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Time to relapse during treatment-free follow-up without remibrutinib in patients with chronic spontaneous urticaria: Subgroup analysis by baseline immunoglobulin-E levels and chronic urticaria index status from a Phase 2b extension study

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Introduction

- **CSU** is characterized by the occurrence of **hives (itchy wheals) and/or angioedema** for **>6 weeks** and has a major detrimental **impact on patients' well-being**[1]
- **Remibrutinib** is a **novel, oral, highly selective BTK inhibitor,**[2] which has demonstrated **safety** and **efficacy** for up to **52 weeks** in the **Phase 2b core and extension studies** (NCT03926611 and NCT04109313)[3,4] and in the **24-week** primary analysis from **Phase 3 clinical studies** (REMIX-1: NCT05030311, REMIX-2: NCT05032157) in **patients with CSU** inadequately controlled by H1-AH[5]
- Here, we report data from **treatment-free follow-up** period of the **52-week Phase 2b extension** (NCT04109313) study

Objective

To evaluate the effect of remibrutinib on time to first relapse (UAS7 ≥16) in subgroups of patients divided by baseline IgE levels and CU index status during treatment-free follow-up period (only on background H1-AH treatment and as needed rescue medication) of the Phase 2b extension study

BTK, Bruton's tyrosine kinase; CSU, chronic spontaneous urticaria; CU, chronic urticaria; H1-AH, H1-antihistamines; Ig, immunoglobulin; UAS7, weekly Urticaria Activity Score.

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.* 2023;150:1498–1506.e2; 4. Jain V, et al. *J Allergy Clin Immunol.* Published online October 20, 2023. 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.

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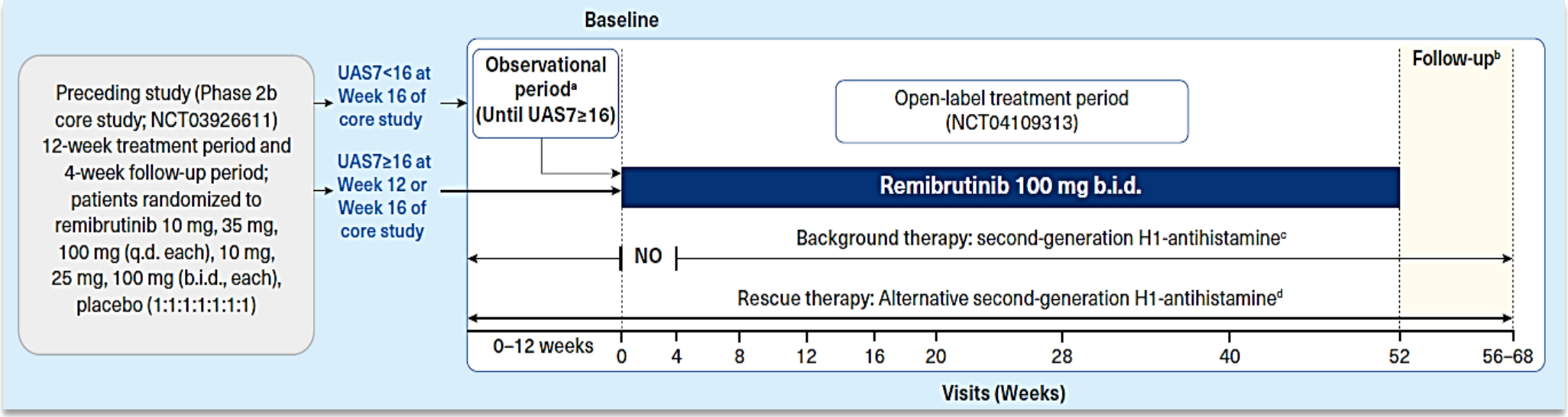
Methods

A 52-week, long-term, open-label extension study of patients who completed the preceding core study[1-4]



[a]**Observation period:** Patients who never relapsed (UAS7 ≥16 at least once) within 12 weeks completed the study at the end of the observational period without entering the extension study
[b]**Follow-up period:** The minimum duration of follow-up period was 4 weeks for all patients who stopped treatment with remibrutinib. Patients who achieved a UAS7 ≤6 at Week 52 of the treatment period extended their follow-up period until they relapsed (UAS7 ≥16) for up to 16 weeks after remibrutinib discontinuation. Follow-up ended at Week 68 for all patients
[c]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
[d]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; N, total number of patients; q.d., once daily; UAS7, weekly Urticaria Activity Score.

