Oral presentation
OP. 010

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Safety and efficacy of remibrutinib in Japanese patients with chronic spontaneous urticaria (BISCUIT study/interim analysis)

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Conflict of interest disclosure

☐ I have no, real or perceived, direct or indirect conflicts of interest that relate to this presentation.

☑ I have the following, real or perceived direct or indirect conflicts of interest that relate to this presentation:

Type of affiliation / financial interest	Name of commercial company
Receipt of grants/research supports:	
Receipt of honoraria or consultation fees:	Kaken, Kyorin, Kyowa Kirin, Meiji Seika Pharma, Mitsubishi-Tanabe, Nihon Pharmaceutical, Novartis, Sanofi, Taiho
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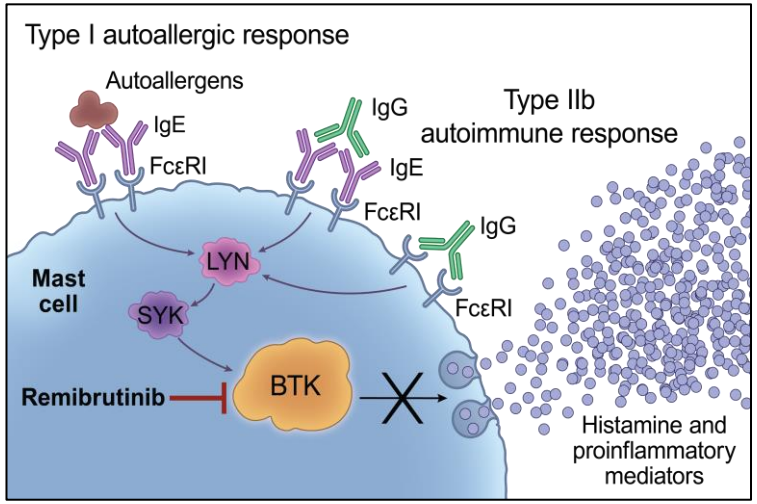
Introduction

- The Japanese Dermatological Association guideline for the treatment of urticaria 2018 defines CSU as ‘spontaneous urticaria persistent for ≥6 weeks’[1]
- In the Phase 3 REMIX-1 (NCT05030311) and REMIX-2 (NCT05032157) studies, remibrutinib demonstrated statistically significant superiority in both primary endpoint scenarios (UAS7 and ISS7/HSS7 at Week 12) versus placebo in patients with CSU remaining symptomatic with second-generation H1-AHs[2]
- To satisfy regulatory requirements in Japan, the BISCUIT study (NCT05048342) aims to assess the safety, tolerability, and efficacy of remibrutinib over 52 weeks in adult Japanese patients with CSU who remain symptomatic despite H1-AH treatment

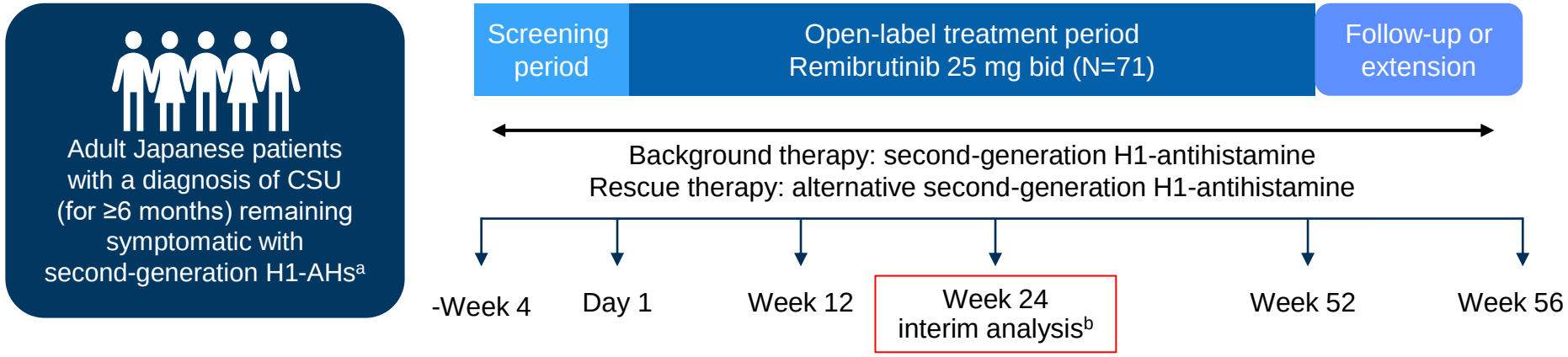


Objective: To present the interim analysis (Week 24) data of the BISCUIT study.

