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# Effect of remibrutinib treatment on disease activity in chronic spontaneous urticaria: Data from the Phase 3 REMIX-1 and REMIX-2 studies

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†Prof. Maurer M sadly passed away during the development of this poster. His invaluable contributions to this study are honored with his recognition as a co-author in memoriam.

## KEY FINDINGS AND CONCLUSIONS

- Remibrutinib was associated with a fast decrease of 10.5 points in UAS7, 5.0 points in ISS7 and 5.5 points in HSS7, a threshold which is considered as clinically meaningful improvement (MID), as early as week 1 in more than half of the patients vs placebo in the Phase 3 REMIX-1 and REMIX-2 studies
- The majority of patients on remibrutinib achieved a decrease of 10.5 points in UAS7, 5.0 points in ISS7 and 5.5 points in HSS7 at any time between weeks 0–12
- Remibrutinib has the potential to be an effective oral treatment option that achieves fast clinically meaningful improvements (reduction) in CSU disease activity as early as week 1

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## INTRODUCTION

- Remibrutinib, a novel, highly selective, oral, Bruton's tyrosine kinase inhibitor, has previously shown superior efficacy versus placebo at week 12 and a favourable safety profile in the 24-week double-blind (DB) period of the pivotal Phase 3 REMIX-1 and REMIX-2 studies in patients with chronic spontaneous urticaria (CSU) who remained symptomatic despite treatment with second-generation H1-antihistamines[1]
  - Improvements in UAS7, ISS7, and HSS7 occurred fast (observed as early as week 1 in a post hoc analysis) with remibrutinib and were sustained to week 52[1]
- Treatment response for CSU in clinical studies is often evaluated by the weekly Urticaria Activity Score (UAS7: range 0–42), with a higher score reflecting higher disease activity[2]
  - A decrease in the range of 9.5–10.5 points in UAS7, 4.5–5.0 points in ISS7 and 5.0–5.5 points in HSS7 (minimal important difference [MID]) is commonly considered to indicate a meaningful clinical response to therapy[2]

## OBJECTIVE

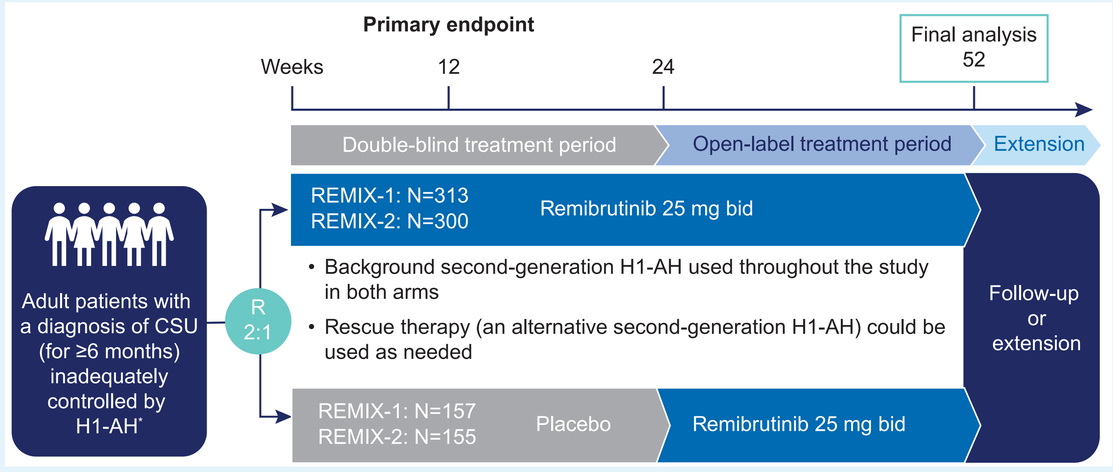
- To assess early clinically meaningful improvement (MID) in CSU disease activity with remibrutinib 25 mg twice daily (bid) vs placebo in the Phase 3 REMIX-1 and REMIX-2 studies

## METHODS

### Study Design

- REMIX-1 and REMIX-2 are two identical, global, double-blind, placebo-controlled Phase 3 studies of remibrutinib 25 mg bid administered orally (**Figure 1**). Adult patients with CSU who remained symptomatic despite treatment with 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)

**Figure 1. Study design[1]**




*Presence of itch and hives for ≥6 consecutive weeks prior to screening despite the use of a second-generation H1-antihistamine; UAS7 score ≥16, ISS7 score ≥6 and HSS7 score ≥6 during the 7 days prior to randomisation (day 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 patients (Randomised set); R, randomisation; UAS7, weekly Urticaria Activity Score.

