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Remibrutinib (LOU064) treatment improves chronic spontaneous urticaria in patients irrespective of previous anti-IgE treatment: Phase 2b study results

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1 Disclosures and acknowledgements

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  - Martin Metz reports personal fees from Amgen, Aralez, Argenx, AstraZeneca, Celldex, Moxie, Novartis, Roche, Sanofi and Uriach, outside the submitted work

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2 Introduction

- **Chronic spontaneous urticaria (CSU)** is characterised by the occurrence of **wheals (hives) and/or angioedema** for **>6 weeks** and has a major detrimental **impact on patients' well-being**[1]
- Guidelines recommend the use of second-generation H_1-AH or updosing of H_1-AH by 4-fold, if needed, as the first-line treatment for CSU[1]
- In patients, unresponsive to up-dosed H_1-AH, omalizumab is recommended as second-line therapy[1]. However, nearly one-third of the patients do not achieve complete control of signs and symptoms of CSU with omalizumab[2]
- **Remibrutinib (LOU064)** is an **oral**, highly selective **BTK inhibitor** that offers fast disease control in CSU patients who remain symptomatic despite H_1-AH[3]
- Remibrutinib showed **clinical efficacy** and a **favorable safety profile** for up to **12 weeks** in the Phase 2b dose-finding study (NCT03926611)[4] and up to **52 weeks** in the open-label Phase 2b extension study (NCT04109313) in patients with **moderate to severe CSU** inadequately controlled by H_1-AH[4]

Anti-IgE, anti-immunoglobulin E; BTK, Bruton's Tyrosine Kinase; CSU, Chronic Spontaneous Urticaria; H1-AH, H1-antihistamine; IgE, Immunoglobulin E.

1. Zuberbier T, et al. Allergy. 2022;77:734–766; 2. Kaplan A, et al. *J Allergy Clin Immunol* 2016; 137:474-81; 3. Angst D, et al. J Med Chem. 2020;63:5102–5118; 4. Maurer M, et al. J Allergy Clin Immunol. 2022; S0091-6749(22)01181–2.

2 Study objective

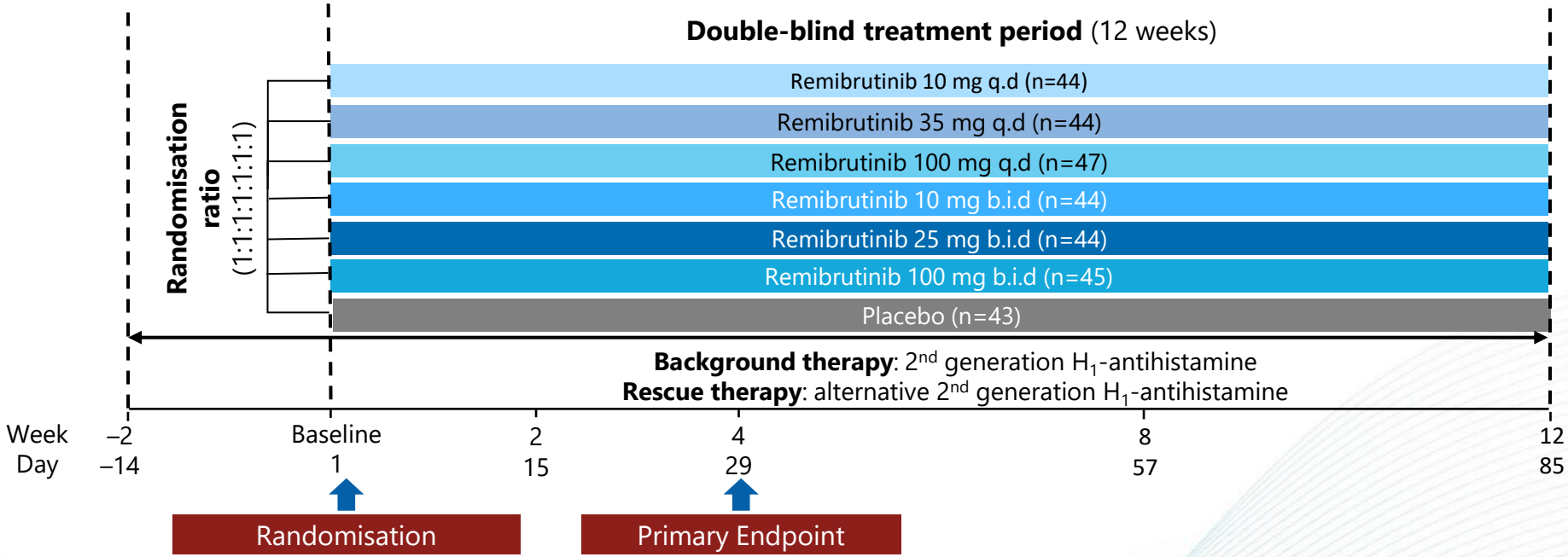
Objective

To evaluate the effect of remibrutinib in patient subgroups with or without previous use of anti-IgE treatment for CSU from the Phase 2b study