AH, antihistamine; BTK, Bruton’s tyrosine kinase; CSU, chronic spontaneous urticaria; FcεRI, high-affinity IgE receptor; H1, histamine-1; Ig, immunoglobulin; LYN, LCK/YES novel tyrosine kinase; SYK, spleen tyrosine kinase.

1. Hide M, et al. *Arerugi*. 2018;67(10):1394–1398. 2. Metz, M. Oral presentation at the annual congress of the European Academy of Allergy and Clinical Immunology (EAACI) 2024; 31 May–03 June 2024. Valencia, Spain.

BISCUIT study design



BISCUIT is a single country, multicentre, open-label, single-arm Phase III study evaluating remibrutinib 25 mg bid in patients with CSU

Primary endpoint

- To evaluate the safety of remibrutinib (25 mg bid) in CSU patients

Secondary endpoints (at Week 12)

- Change from baseline in UAS7,[c] ISS7 and HSS7
- Proportion of patients achieving
  - well-controlled disease (UAS7≤6)
  - complete response (UAS7=0)

AH, antihistamine; bid, twice daily; CSU, chronic spontaneous urticaria; H1, histamine 1; HSS7, weekly Hives Severity Score; ISS7, weekly Itch Severity Score; 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-AH; UAS7 score ≥16, ISS7 score ≥6, and HSS7 score ≥6 during the 7 days prior to randomisation (day 1). [b]An interim analysis was conducted when all patients had completed Week 24 visit or discontinued early. [c]The UAS7 is the sum of the HSS7 and the ISS7 and is a widely accepted tool for assessing symptoms of CSU and ranges from 0 to 42 (a higher score indicates more activity).

Patient demographics and baseline characteristics (safety set)

Characteristic	Remibrutinib 25 mg bid (N=71)
Age (years); mean±SD	43.5±12.52
Gender (female); n (%)	54 (76.1)
Baseline UAS7 score; mean±SD	28.4±7.18
Baseline UAS7 disease status; n (%)	
Moderate disease (16 ≤ UAS7 < 28)	32 (45.1)
Severe disease (28 ≤ UAS7 ≤ 42)	39 (54.9)
Baseline ISS7 score; mean±SD	12.6±3.46
Baseline HSS7 score; mean±SD	15.8±4.75
Duration of CSU (years); mean±SD	4.7±4.34
Previous exposure to anti-IgE biologics for CSU; n (%)	6 (8.5)
Previous experience of angioedema; n (%)	5 (7.0)
Diagnosis of concomitant CIndU; n (%)	9 (12.7)

bid, twice daily; CIndU; chronic inducible urticaria; CSU, chronic spontaneous urticaria; HSS7, weekly Hives Severity Score; ISS7, weekly Itch Severity Score; IgE, immunoglobulin E; UAS7, weekly Urticaria Activity Score.

Overview of AEs

	Remibrutinib 25 mg bid (N=71), n (%)
Patients with AE(s)	60 (84.5%)
Mild	36 (50.7%)
Moderate	24 (33.8%)
Severe	0
SAEs	3 (4.2%)
Discontinuation of study treatment due to any AE(s)	1 (1.4%)

- The median duration of exposure for remibrutinib 25 mg bid was 24 weeks
- All AEs were mild or moderate, none were severe
- All three SAEs (Meniere's disease, epiretinal membrane, and rhegmatogenous retinal detachment) were considered unrelated to remibrutinib
- One AE leading to study treatment discontinuation was a case of (worsening) moderate dermatitis atopic and was not considered to be related to the study treatment by the investigator

AE, adverse event; bid, twice daily; SAE, serious adverse event.

