EAACI Congress 2024

Valencia, Spain

31 May - 3 June

Revolutionising Patient Care
Through the Power of Data Science

EAACI
EUROPEAN ACADEMY OF ALLERGY AND CLINICAL IMMUNOLOGY

#EAACIcongress

www.eaaci.org

Effect of Remibrutinib on Sleep and Daily Activities in Patients with Chronic Spontaneous Urticaria: Results from the Phase 3 Studies

Presenter: Prof. Ana M Giménez-Arnau

Ana M Giménez-Arnau,[1] Michihiro Hide,[2, 3] Mark Lebwohl,[4] Gordon Sussman,[5] Sarbjit Saini,[6] Sibylle Haemmerle,[7] Noriko Seko,[8] Pengpeng Wang,[9] El-Djouher Martzloff,[7] Marcus Maurer[10, 11]

[1]Department of Dermatology, Hospital del Mar Research Institute, Universitat Pompeu Fabra, Barcelona, Spain; [2]Department of Dermatology, Hiroshima University, Hiroshima, Japan; [3]Department of Dermatology, Hiroshima City Hiroshima Citizens Hospital, Hiroshima, Japan; [4]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, USA; [5]Division of Allergy and Clinical Immunology, University of Toronto, Toronto, Ontario, Canada; [6]Johns Hopkins Asthma and Allergy Center, Baltimore, Maryland, USA; [7]Novartis Pharma AG, Basel, Switzerland; [8]Novartis Pharma KK, Tokyo, Japan; [9]Novartis (China) Biomedical Research, Shanghai, China; [10]Urticaria Center of Reference and Excellence (UCARE), Institute of Allergology, Charité–Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt–Universität zu Berlin, Berlin, Germany; [11]Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Immunology and Allergology, Berlin, Germany.

ORAL Session OAS10 (000546)
Advances in Chronic Urticaria treatment
Saturday, 01 June 2024

Table of Contents

1 Disclosures and Acknowledgements

In relation to this presentation, the following real or perceived conflicts of interest were declared:

AGA is or recently was a speaker and/or advisor for and/or has received research funding from Almirall, Amgen, AstraZeneca, Avene, Celldex, Escient Pharmaceutials, Genentech, GSK, Instituto Carlos III- FEDER, Leo Pharma, Menarini, Mitsubishi Tanabe Pharma, Novartis, Sanofi–Regeneron, Servier, Thermo Fisher Scientific and Uriach Pharma / Neucor; **MH** has received lecture and/or consultation fees from Kyowa-Kirin, Kaken Pharmaceutical, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Novartis, TAIHO Pharmaceutical, Teikoku Seiyaku and Sanofi/Regeneron; **ML** is an employee of Mount Sinai and receives research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant Sciences, Eli Lilly, Incyte, Janssen Research & Development, LLC, Ortho Dermatologics, Regeneron, and UCB, Inc., and is a consultant for Aditum Bio, Almirall, AltruBio Inc., AnaptysBio, Arcutis, Aristea Therapeutics, Arrive Technologies, Avotres Therapeutics, BiomX, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Dr. Reddy's Laboratories, Evelo Biosciences, Evommune, Inc., Facilitation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Helsinn Therapeutics, Hexima Ltd., LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Seanergy and Verrica; **GS** has received research support from Aimmune, Amgen, AstraZeneca, DBV Technologies, Genentech, Kedrion S.p.A, Leo Pharma, Novartis, Nuvo Pharmaceuticals, Sanofi, Stallergenes, Merck, Schering Plough, Regeneron and ALK; is a medical advisor and/or has received payment for lectures from Merck, Novartis, CSL Behring, Pfizer, Anaphylaxis Canada, the Allergy Asthma and Immunology Society of Ontario and the Canadian Hereditary Angioedema Network; **SS** has received grant/research/clinical trial support from the National Institutes of Health, Novartis, Sanofi, Amgen, and Regeneron and is a consultant/advisory board member for Allakos, Granular Therapeutics, Novartis, Aquestive, Regeneron, Escient, Innate, Celltrion and Sanofi; **SH** and **E-D M** are employees of Novartis Pharma AG; **NS** is an employee of Novartis Pharma KK; **PW** is an employee of Novartis (China) Biomedical Research; **MM** is or recently was a speaker and/or advisor for and/or has received research funding from Allakos, Alvotech, Amgen, Aquestive, Aralez, AstraZeneca, Bayer, Celldex, Celltrion, Evommune, GSK, Ipsen, Kyowa Kirin, Leo Pharma, Lilly, Menarini, Mitsubishi Tanabe Pharma, Moxie, Noucor, Novartis, Orion Biotechnology, Resoncance Medicine, Sanofi/Regeneron, Septerna, Third HarmonicBio, ValenzaBio, Yuhan Corporation and Zurabio.

