Remibrutinib (LOU064) reduces the use of rescue medication in patients with chronic spontaneous urticaria: Findings from a Phase 2b study

Presenter: Prof. Marcus Maurer

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Disclosures and acknowledgements

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2 Introduction and study objective

- **Chronic spontaneous urticaria (CSU)** is characterised by the spontaneous occurrence of **wheals (hives)** and/or **angioedema** for $\geq 6$ weeks and has a major **impact on patients’ well-being**\(^1\)

- Second-generation H\(_1\)-antihistamines (H\(_1\)-AH) are recommended as first-line treatment for CSU\(^1\)

- **Remibrutinib (LOU064)** is a novel, highly selective and potent covalent oral **BTK inhibitor**, that has demonstrated **clinical efficacy and a favorable safety profile** in a Phase 2b dose-finding study (NCT03926611) of patients with **moderate to severe CSU** inadequately controlled by H\(_1\)-antihistamines\(^2-4\)

**Objective**

To report the use of second-generation H\(_1\)-AH as rescue medication in patients with moderate to severe CSU from a Phase 2b study

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BTK, bruton tyrosine kinase; CSU, chronic spontaneous urticaria.

Remibrutinib dose showed rapid and significant improvement in UAS7 score over 12 weeks versus placebo

![UAS7 change from baseline over time during the treatment period](image)

<table>
<thead>
<tr>
<th>Treatment arm</th>
<th>LS mean change (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remibrutinib 10 mg q.d. (N=44)</td>
<td>-18.1 (1.9)</td>
</tr>
<tr>
<td>Remibrutinib 35 mg q.d. (N=44)</td>
<td>-18.0 (1.9)</td>
</tr>
<tr>
<td>Remibrutinib 100 mg q.d. (N=47)</td>
<td>-15.3 (1.9)</td>
</tr>
<tr>
<td>Remibrutinib 10 mg b.i.d. (N=44)</td>
<td>-17.7 (1.9)</td>
</tr>
<tr>
<td>Remibrutinib 25 mg b.i.d. (N=43)</td>
<td>-20.2 (2.0)</td>
</tr>
<tr>
<td>Remibrutinib 100 mg b.i.d. (N=45)</td>
<td>-17.4 (2.0)</td>
</tr>
<tr>
<td>Placebo (N=42)</td>
<td>-7.9 (2.0)</td>
</tr>
</tbody>
</table>

- UAS7 scores improved from baseline up to Week 12 in all remibrutinib doses compared with placebo
- A rapid improvement in UAS7 was observed as early as at Week 1, which was maintained up to Week 12

b.i.d., twice daily; CI, confidence interval; LS, least square; N, number of patients; q.d., once daily; SE, standard error; UAS7, weekly Urticaria Activity Score.
Methods: Study design

A dose-finding, multicenter, randomised, double-blind, placebo-controlled Phase 2b study in patients with CSU\textsuperscript{1,2}

- Patients received second generation H\textsubscript{1}-AH at a locally approved licensed dose and posology as background therapy throughout the study\textsuperscript{1,2}

*Eligible patients rolled over into an extension study at Week 12 or at Week 16, following roll-over criteria defined in the extension study protocol and dependent on HAs/EC approval from participating countries. Background therapy was a 2nd generation H\textsubscript{1}-AH at a locally approved licensed posology that had to be administered daily with a stable treatment regimen throughout the study. Rescue therapy was a 2nd generation H\textsubscript{1}-AH at a locally approved licensed posology that differed from the background H\textsubscript{1}-AH, 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; AH, antihistamines; CSU, chronic spontaneous urticaria; n, number of patients randomized in each group; q.d, once daily.