1. Maurer M, et al. *J Allergy Clin Immunol*. 2022 Dec;150(6):1498–1506.e2; 2. Giménez-Arnau A, et al. Poster presented at: EADV 2022; September 7–11, 2022, Milan, Italy. #P1722; 3. Giménez-Arnau A, et al. Oral presentation at EAACI 2022: July 1–3, 2022; Prague, Czech Republic; 4. Jain V, et al. *J Allergy Clin Immunol*. Accepted manuscript. Published online October 12, 2023. doi:10.1016/j.jaci.2023.10.007.

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Methods

Patient population

- Patients with well-controlled disease (UAS7≤6) at Week 52 (end of open-label treatment period) were followed up until relapse (UAS7≥16) during treatment-free follow-up period (up to 16 weeks)

Exploratory outcomes and data analysis

- Time to first relapse (defined as the time to reach UAS7≥16 for the first time after the 52-week treatment period) during treatment-free follow up period was assessed in all patients with a UAS7≤6 at treatment completion as well as subgroups of patients with markers of autoallergy (baseline IgE levels >43 IU/mL and CU index negative [<10]) and autoimmunity (IgE levels ≤43 IU/mL and CU index positive [≥10])
- All analysis were performed at a descriptive level. Data are presented as observed

CU, chronic urticaria; IgE, immunoglobulin E; UAS7, weekly Urticaria Activity Score

Results

- In the extension study, **156/194 (80.4%)** patients completed open-label treatment with remibrutinib 100 mg b.i.d. Of them, **100 patients** had well-controlled disease **(UAS7≤6)** at Week 52, and **98** were included in **treatment-free follow-up** period analysis

Demographics and baseline characteristics	Extension study[1] Remibrutinib 100 mg b.i.d. (N=194)
Age (years)	45.5±14.12
Sex (female), n (%)	139 (71.6)
Weight (kg)	77.8±17.86
Duration of CSU (years)	5.8±6.68
UAS7 score	27.9±8.23
Previous exposure to anti-IgE therapy, n (%)	54 (27.8)

Data are expressed as mean±SD unless stated otherwise.

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.

1. Jain V, et al. *J Allergy Clin Immunol*. Accepted manuscript. Published online October 12, 2023. doi:10.1016/j. jaci.2023.10.007.

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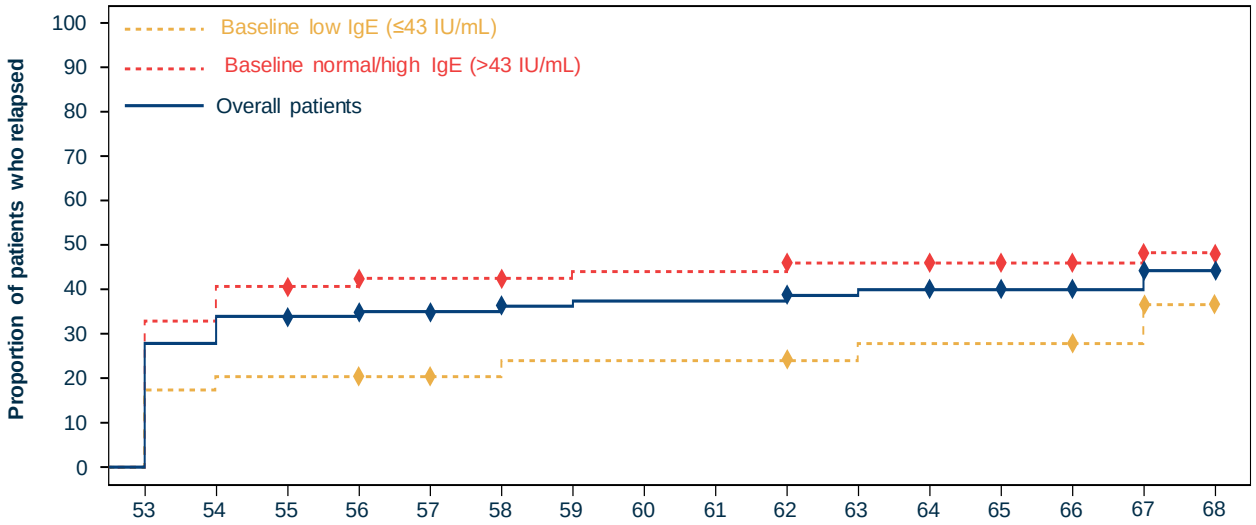
Results

- Of **all patients (n=98)** included in this analysis, KM estimate of cumulative number of patients with relapse was **43.9% (n=41)**; **34.7% (n=34)** experienced **a relapse within the first 4 weeks**
- More patients with a **normal/high IgE (42.2%; 27/64)** at baseline relapsed within the first 4 weeks compared with those with **low baseline IgE levels (20.6%; 7/34)**
- Since **relapse** occurred in **less than 50% of the patients** from **both IgE subgroups**, median time to relapse was not evaluable