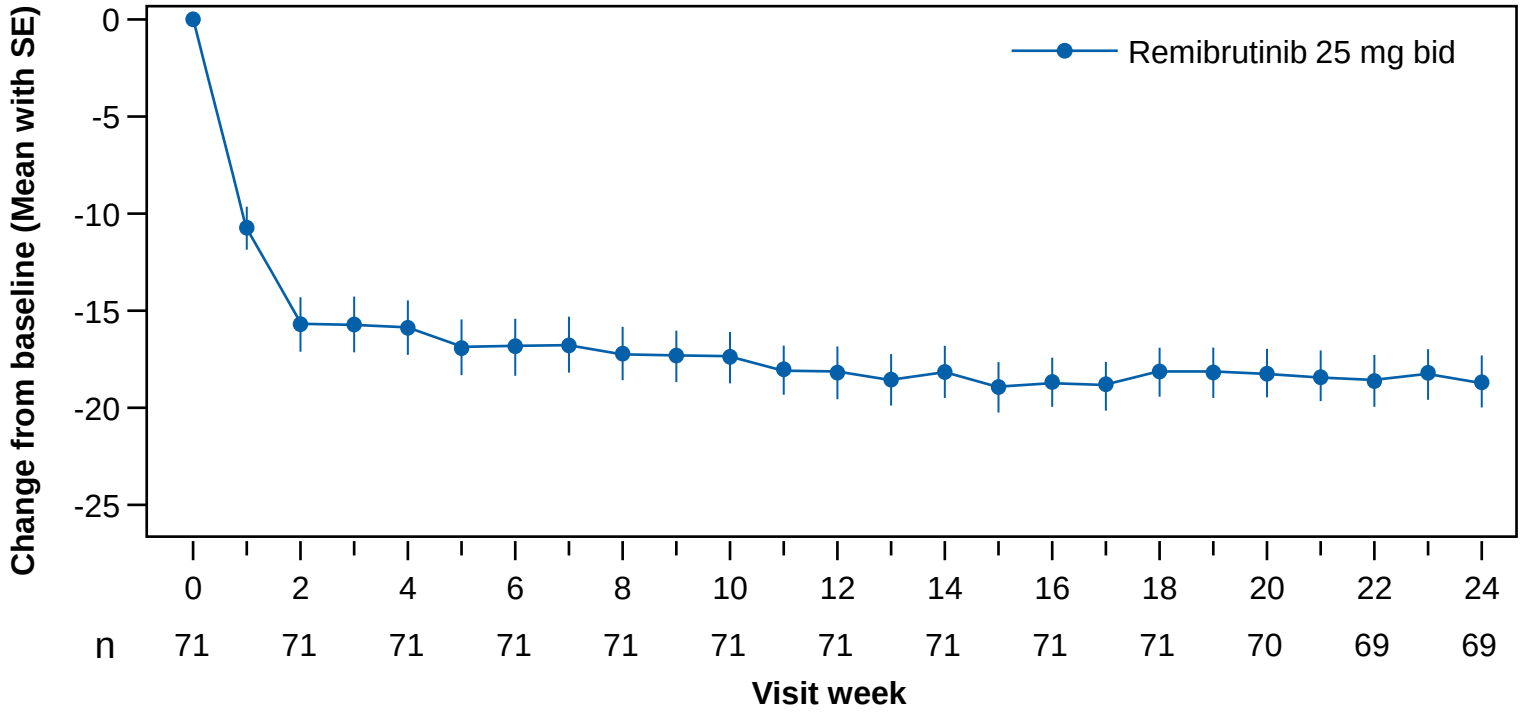
Most common AEs by system organ class (≥5%; safety set)

Preferred terms	Remibrutinib 25mg bid N=71, n (%)
COVID-19	10 (14.1)
Headache	9 (12.7)
Dermatitis atopic	6 (8.5)
Diarrhoea	6 (8.5)
Acne	5 (7.0)
Eczema	5 (7.0)
Dyslipidaemia	4 (5.6)
Eczema asteatotic	4 (5.6)
Nasopharyngitis	4 (5.6)
Purpura	4 (5.6)
Tonsillitis	4 (5.6)

- Most common AE by primary SOC was skin and subcutaneous tissue disorders (49.3%) represented by PT such as dermatitis atopic, acne, eczema, eczema steatotic, purpura
- Study was conducted during the COVID-19 pandemic

Preferred terms are sorted in descending frequency. A patient with multiple AEs within a preferred term is counted only once for the preferred term.
MedDRA Version 26.0 has been used for the reporting.
AE, adverse event; bid, twice daily; MedDRA, medical dictionary for regulatory activities.