CSU, Chronic Spontaneous Urticaria; IgE, immunoglobulin E

3 Study design and patient population

A dose-finding, multicenter, randomised, double-blind, placebo-controlled Phase 2b study



- The study included patients aged ≥18 years with moderate/severe CSU for ≥6 months that was inadequately controlled by second-generation H_1-antihistamines, and who were on background H_1-AH and rescue therapy when needed

Background therapy was a second generation H_1-antihistamines at a locally approved licensed posology that had to be administered daily with a stable treatment regimen throughout the study. Rescue therapy was a second generation H_1-antihistamines at a locally approved licensed posology that differed from the background H_1-antihistamines, was eliminated primarily via renal excretion, and could only be given to treat unbearable symptoms (itch) of CSU on a day-to-day basis; b.i.d., twice daily; CSU, chronic spontaneous urticaria; n, number of patients randomised in each group; q.d., once daily

Maurer M, et al. *J Allergy Clin Immunol.* 2022;150(6):1498-1506.e2.

3 Study outcomes and data analysis

- The outcomes included
  - Proportion of patients achieving complete response (UAS7=0) at Week 12
  - Proportion of patients achieving well-controlled CSU (UAS7≤6) at Week 12
  - Change from baseline in UAS7 at Week 12
- All the above data were analysed in patient subgroups with or without previous use of anti-IgE treatment
- Data were analysed using summary statistics

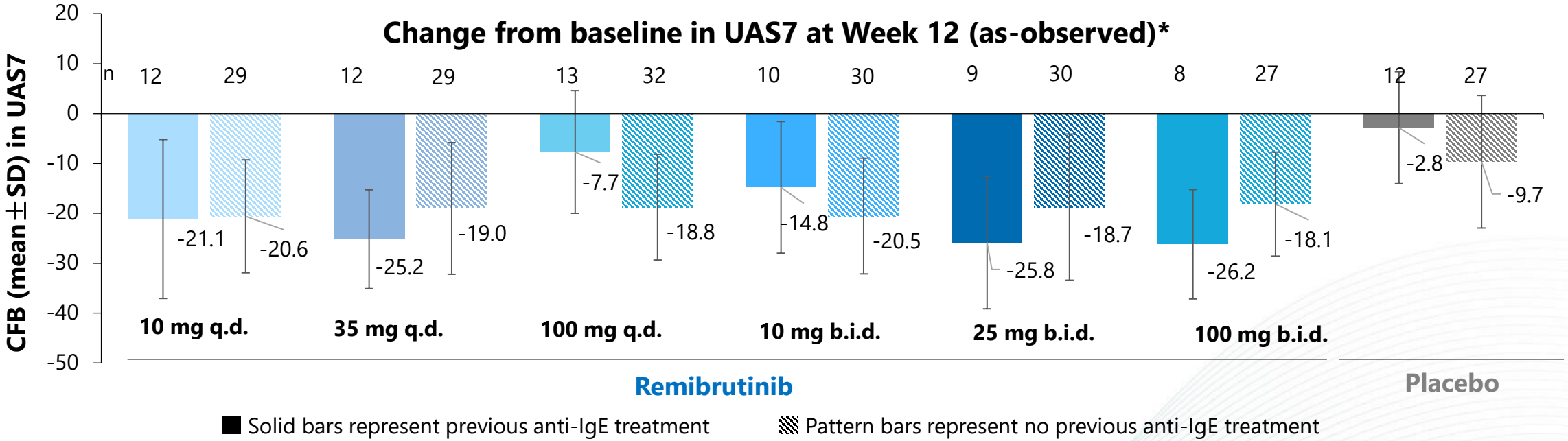
CSU, Chronic Spontaneous Urticaria; IgE, immunoglobulin E; UAS7, weekly Urticaria Activity Score

4 Patient demographics and baseline disease characteristics were generally balanced between remibrutinib and placebo arms