We thank all the study investigators and patients for their participation in these clinical studies

- Editorial and medical writing support was provided by Suparna Mukherjee and Mohammad Fahad Haroon (both of Novartis Healthcare Pvt. Ltd., Hyderabad, India) in accordance with Good Publication Practice (GPP3) guidelines (www.ismpp.org/gpp3). The final responsibility for the content lies with the authors
- This study is funded by Novartis Pharma AG, Basel, Switzerland

Scan to obtain

- **Abstract**
- **Presentation slides**

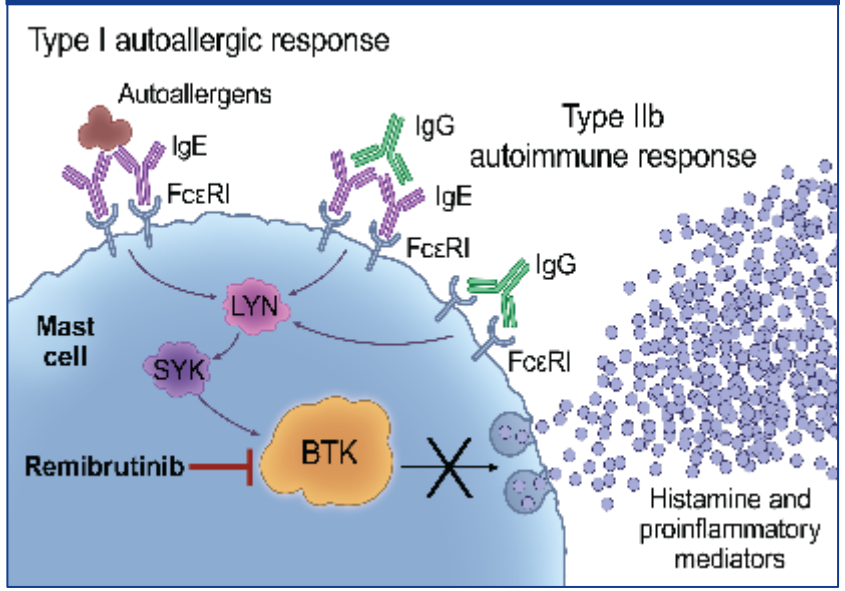
https://bit.ly/UKCEAACI

2 Introduction

CSU symptoms can adversely affect sleep and daily activities[1,2]

- **CSU** causes substantial **sleep interference,** which occurs almost **twice as frequently** as that seen in **individuals without CSU[2]**
- **Reduction** of **urticaria disease activity** helps to **alleviate sleep** and **daily activity** interference[1]
- **Remibrutinib** is an **oral, highly selective Bruton's tyrosine kinase inhibitor** that offers early (Week 2) and **sustained symptom control** in patients with CSU who remain symptomatic despite treatment with **second-generation H1-antihistamines.**

Remibrutinib is a novel, oral, highly selective BTK inhibitor



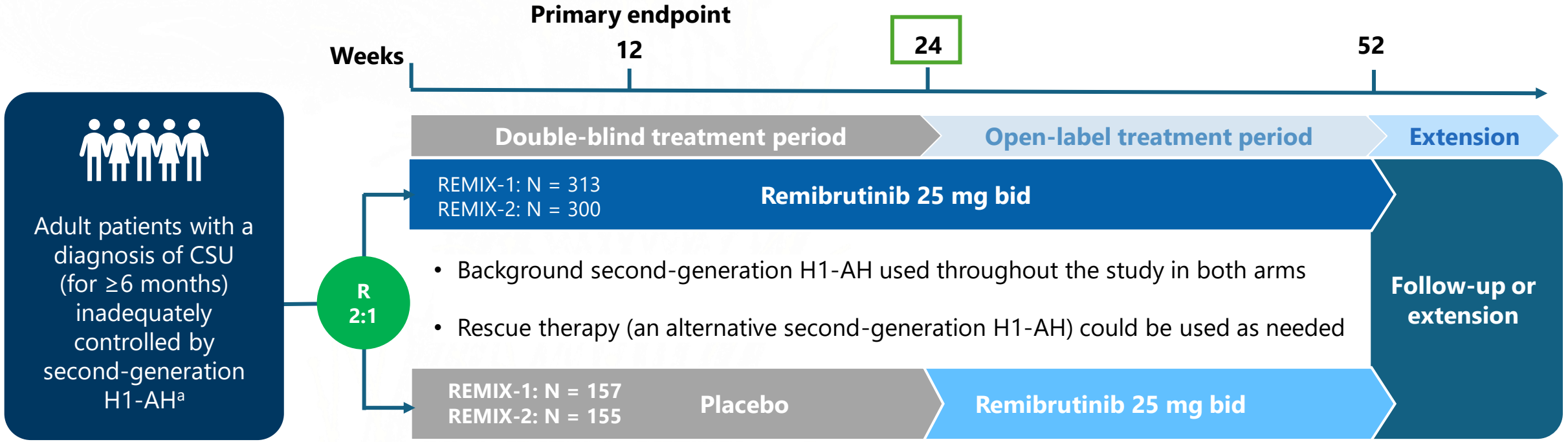
Herein, we present the **effect of remibrutinib** on **sleep and daily activities** in patients with **CSU** up to **Week 24** of the **Phase 3 REMIX-1** (NCT05030311)[3] and **REMIX-2** (NCT05032157)[4] studies

