novartis Pharma AG, Basel, Switzerland. **Swapnil Dahale** is an employee of IQVIA, Mumbai, India. **Koremasa Hayama** was a speaker and/or advisor for and/or has received research funding from AbbVie, Boehringer Ingelheim, Eisai, Janssen Pharmaceutical, Kaken Pharmaceutical, Kyorin, Kyowa-Kirin, Maruho, Mitsubishi-Tanabe, Nihon Pharmaceutical, Novartis, Sanofi, Sun Pharma, and Taiho. **Robert Snyder** is a speaker and/or advisor for and/or has received research funding from Janssen Biotech, Amgen, Novartis, Galderma, Abbvie, Leo Pharma, Sun Pharma, Regeneron, Sanofi, Mindera, Pfizer, Incyte, Castle Biosciences, and UCB.

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References

1. Zuberbier T, et al. *Allergy.* 2022;77:734–766.
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. doi: 10.1016/j.jaci.2023.10.007. Epub ahead of print.
5. Saini S, et al. ACAAI 2023. Oral Presentation LB001 – Late-breaker; November 12, 2023; Anaheim, CA.
6. McDonald C, et al. *Immunology.* 2021;164:722–736.