Baseline characteristics	Remibrutinib						Placebo N=43
	10 mg q.d. n=44	35 mg q.d. n=44	100 mg q.d. n=47	10 mg b.i.d. n=44	25 mg b.i.d. n=44	100 mg b.i.d. n=45	
Age (years)*	42.5±16.0	44.0±16.5	45.2±13.4	46.1±15.2	47.4±14.6	44.9±13.8	45.1±15.2
Female, n (%)*	35 (79.5)	30 (68.2)	39 (83.0)	32 (72.7)	32 (72.7)	29 (64.4)	25 (58.1)
Duration of CSU (years)*	6.2±7.7	5.9±8.8	5.3±5.8	4.9±5.5	3.8±4.5	4.5±5.2	3.6±4.8
IgE level (IU/mL) median (min, max)*	149.7 (4.7, 7743.7)	67.3 (1.0, 5453.3)	80.3 (1.0, 1754.1)	79.4 (1.0, 1657.8)	122.0 (2.8, 1288.2)	109.2 (1.0, 3452.4)	110.6 (1.0, 6027.7)
Previous exposure to anti IgE therapy, yes, n (%)*	13 (29.5)	13 (29.5)	13 (27.7)	11 (25.0)	10 (22.7)	12 (26.7)	12 (27.9)
UAS7 score (all patients)*	31.4±7.1	31.2±7.2	28.5±7.0	29.8±6.7	29.3±7.9	29.3±6.0	27.6±7.6
UAS7 with previous use of anti-IgE treatment#	33.3±6.6	32.2±8.5	30.0±7.3	32.0±6.2	34.9±8.1	29.4±5.9	27.9±8.0
UAS7 without previous use of anti-IgE treatment#	30.6±7.2	30.8±6.7	27.9±6.9	29.1±6.8	27.6±7.2	29.2±6.1	27.7±7.6

*Randomised set; #Full Analysis Set; Data are expressed as mean±SD, unless stated otherwise. b.i.d., twice daily; CSU, chronic spontaneous urticaria; n, number of patients randomized to each arm; q.d., once daily; SD, standard deviation; UAS7, weekly Urticaria Activity Score

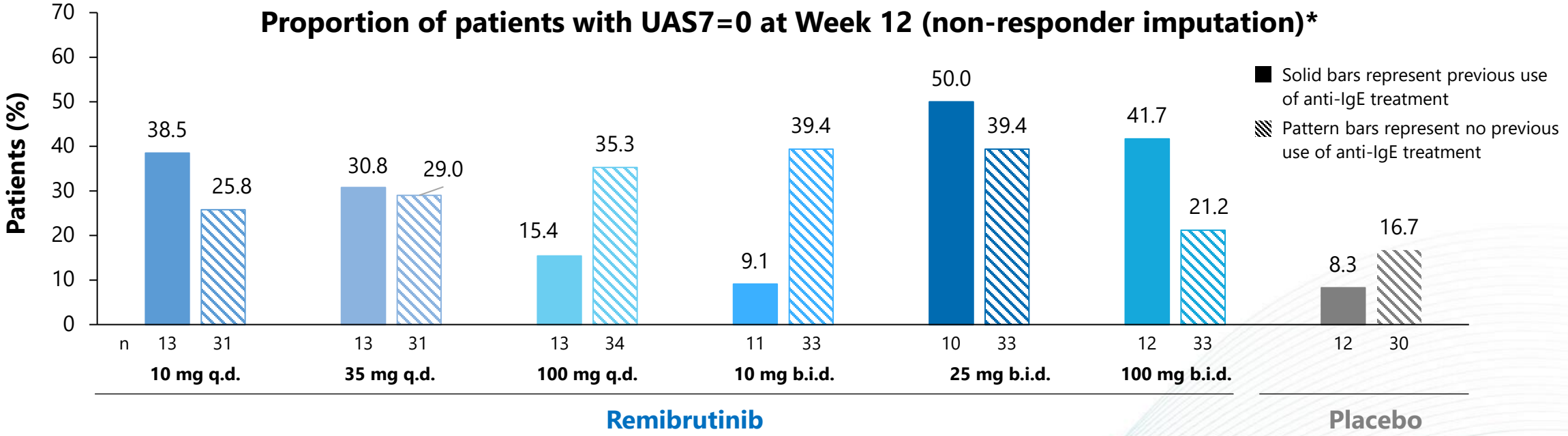
4 Remibrutinib (all doses) showed improvement in UAS7 CFB in both subgroups with or without previous use of anti-IgE treatment at Week 12; no consistent difference observed between subgroups



- At Week 12, no consistent difference in UAS7 change from baseline was observed between subgroups with or without previous use of anti-IgE treatment across remibrutinib doses (reduction: 7.7 to 26.2) and placebo (reduction: 2.8 to 9.7 respectively)