### Study Assessments and Data Analysis

- The proportion of patients who achieved a decrease of 10.5 points in UAS7, 5.0 points in ISS7 and 5.5 points in HSS7 early (between weeks 0–1 and weeks 0–2) and at any time up to week 12 (between weeks 0–12) was assessed
- Kaplan-Meier plot of time to first decrease of 10.5 points in UAS7, 5.0 points in ISS7 and 5.5 points in HSS7, and log-rank test to compare the two treatment groups

## RESULTS

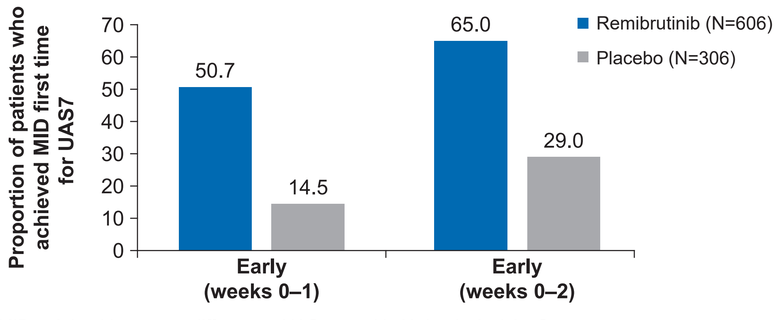
- This pooled analysis included randomised patients who received at least one dose of remibrutinib 25 mg bid (N=606) or placebo for 24 weeks (N=306) in the REMIX-1 and 2 studies (Full analysis set)
- Patient demographics and baseline disease characteristics were well balanced between the remibrutinib and placebo groups in both REMIX studies (**Table 1**)
- Half of all patients achieved a decrease of 10.5 points in UAS7 as early as week 1 with remibrutinib (50.7% **Figure 2**); at any time between weeks 0–12 a decrease of 10.5 points in UAS7 (87.1%) vs placebo (69.6%) was seen.
- Median time to first decrease of UAS7 by 10.5 points was significantly shorter for remibrutinib vs placebo (1 week vs 5 weeks; nominal *P*<0.001; **Figure 3**)
- Similarly, half of all patients achieved a decrease of 5.0 points in ISS7 as early as week 1 with remibrutinib (**Figure 4**)
- Median time to first decrease of ISS7 by 5.0 points was significantly shorter for remibrutinib vs placebo (1 week vs 4 weeks; nominal *P*<0.001; **Figure 5**)
- More than half of all patients achieved a decrease of 5.5 points in HSS7 as early as week 1 with remibrutinib (**Figure 6**)
- Median time to first decrease of HSS7 by 5.5 points was significantly shorter for remibrutinib vs placebo (1 week vs 5 weeks; nominal *P*<0.001; **Figure 7**)

**Table 1. Patient demographics and baseline characteristics**

| Patient demographics[a] | Pooled REMIX-1 and REMIX-2 | |
|---|---|---|
| | Remibrutinib 25 mg bid (N=606) | Placebo (N=306) |
| Age (years), mean±SD | 43.3±14.4 | 43.7±14.1 |
| Female, n (%) | 403 (66.5) | 204 (66.7) |
| Duration of CSU (years), mean±SD | 6.2±8.6 | 5.3±6.7 |
| UAS7, mean±SD | 30.6±7.8 | 29.7±7.6 |
| ISS7, mean±SD | 14.6±4.2 | 14.1±4.05 |
| HSS7, mean±SD | 16.0±4.6 | 15.6±4.5 |
| Previous experience of angioedema, n (%) | 313 (51.7) | 135 (44.1) |
| Previous exposure to anti-IgE biologics, n (%) | 187 (30.9) | 98 (32.0) |

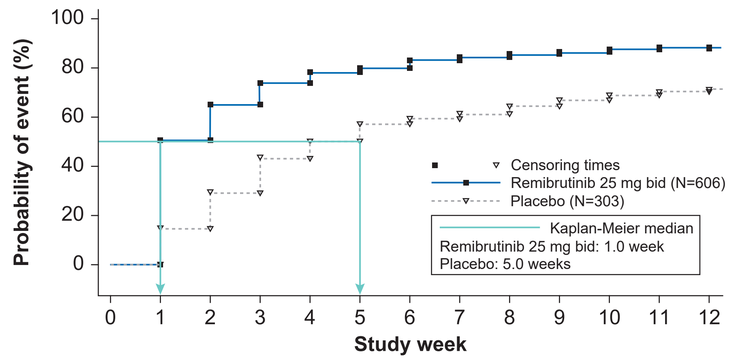
[a]Full analysis set.
bid, twice daily; CSU, chronic spontaneous urticaria; HSS7, weekly Hives Severity Score; IgE, immunoglobulin E; ISS7, weekly Itch Severity Score; SD, standard deviation; UAS7, weekly Urticaria Activity Score.

**Figure 2. Proportion of patients who achieved a decrease of 10.5 points in UAS7 at early timepoints (Observed data)**




MID, minimal important difference; UAS7, weekly Urticaria Activity Score.