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.Giménez-Arnau A, et al. *Clin Transl Allergy.* 2022;12(2):e12121; 2. Balp MM, et al. Patient. 2015;8(6):551-8. 3. ClinicalTrials.gov. NCT05030311. Accessed April 22, 2024. https://classic.clinicaltrials.gov/ct2/show/NCT05030311. 4. ClinicalTrials.gov. NCT05032157. Accessed April 22, 2024. https://classic.clinicaltrials.gov/ct2/show/NCT05032157

2 Study Design

REMIX-1 and REMIX-2 are two Phase 3, randomised, placebo-controlled studies of remibrutinib 25 mg bid administered orally



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; 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-antihistamine; UAS7 score ≥16, ISS7 score ≥6, and HSS7 score ≥6 during the 7 days prior to randomization (day 1).

3 Assessments

The following exploratory outcomes from REMIX-1 and REMIX-2 were assessed:

Weekly Sleep Interference Score (SIS7)

- **Daily sleep interference** was scored on a **scale of 0 to 3**

Question in patients' e-diary

Q. Please rate how much your hives or itch interfered with your sleep during the past 24 hours.

Scoring	Effect on patients' sleep
0	**No interference**
1	**Mild**, little interference with sleep
2	**Moderate**, awoke occasionally, some interference with sleep
3	Substantial, woke up often, **severe** interference with sleep

Weekly Activity Interference Score (AIS7)

- **Daily activity interference** was scored on a **scale of 0 to 3**
  - *Daily activities could include work, school, sports, hobbies and activities with friends and family*

Q. Please rate how much your hives or itch interfered with your daily activities during the past 24 hours.

Scoring	Effect on patients' daily activities
0	**No interference**
1	**Mild,** little interference with daily activities
2	**Moderate,** some interference with daily activities
3	Substantial, **severe** interference with daily activities

The weekly scores, **SIS7** and **AIS7** ranged from **0 to 21**
Lower scores indicate **lower impact** on sleep or activity

Assessments
- Change from baseline in SIS7 (**CFB-SIS7**) over time
- Proportion of patients with no impact of CSU on sleep (**SIS7=0**) over time

Assessments
- Change from baseline in AIS7 (**CFB-AIS7**) over time
- Proportion of patients with no impact of CSU on daily activities (**AIS7=0**) over time

4 Patient Demographics and Baseline Characteristics

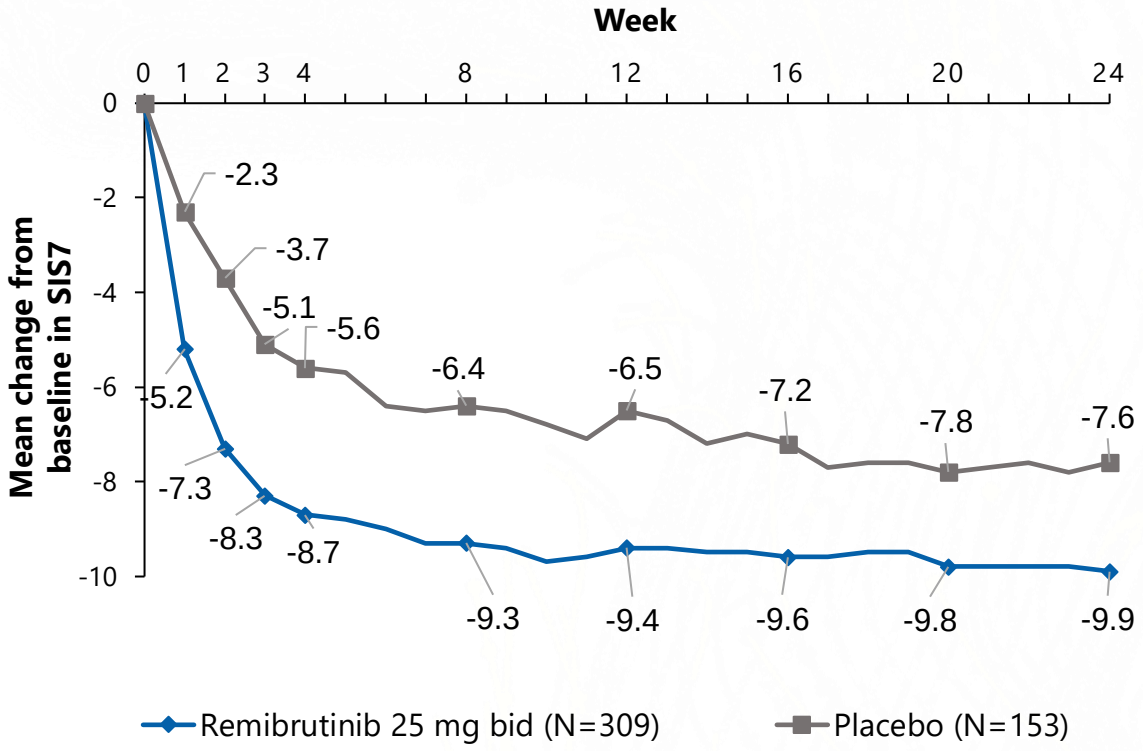
Patient demographics[a]	REMIX-1		REMIX-2	
	Remibrutinib 25 mg bid (N=313)[a]	Placebo (N=157)[a]	Remibrutinib 25 mg bid (N=300)[a]	Placebo (N=155)[a]
Age[a] (years), mean ± SD	**44.6** ± 14.3	**45.9** ± 13.4	**41.9** ± 14.5	**41.3** ± 14.6
Gender[a] (female), n (%)	212 (**67.7**)	109 (**69.4**)	197 (**65.7**)	100 (**64.5**)
Duration of CSU[a] (years), mean ± SD	**6.9** ± 9.3	**6.1** ± 7.1	**5.5** ± 7.6	**4.6** ± 6.2
UAS7[a], mean ± SD	**30.6** ± 7.9	**29.6** ± 7.7	**30.2** ± 8.0	**29.5** ± 7.6
SIS7[b], mean ± SD	**12.7** ± 5.4	**12.3** ± 5.4	**11.8** ± 5.6	**12.1** ± 5.0
AIS7[b], mean ± SD	**13.1** ± 4.9	**13.0** ± 4.8	**12.5** ± 5.3	**12.3** ± 4.8
DLQI[a], mean ± SD	**14.2** ± 7.0	**13.5** ± 6.8	**14.0** ± 7.5	**13.6** ± 6.7