*Full analysis set
b.i.d., twice daily; CFB, change from baseline; q.d., once daily; UAS7, weekly Urticaria Activity Score

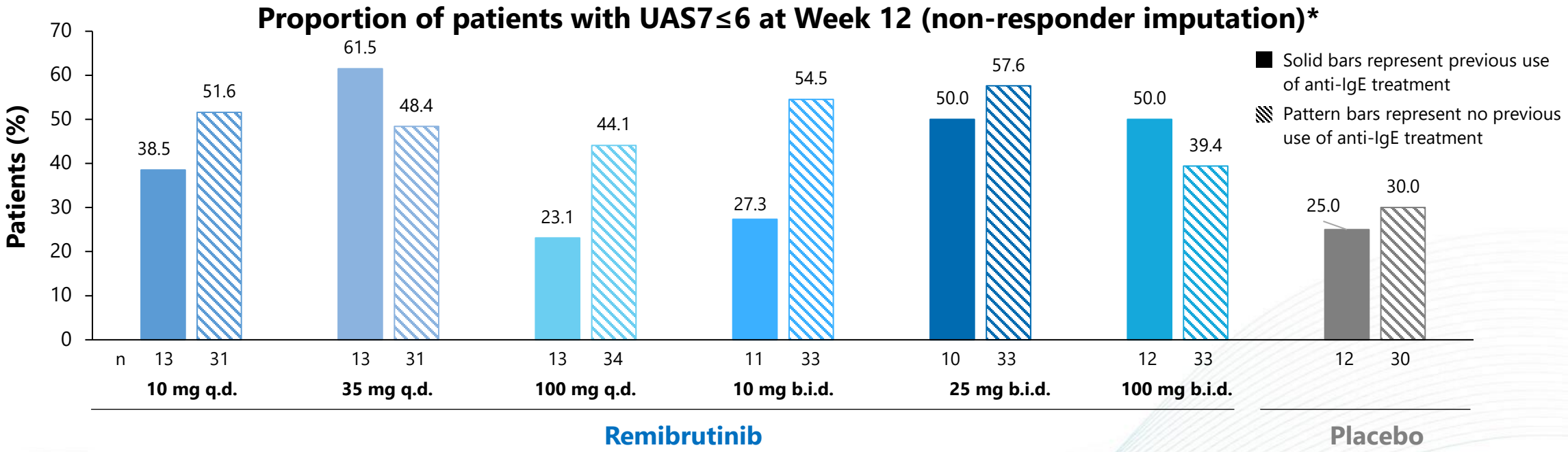
4 No different trends were observed in proportion of patients achieving UAS7=0 between subgroups with and without previous use of anti-IgE treatment across remibrutinib doses and placebo at Week 12



- Proportion of patients achieving UAS7=0 was higher across remibrutinib doses in both subgroups with and without previous anti-IgE treatment (9.1% to 50.0% and 21.2% to 39.4%, respectively) versus placebo (8.3% and 16.7%, respectively) at Week 12

*Full analysis set
b.i.d., twice daily; q.d., once daily; IgE, immunoglobulin E; UAS7, weekly Urticaria Activity Score

4 No different trends were observed in proportion of patients achieving UAS7≤6 between subgroups with and without previous use of anti-IgE treatment across remibrutinib doses and placebo at Week 12



- Proportion of patients achieving UAS7≤6 was higher across remibrutinib doses in both subgroups with and without previous anti-IgE treatment (23.1% to 61.5% and 39.4% to 57.6%, respectively) versus placebo (25.0% and 30.0%, respectively) at Week 12

*Full analysis set
b.i.d., twice daily; q.d., once daily; IgE, immunoglobulin E; UAS7, weekly Urticaria Activity Score

5 Conclusions

- **Remibrutinib** (all doses) showed **improvement in UAS7** with no consistent different trends observed among the remibrutinib doses
- **More patients on remibrutinib** achieved **UAS7=0** versus placebo in both the subgroups with and without previous anti-IgE treatment
- Similarly, **more patients on remibrutinib** achieved **UAS7≤6** versus placebo in both the subgroups with (except 100 mg q.d.) and without previous anti-IgE treatment
- **Remibrutinib** can be an **effective treatment option for CSU** patients regardless of whether they had previously received anti-IgE treatment
- Larger studies are required to confirm the findings of these data due to limited number of patients in the subgroup of patients with previous use of anti-IgE treatment from the Phase 2b study

CSU, chronic spontaneous urticaria; IgE, immunoglobulin E; q.d., once daily; UAS7, weekly Urticaria Activity Score

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