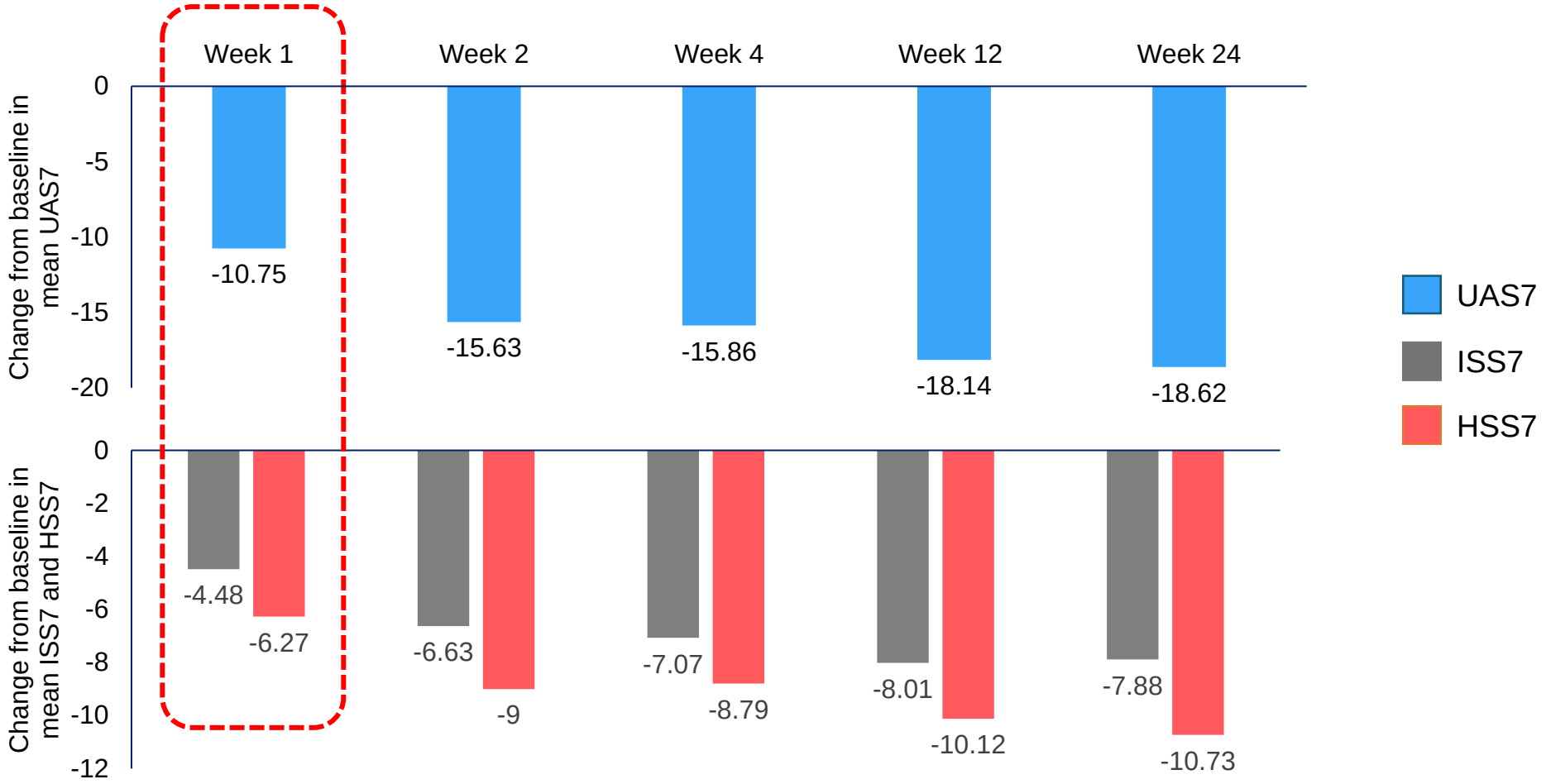
Change from baseline in mean UAS7 with remibrutinib



The absolute mean UAS7 at baseline was 28.37, with an improvement observed as early as Week 1 (mean change from baseline −10.75), further improving at Week 12 (−18.1) and sustained through Week 24 (−18.6).

Week 0 corresponds to the baseline value.
bid, twice daily; n, number of evaluable patients at each visit; SE, standard error; UAS7, weekly Urticaria Activity Score.

