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Safety of Remibrutinib in Patients with Chronic Spontaneous Urticaria: Results from the Phase 3 REMIX-1 and REMIX-2 Studies

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INTRODUCTION

- Remibrutinib is a novel, oral, highly selective Bruton's tyrosine kinase inhibitor that has demonstrated superior efficacy vs placebo and favourable safety with up to 24-weeks of treatment in the Phase 3 REMIX-1 and REMIX-2 studies in patients with chronic spontaneous urticaria (CSU) inadequately controlled by H1-antihistamines[1]
- Remibrutinib has shown a favourable safety profile and was well-tolerated in previous clinical studies,[2,3] including REMIX-1 and -2[1]

OBJECTIVE

- To report the pooled analysis of safety data up to Week 24 from final analysis of the Phase 3 REMIX studies in patients with CSU receiving remibrutinib 25 mg twice daily (bid)

METHODS

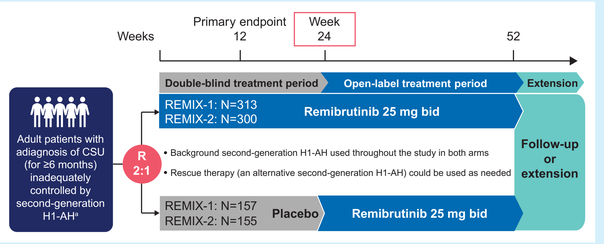
Study design

- REMIX-1 and REMIX-2 are two identical, global, double-blind, placebo-controlled Phase 3 studies (**Figure 1**). Adult patients with CSU inadequately controlled by second-generation antihistamines were randomised 2:1 to oral remibrutinib 25 mg bid or placebo for 24 weeks, followed by an open-label treatment with remibrutinib 25 mg bid for 28 weeks (patients on placebo transitioned to remibrutinib at Week 24)

Study assessments and data analysis

- Safety assessments comprised adverse events (AEs), serious AEs (SAEs), and laboratory parameters (all data presented as remibrutinib vs placebo)
- Data were analyzed using summary statistics

Figure 1. Study design[1]



AH, antihistamine; bid, twice daily; CSU, chronic spontaneous urticaria; H1, histamine 1; HSS7, weekly Hives Severity Score; ISS7, weekly Itch Severity Score; N, number of randomized patients; R, randomisation; UAS7, weekly Urticaria Activity Score.

[a]Presence of itch and hives for ≥6 consecutive weeks prior to screening despite the use of a second-generation H1-antihistamines; UAS7 score ≥16, ISS7 score ≥6, and HSS7 score ≥6 during the 7 days prior to randomization (day 1).

RESULTS

- This pooled safety analysis included randomised patients who received at least one dose of remibrutinib 25 mg bid (N=606) or placebo (N=306) for 24 weeks in the REMIX-1 & 2 studies
- Patient demographics and baseline disease characteristics were well-balanced between remibrutinib and placebo in both REMIX studies (**Table 1**)

Table 1. Patient demographics and baseline characteristics

This table has been published in the New England Journal of Medicine.
It can be found by clicking here: Metz M, et al. N Engl J Med. 2025;392(10):984-94).

- During the 24-week double-blind period, the duration of treatment exposure, percentage of AEs, SAEs and AEs leading to treatment discontinuation were comparable between remibrutinib and placebo groups **(Table 2)**
- No SAE was considered related to study medication
- AEs were predominantly mild or moderate with severe AEs reported in 2.8% of patients from remibrutinib and 2.3% from placebo groups

Table 2. Overview of safety from 24-week double-blind period

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Most common AEs

- Most common AEs by system organ class (SOC) and preferred term (PT) were generally comparable between remibrutinib and placebo groups **(Table 3)**
- Infections were the most commonly reported AEs, primarily those affecting respiratory tract – COVID-19 (studies conducted during COVID-19 pandemic) and nasopharyngitis
- Petechiae (3.8% vs 0.3%) and nasopharyngitis (6.6% vs 4.6%) were more frequent with remibrutinib, and urticaria (representing CSU exacerbations, 2.5% vs 4.9%) was more common in the placebo group
  - Petechia and, similarly, AEs of purpura and ecchymosis (both reported in < 3% of patients in any treatment group), were all mild or moderate in severity and, when seen, tended to occur early on treatment (within first 3 months)
- Newly occurring liver transaminase (ALT or AST) elevations were balanced between remibrutinib and placebo during the double-blind treatment period (**Table 4**)
- All observed liver transaminase (ALT or AST) elevations across both studies were asymptomatic and transient/reversible

Table 3. Most common (≥10%) AEs with remibrutinib treatment by SOC ≥10% and/or PT ≥3% in any treatment group

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Table 4. Newly occurring liver transaminase elevations[a]

This table has been published in the New England Journal of Medicine.
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CONCLUSIONS

- In the pivotal REMIX studies, remibrutinib showed favourable safety and tolerability with up to 24 weeks of treatment, consistent with the known safety profile
- Remibrutinib has the potential to become a well-tolerated novel oral treatment option for patients with CSU inadequately controlled by second-generation H1-antihistamines

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