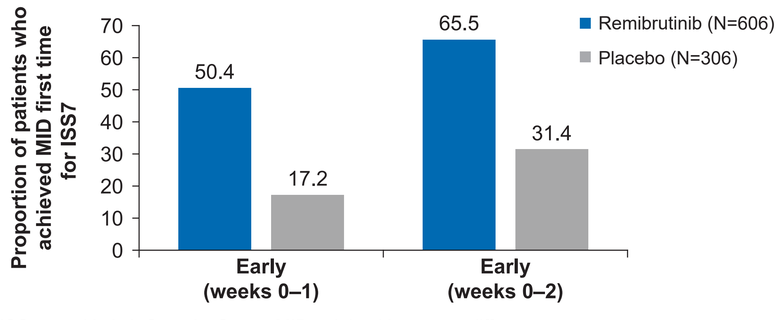
**Figure 3. Kaplan-Meier plot of time to first decrease of 10.5 points in UAS7 (Observed data)**




Number of patients still at risk

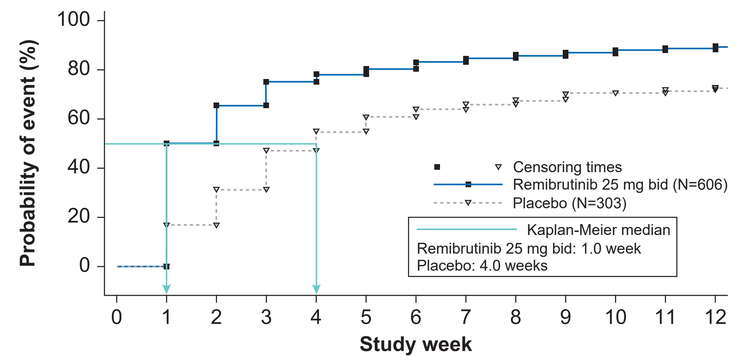
| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Remibrutinib 25 mg bid | 606 | 298 | 208 | 151 | 126 | 110 | 93 | 85 | 80 | 75 | 68 | 64 | 62 |
| Placebo | 303 | 259 | 211 | 169 | 147 | 126 | 119 | 111 | 101 | 94 | 86 | 82 | 80 |

**Figure 4. Proportion of patients who achieved a decrease of 5.0 points in ISS7 at early timepoints (Observed data)**




ISS7, weekly Itch Severity Score; MID, minimal important difference.

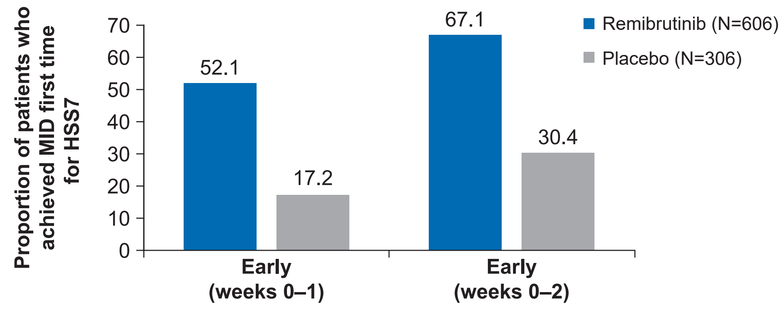
**Figure 5. Kaplan-Meier plot of time to first decrease of 5.0 points in ISS7 (Observed data)**




Number of patients still at risk

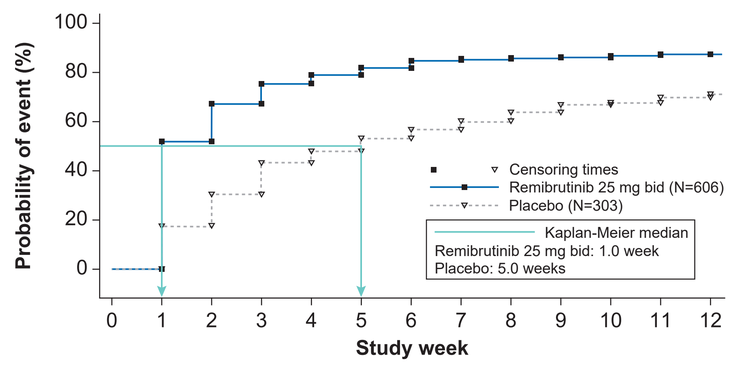
| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Remibrutinib 25 mg bid | 606 | 300 | 205 | 145 | 129 | 109 | 94 | 84 | 78 | 72 | 67 | 62 | 58 |
| Placebo | 303 | 251 | 204 | 157 | 134 | 116 | 106 | 98 | 92 | 85 | 81 | 78 | 76 |

**Figure 6. Proportion of patients who achieved a decrease of 5.5 points in HSS7 at early timepoints (Observed data)**




HSS7, weekly Hives Severity Score; MID, minimal important difference.

**Figure 7. Kaplan-Meier plot of time to first decrease of 5.5 points in HSS7 (Observed data)**




Number of patients still at risk

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Remibrutinib 25 mg bid | 606 | 290 | 194 | 142 | 120 | 98 | 81 | 79 | 76 | 74 | 70 | 67 | 66 |
| Placebo | 303 | 251 | 207 | 169 | 152 | 137 | 125 | 115 | 103 | 94 | 90 | 84 | 80 |

## References

1. Metz M, et al. Oral presentation at: EACCI congress 2024; 31 May–03 June 2024; Valencia, Spain. Abstract 100107.
2. Mathias SD, et al. *Ann Allergy Asthma Immunol*. 2012;108(1):20–24.

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## Disclosures

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