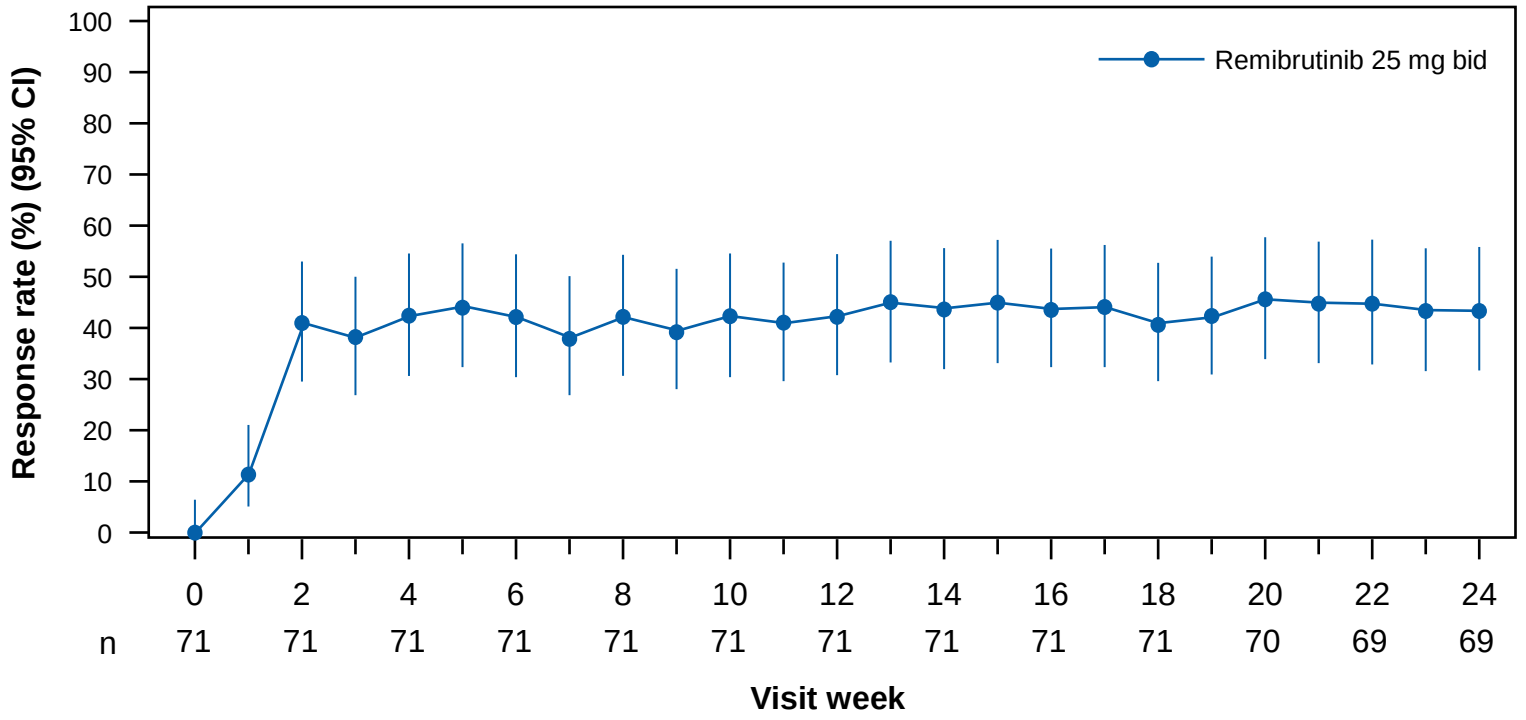
Early improvement in USA7, ISS7 and HSS7 with remibrutinib



Mean baseline values: UAS7 = 28.37; ISS7 = 12.58; HSS7 = 15.80.

HSS7, weekly Hives Severity Score; ISS7, weekly Itch Severity Score; UAS7, weekly Urticaria Activity Score.