- Patient demographics and baseline characteristics were well-balanced between remibrutinib and placebo in both studies

AIS7, weekly Activity Interference Score; bid, twice daily; CSU, chronic spontaneous urticaria; DLQI, Dermatology Life Quality Index; N, total number of patients in each treatment arm; n, number of evaluable patients; SD, standard deviation; SIS7, weekly Sleep Interference Score; UAS7, weekly Urticaria Activity Score.
[a]Randomised set; [b]Full analysis set (observed data).

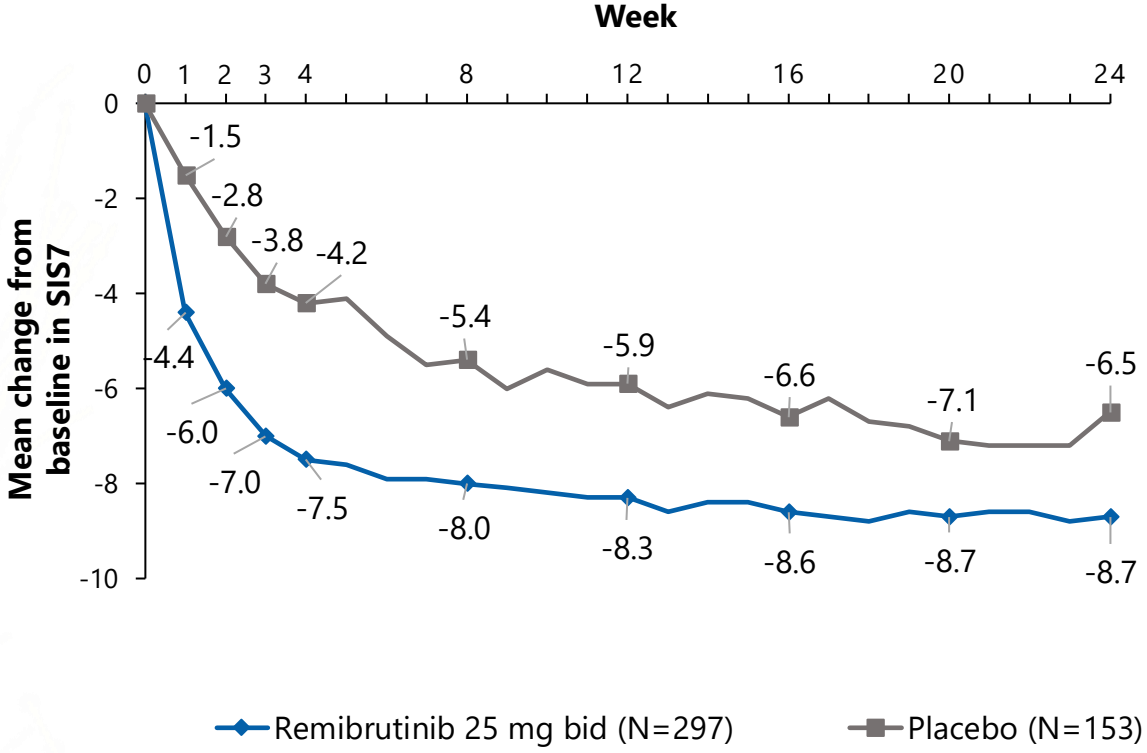
4 Remibrutinib Reduced the Impact of CSU on Sleep (CFB-SIS7), Observed as Early as Week 1, with Continued Improvements up to Week 24[a]