Methods: Study outcomes and data analysis

Study outcome

- Number of rescue H\textsubscript{1}-AH tablets used over the preceding 24 hours to control itch or hives was evaluated from baseline to Week 12
- Rescue medication allowed was second generation H\textsubscript{1}-AH eliminated primarily via renal excretion. The rescue medication had to be different from the background H\textsubscript{1}-AH and was given as needed for the treatment of unbearable symptoms during screening, treatment and follow-up periods

Data analysis

- The weekly use of rescue medication was calculated as the sum of the doses per day, over 7 days described using summary statistics
## Results

### Baseline demographics and disease characteristics (randomised set) were generally balanced between treatment arms

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Remibrutinib</th>
<th>Placebo</th>
<th>Total Randomised</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 mg q.d. n=44</td>
<td>35 mg q.d. n=44</td>
<td>100 mg q.d. n=47</td>
</tr>
<tr>
<td>Age (years)</td>
<td>42.5 ± 16.04</td>
<td>44.0 ± 16.47</td>
<td>45.2 ± 13.40</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>35 (79.5)</td>
<td>30 (68.2)</td>
<td>39 (83.0)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.4 ± 19.43</td>
<td>79.0 ± 20.20</td>
<td>76.6 ± 14.66</td>
</tr>
<tr>
<td>Baseline DLQI score</td>
<td>14.9 ± 7.1</td>
<td>12.6 ± 6.5</td>
<td>12.7 ± 7.1</td>
</tr>
<tr>
<td>Baseline UAS7 score</td>
<td>31.4 ± 7.1</td>
<td>31.2 ± 7.2</td>
<td>28.5 ± 7.0</td>
</tr>
<tr>
<td>Duration of CSU (years)</td>
<td>6.2 ± 7.7</td>
<td>5.9 ± 8.8</td>
<td>5.3 ± 5.8</td>
</tr>
<tr>
<td>Previous exposure to anti-IgE therapy, n (%)</td>
<td>13 (29.5)</td>
<td>13 (29.5)</td>
<td>13 (27.7)</td>
</tr>
</tbody>
</table>

Data are presented as means±SD, unless stated otherwise. b.i.d., twice a day; CSU, chronic spontaneous urticaria; DLQI, dermatology life quality index; n, number of patients; N, total number of patients; q.d., once a day; SD, standard deviation; UAS7, weekly Urticaria Activity Score. Maurer M, et al. EADV. 29 September – 2 October 2021. Maurer M, et al. Poster presented at American Academy of Allergy, Asthma and Immunology. 2022 (Poster #536).
Reduction in weekly use of rescue medication tablets was observed early in all remibrutinib arms and remained low throughout the study.

Compared to baseline, there was decreased use of rescue medication as early as Week 1 across all remibrutinib arms which remained low during the study whereas the placebo arm showed an increased use of rescue medication.

Full analysis set.
BL, baseline; b.i.d., twice a day; q.d., once a day.
At Week 12, the mean weekly use of rescue medication was numerically lower across remibrutinib arms compared to baseline and placebo.

**Week 12 use of rescue medication tablets at baseline, W4 and W12**

<table>
<thead>
<tr>
<th>Remibrutinib (Mean)</th>
<th>10 mg q.d.</th>
<th>35 mg q.d.</th>
<th>100 mg q.d.</th>
<th>10 mg b.i.d.</th>
<th>25 mg b.i.d.</th>
<th>100 mg b.i.d.</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL</td>
<td>8.7</td>
<td>6.6</td>
<td>6.4</td>
<td>7.6</td>
<td>9.0</td>
<td>9.4</td>
<td>12.3</td>
</tr>
<tr>
<td>W4</td>
<td>5.2</td>
<td>3.7</td>
<td>2.9</td>
<td>5.1</td>
<td>4.5</td>
<td>7.7</td>
<td>9.0</td>
</tr>
<tr>
<td>W12</td>
<td>5.8</td>
<td>3.9</td>
<td>4.0</td>
<td>5.6</td>
<td>4.5</td>
<td>7.1</td>
<td>11.9</td>
</tr>
</tbody>
</table>

**Full analysis set.**
BL, baseline; b.i.d., twice a day; q.d., once a day; W, week.
The present analysis from a first-in-patient, Phase 2b dose-finding remibrutinib trial demonstrated:

- **Remibrutinib reduced the need for rescue medication as early as Week 1**, compared to baseline and placebo across all doses over 12 weeks in patients with CSU.
- Despite reduced use of H₁-AH, an improvement in CSU symptoms was observed in all treatment arms, as reported previously.

Remibrutinib showed a favorable safety profile across all doses.

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CSU, chronic spontaneous urticaria; H₁-AH, H₁-antihistamines.