Patients achieving well-controlled disease (UAS7 ≤6) (%) with remibrutinib

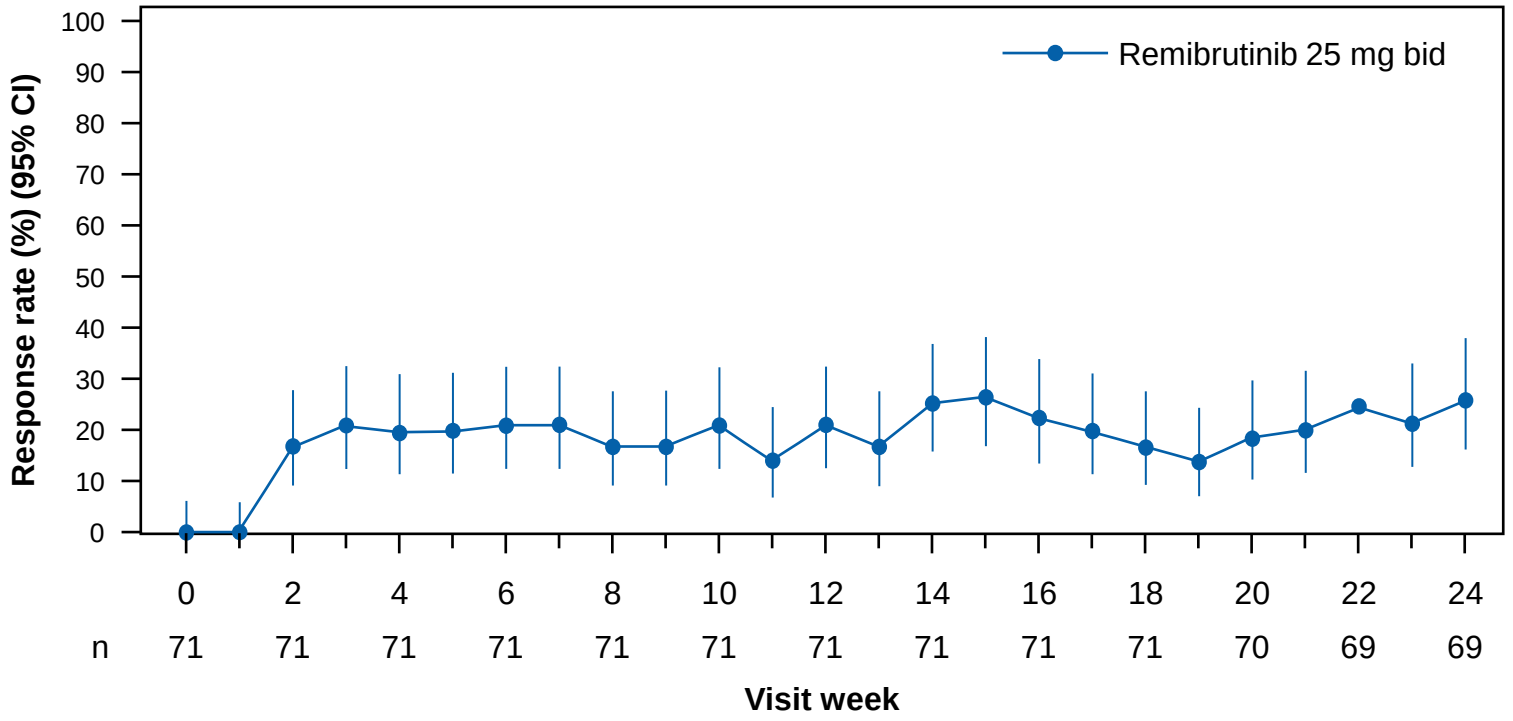


43.5%
of patients achieved UAS7≤6

A total of 29/71 patients (40.8%) achieved well-controlled disease (UAS7 ≤ 6) as early as Week 2 and sustained through until Week 12 (30/71, 42.3%) and Week 24 (30/69, 43.5%).

Week 0 corresponds to the baseline value
bid, twice daily; n, number of evaluable patients at each visit; UAS7, weekly urticaria activity score.