REMIX-1



BL SIS7[a] (mean ± SD): **12.7 ± 5.4** (remibrutinib); **12.3 ± 5.4** (placebo)

REMIX-2

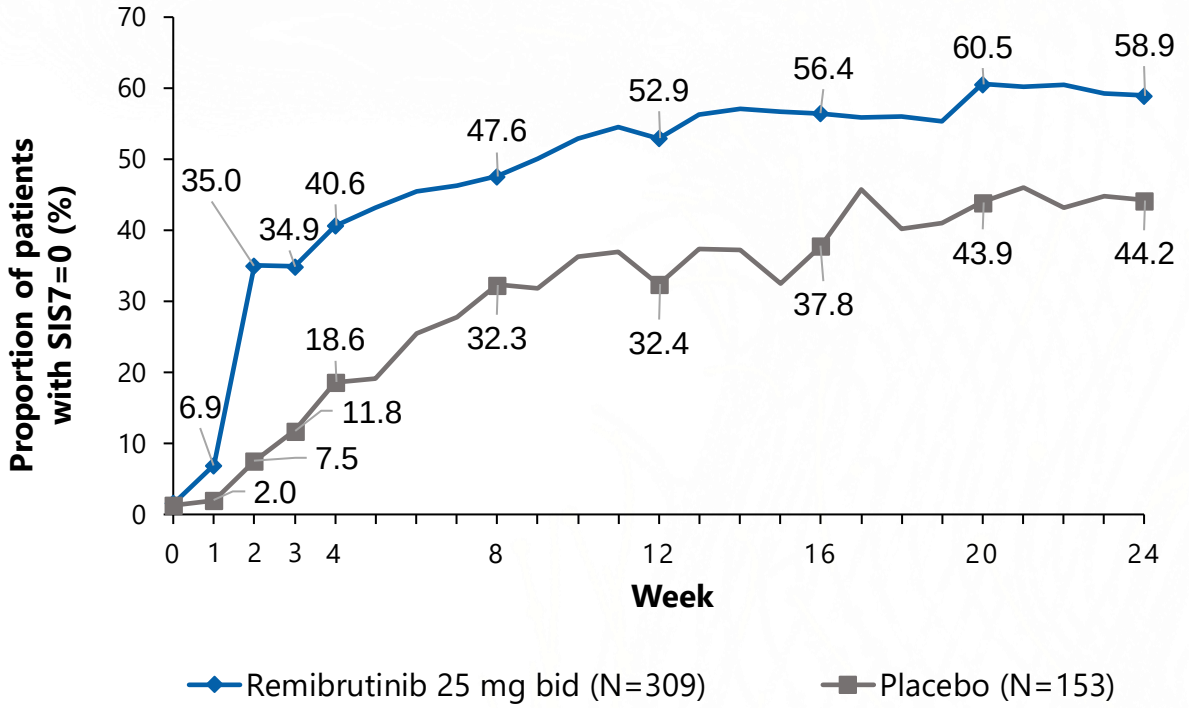


BL SIS7[a] (mean ± SD): **11.8 ± 5.6** (remibrutinib); **12.1 ± 5.0** (placebo)

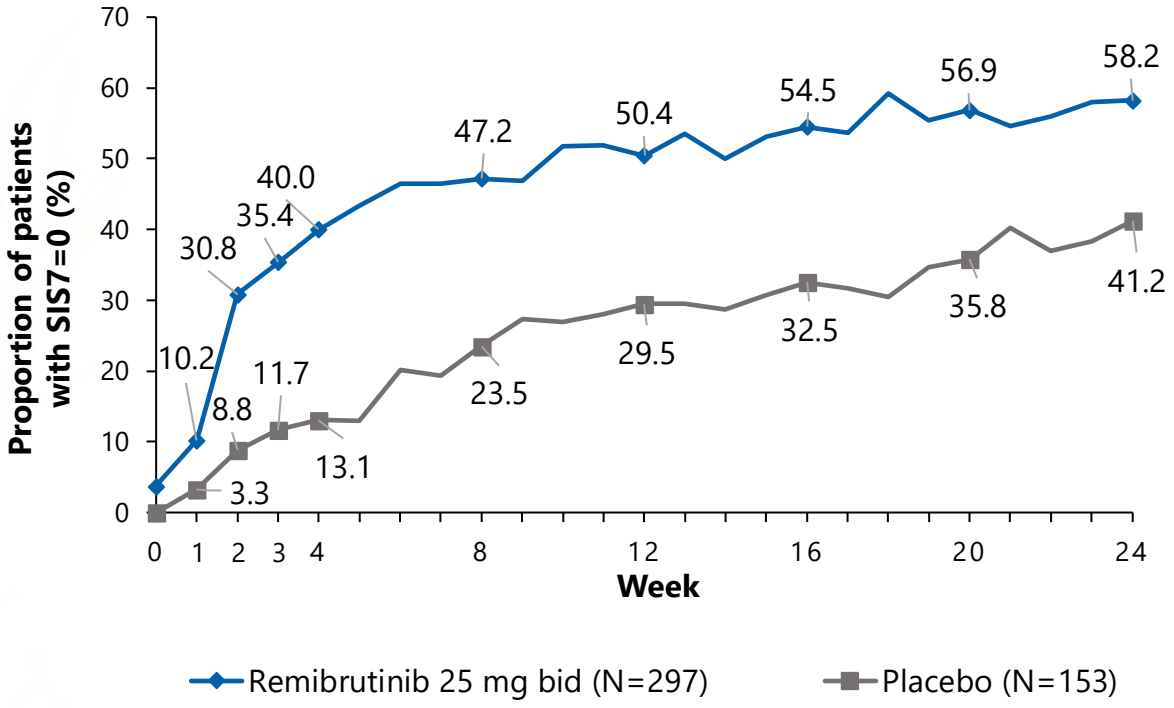
bid, twice daily; BL, baseline; CFB, change from baseline; CSU, chronic spontaneous urticaria; N, number of patients on each treatment arm; SIS7, weekly Sleep Interference Score.
[a]Full analysis set; observed data.