Subgroups of patients by baseline IgE normal/high (>43 IU/mL) and low (≤43 IU/mL) levels



Number of patients at risk																
IgE low (≤43 IU/mL)	34	28	27	27	23	22	21	21	21	21	20	19	19	19	17	12
IgE normal/high (>43 IU/mL)	64	43	38	36	33	33	32	31	31	31	29	29	28	27	25	21
Overall patients	98	71	65	63	56	55	53	53	53	52	49	48	47	46	42	33

b.i.d., twice daily; IgE, immunoglobulin E; KM, Kaplan-Meier

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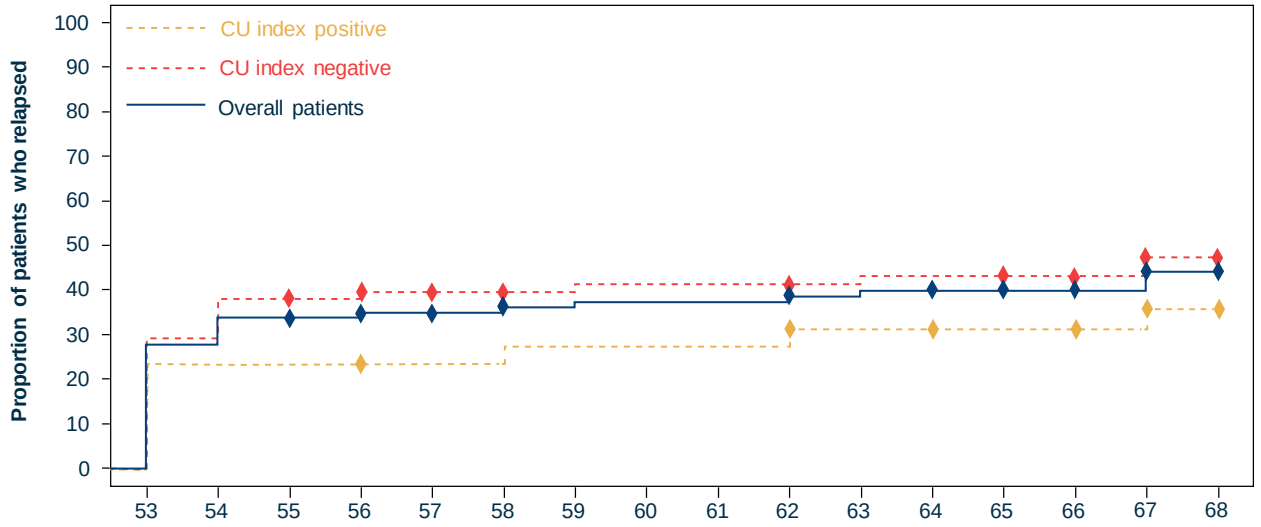
Results

- The **relapse rate** within the first 4 weeks was **39.7%** (27/68) for patients with a **CU index negative** status at baseline versus **23.3%** (7/30) for those with a **CU index positive** status
- Since **relapse** occurred in **less than 50%** of the patients from **both CU index subgroups**, median time to relapse was not evaluable

Subgroups of patients by CU index positive and negative status



Number of patients at risk																
CU index positive	30	23	23	23	20	20	19	19	19	19	17	17	16	16	15	12
CU index negative	68	48	42	40	36	35	34	33	33	33	32	31	31	30	27	21
Overall patients	98	71	65	63	56	55	53	53	53	52	49	48	47	46	42	33

b.i.d., twice daily; CU, chronic urticaria; KM, Kaplan-Meier

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Conclusions

- During **treatment-free follow-up** period when patients were only on background H1-AH treatment and as needed rescue medication, **<50%** of the **patients relapsed** after cessation of remibrutinib at Week 52. Patients who relapse, **relapse quickly** during the **first 4 weeks**. If a patient has **not relapsed** after being **off therapy** for 4 weeks, the **likelihood of relapse thereafter is low**
- Results of this exploratory analysis indicate that patients with markers of **autoallergy (baseline IgE levels >43 IU/mL and CU-index negative [<10])** showed a trend of **higher susceptibility to relapse** in comparison to patients with markers of **autoimmunity (IgE levels ≤43 IU/mL and CU-index positive [≥10])**

AH, antihistamines; CU, chronic urticaria; IgE, immunoglobulin E

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Disclosures

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