Patients achieving a complete response (UAS7=0) (%) with remibrutinib



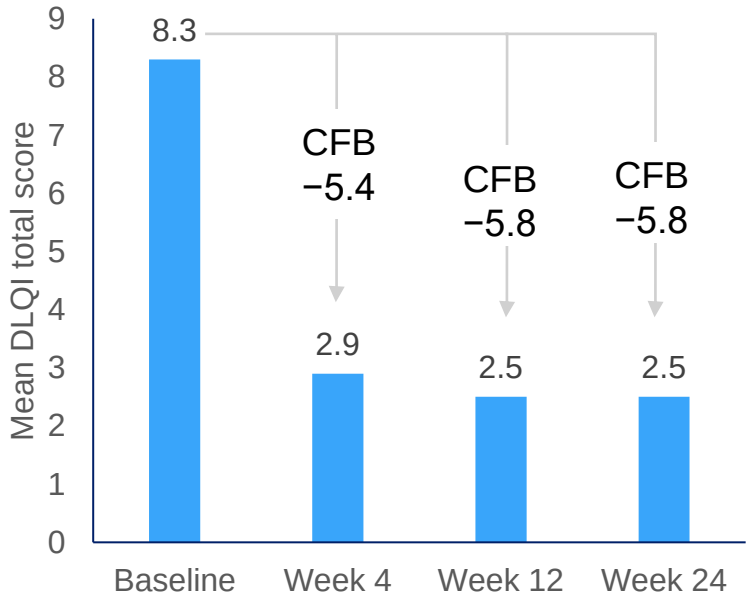
26.1%
of patients achieved UAS7=0

A total of 12/71 patients (16.9%) achieved complete absence of itch and hives (UAS7 = 0) as early as Week 2, which increased further at Week 12 (15/71, 21.1%) and sustained through Week 24 (18/69, 26.1%).

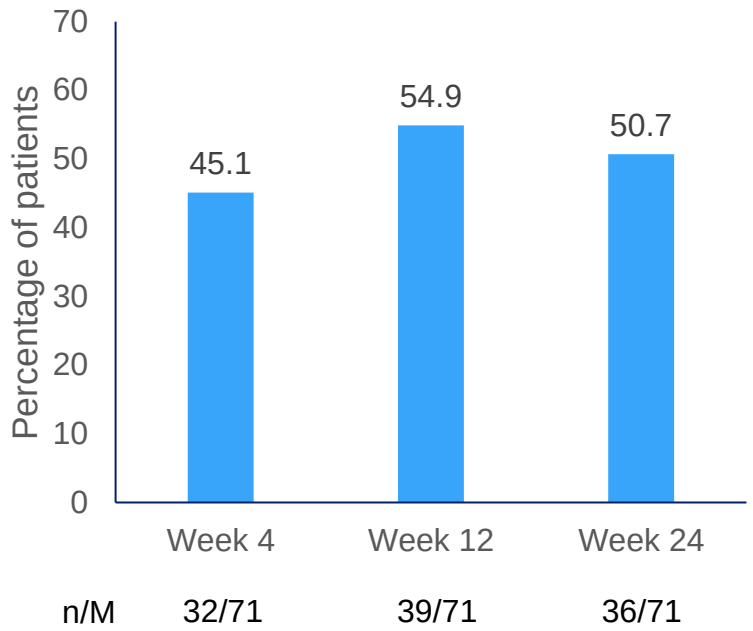
Week 0 corresponds to the baseline value.
bid, twice daily; n, number of evaluable patients at each visit; UAS7, weekly urticaria activity score.

Majority of patients on remibrutinib achieved no impact of CSU on dermatology-related QoL

Mean DLQI scores



Proportion of patients achieving DLQI = 0–1



n/M	32/71	39/71	36/71

The mean change from baseline in the DLQI total score was −5.8 at Week 24; importantly, more than 50% patients reported no impact of CSU on their QoL.

For each post-baseline week, only patients with a value at both baseline and the respective week are included.
CFB, change from baseline; CSU, chronic spontenous urticaria; DLQI, Dermatology Life Quality Index; QoL, qualtiy of life.

CONCLUSIONS

- The BISCUIT **interim analysis at Week 24** showed **favourable safety and tolerability** profile of **remibrutinib 25 mg bid** in adult **Japanese** patients with **CSU** remaining symptomatic despite H1-AH treatment, findings consistent with the known safety profile of remibrutinib
- Most of the **AEs** were either **mild** or **moderate**, all SAEs were considered not related to study treatment and were uncommon
- Patients experienced **improvements in symptoms** with remibrutinib, **as early as Week 1**, **sustained up to Week 24**, enabling a substantial proportion of Japanese patients to achieve well-controlled disease
- **Remibrutinib** also enhanced the QoL of patients, with **half of all patients** at Week 24 experiencing no further impact of CSU on their QoL (**DLQI = 0–1**), despite reporting poor QoL at baseline
- These findings suggest the potential of remibrutinib to become **a novel oral treatment option** that provides **fast** (observed as early as Week 1) and **sustained symptom relief** for **Japanese** patients with **CSU**

AE, adverse events; CSU, chronic spontaneous urticaria, DLQI, Dermatology Life Quality Index; QoL, quality of life; SAE, serious AE; UAS7, weekly urticaria activity score.