Greater Proportion of Patients on Remibrutinib vs Placebo Experienced Undisturbed Sleep (SIS7=0)[a] Through to Week 24

REMIX-1



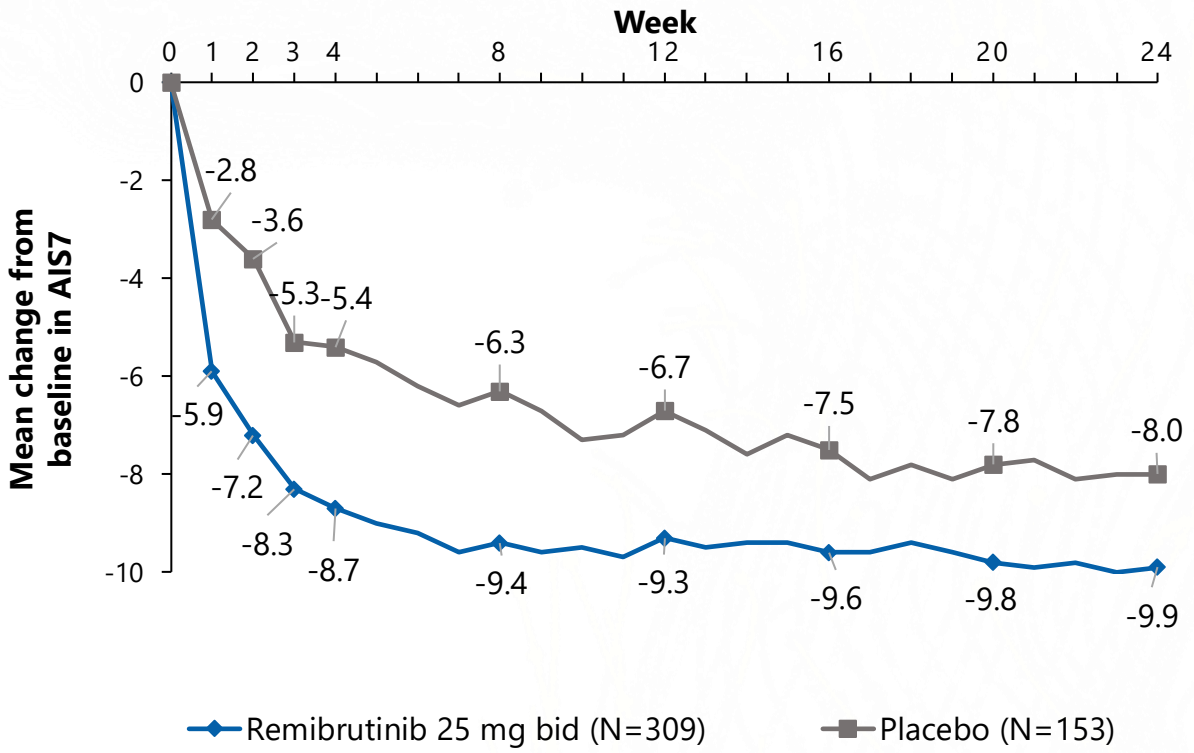
REMIX-2



bid, twice daily; N, number of patients on each treatment arm; SIS7, weekly Sleep Interference Score.
[a]Full analysis set; observed data.

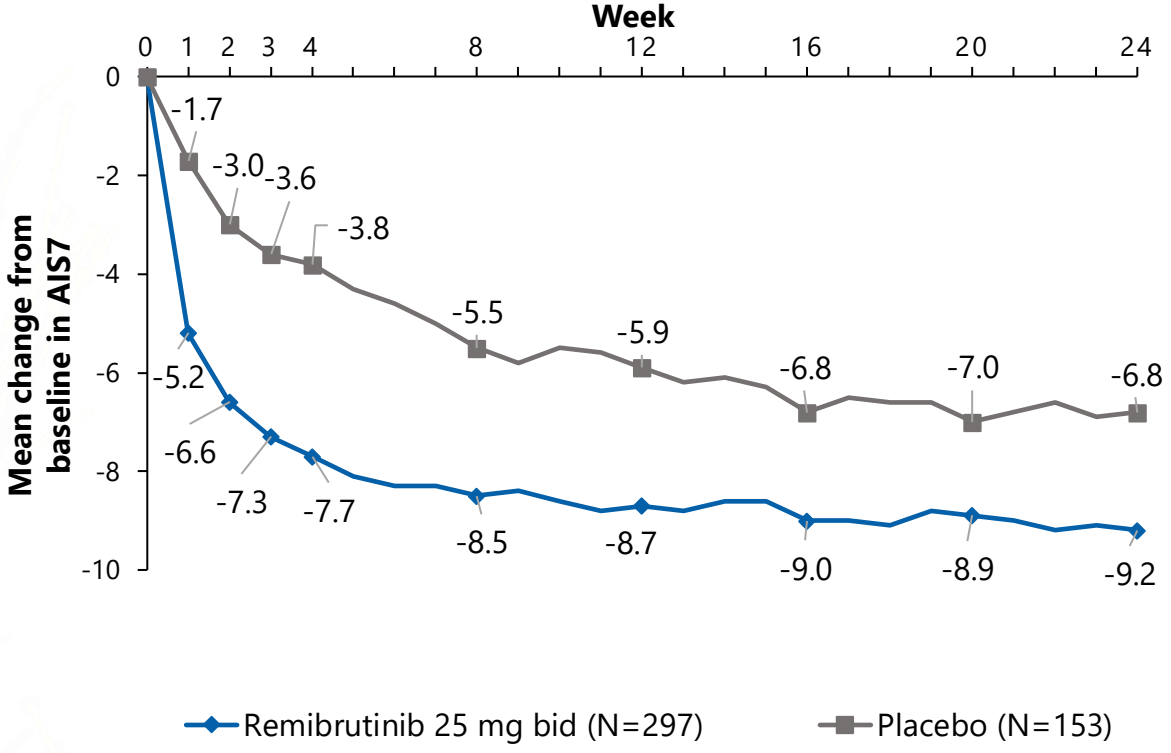
4 Remibrutinib Reduced the Impact of CSU on Daily Activities (CFB-AIS7), Observed as Early as Week 1, with Continued Improvements up to Week 24[a]

REMIX-1



BL AIS7[a] (mean ± SD): **13.1 ± 4.9** (remibrutinib); **13.0 ± 4.8** (placebo)

REMIX-2

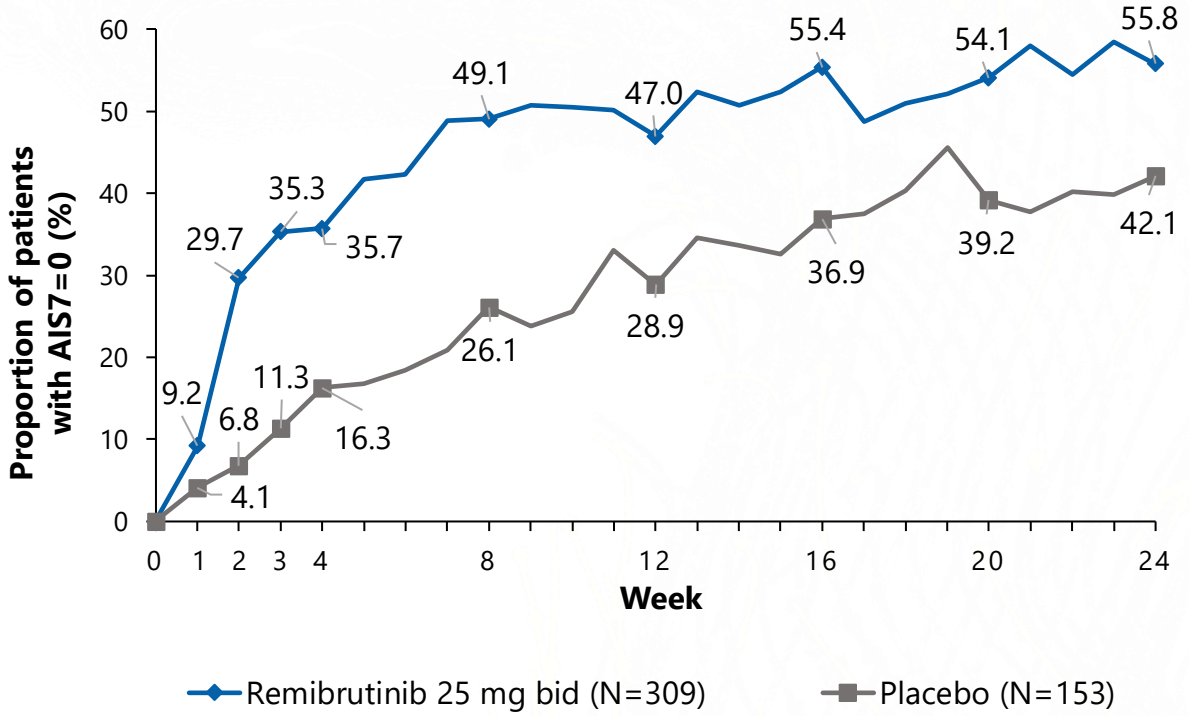


BL AIS7[a] (mean ± SD): **12.5 ± 5.3** (remibrutinib); **12.3 ± 4.8** (placebo)

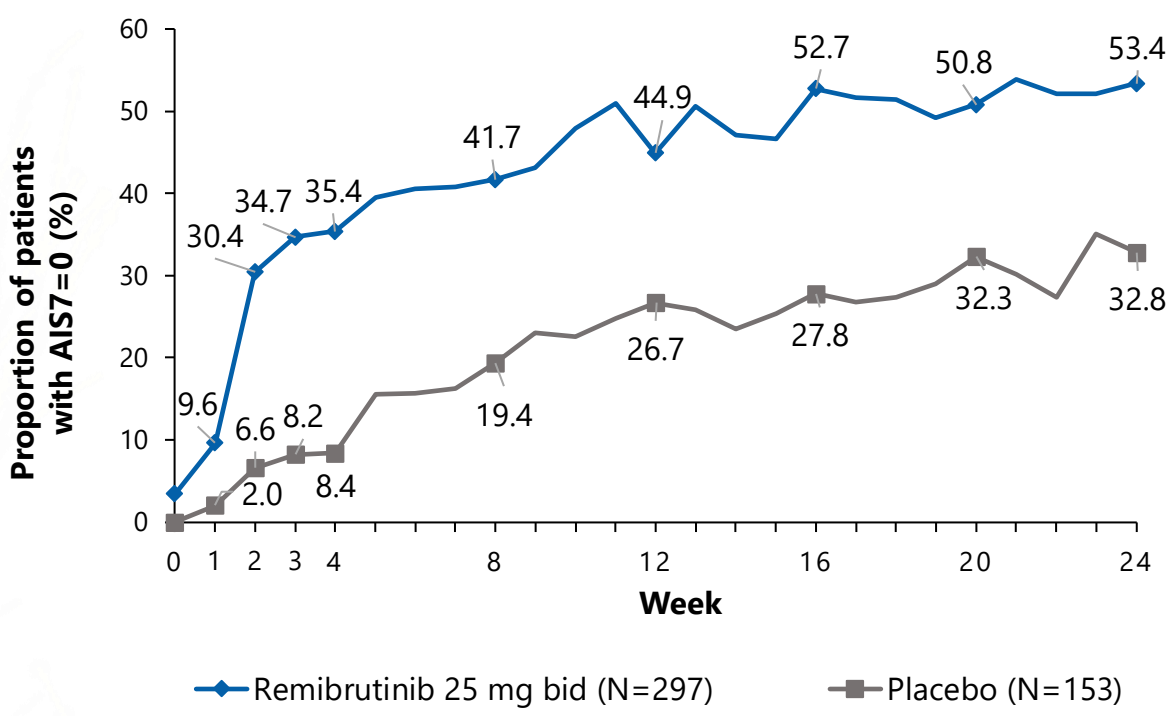
AIS7, weekly Activity Interference Score; bid, twice daily; BL, baseline; CFB, change from baseline; CSU, chronic spontaneous urticaria; N, number of patients on each treatment arm.
[a]Full analysis set; observed data.

4 Greater Proportion of Patients on Remibrutinib vs Placebo Achieved No Impact of CSU on Daily Activities (AIS7=0)[a]

REMIX-1



REMIX-2



AIS7, weekly Activity Interference Score; bid, twice daily; BL, baseline; CSU, chronic spontaneous urticaria; N, number of patients on each treatment arm.
[a]Full analysis set; observed data.

5 Conclusions

- In the pivotal **REMIX** studies, **remibrutinib** 25 mg bid **reduced** the **impact of CSU** on **sleep** and **daily activities** versus placebo, which was observed as early as **Week 1** and improved up to **Week 24**
- Treatment with remibrutinib led to **early achievement** of **SIS7=0** (***no impact on sleep***) and **AIS7=0** (***no impact on daily activities***) in a **greater proportion of patients** versus placebo, which further **improved** through to **Week 24**
- **Remibrutinib** has the potential to be an **effective oral treatment option** that may improve **sleep** and **daily activities** in patients with **CSU**

AIS7, weekly Activity Interference Score; bid, twice daily; CSU, chronic spontaneous urticaria; N, number of patients on each treatment arm; SIS7, weekly Sleep Interference Score.

EAACI Congress 2024

Valencia, Spain

31 May - 3 June

Revolutionising Patient Care
Through the Power of Data Science

EAACI
EUROPEAN ACADEMY OF ALLERGY AND CLINICAL IMMUNOLOGY

#EAACIcongress

www.eaaci.org