Remibrutinib treatment improves quality of life in patients with chronic spontaneous urticaria

Maurer M.¹,², Giménez-Arnau A.³, Jain V.⁴, Tillinghast J.⁵, Tolcachier A.⁶, Nigen S.⁷, Hayama K.⁸, Lheritier K.⁹, Walsh P.¹⁰, Haemmerle S.⁹

¹Urticaria 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; ²Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Allergology and Immunology, Berlin, Germany; ³Department of dermatology, Hospital del Mar, IMIM, Universitat Pompeu, Barcelona, Spain; ⁴Division of Clinical Immunology and Allergy, Department of Medicine, McMaster University, Hamilton, Canada; ⁵The Clinical Research Center, St. Louis, Missouri, USA; ⁶Sección Alergia, Hospital General de Agudos, Dr. Carlos G. Durand, Buenos Aires, Argentina; ⁷Hôpital de Verdun, Service de dermatologie, Département de médecine, Université de Montréal, Montréal, Canada; ⁸Division of Cutaneous Science, Department of Dermatology, Nihon University School of Medicine, Tokyo, Japan; ⁹Novartis Pharma AG, Basel, Switzerland; ¹⁰Novartis Ireland Limited, Dublin, Ireland.

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Introduction

- CSU is a distressing and unpredictable disease characterized by the spontaneous appearance of wheals (hives) and/or angioedema for >6 weeks due to known or unknown causes in the absence of specific and definite stimuli\(^1\)
- CSU can have a substantial **negative impact** on patients’ QoL, and it often does\(^2\)
- Current treatments often **inadequately control symptoms** that impact patients’ QoL\(^3,4\)
- Remibrutinib, a Bruton’s tyrosine kinase inhibitor (BTKi) that leads to **blockade of mast cell and basophil activation**, is a potential **new treatment option** for patients with CSU\(^5\)
- This study explores the **effect of remibrutinib** on patients’ QoL using DLQI\(^*\)

\(^*\)Changes in DLQI score from baseline to Week 4 and 12 and proportions of patients achieving DLQI=0-1 at Week 4 and 12 were analyzed. The outcome reported here is DLQI (range 0-30) in which a decreased score indicates improved QoL and a score of 0-1 indicates no disease effect on QoL.

BTK, Bruton’s tyrosine kinase; CSU, chronic spontaneous urticaria; DLQI, Dermatology Life Quality Index; QoL, quality of life.


A dose-finding, multicentre, randomised, double-blind, placebo-controlled Phase 2b study in adult patients with moderate to severe CSU

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 second generation H1-antihistamine 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 H1-antihistamine at a locally approved licensed posology that differed from the background H1-antihistamine, 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; EC, ethical committee; HAs, health authorities; n, number of patients randomized in each group; q.d., once daily.

Patient disposition: Overall, 309/519 patients screened were included in the full analysis up to Week 12.

- **Screened patients (N=519)**
- **Screen failures (n=208)**
- **Randomized patients (N=311)**
- **Patients not treated (n=2)**

### Remibrutinib

**10 mg**
- Remibrutinib q.d. (n=44)
  - Discontinued (n=3)
    - Patient decision (n=1)
    - Lack of efficacy (n=1)
    - Protocol deviation (n=1)
  - Patient decision (n=1)
  - Lack of efficacy (n=1)

**35 mg**
- Remibrutinib q.d. (n=44)
  - Discontinued (n=3)
    - Lack of efficacy (n=1)
    - Patient decision (n=1)
    - Other (n=1)
  - Patient decision (n=1)
  - Other (n=1)

**100 mg**
- Remibrutinib q.d. (n=47)
  - Discontinued (n=4)
    - Adverse event (n=3)
    - Lack of efficacy (n=1)
    - Protocol deviation (n=1)
  - Other (n=1)
  - Protocol deviation (n=1)

**10 mg**
- Remibrutinib b.i.d. (n=44)
  - Discontinued (n=4)
    - Adverse event (n=1)
    - Lack of efficacy (n=1)
    - Protocol deviation (n=1)
    - Other (n=1)
  - Other (n=1)
  - Patient decision (n=1)
  - Protocol deviation (n=1)
  - Technical problems (n=1)

**25 mg**
- Remibrutinib b.i.d. (n=44)
  - Discontinued (n=4)
    - Adverse event (n=3)
    - Other (n=2)
    - Physician decision (n=1)
    - Patient decision (n=1)
    - Protocol deviation (n=1)
  - Lack of efficacy (n=1)

**100 mg**
- Remibrutinib b.i.d. (n=45)
  - Discontinued (n=9)
    - Adverse event (n=3)
    - Other (n=2)
    - Physician decision (n=1)
    - Patient decision (n=1)
    - Protocol deviation (n=1)
    - Lack of efficacy (n=1)

**Placebo**
- (n=43)
  - Discontinued (n=5)
    - Patient decision (n=3)
    - Protocol deviation (n=1)
  - Lack of efficacy (n=1)

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b.i.d., twice daily; mg, milligrams; q.d., once daily; N, number of patients; n, number of patients randomized to each arm.
Randomized patients were aged 45.0±14.9 (mean±SD) years, 71.4% female, and had lived with CSU for 4.9±6.2 years.

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Remibrutinib 10 mg q.d. (n=44)</th>
<th>Remibrutinib 35 mg q.d. (n=44)</th>
<th>Remibrutinib 100 mg q.d. (n=47)</th>
<th>Remibrutinib 10 mg b.i.d. (n=44)</th>
<th>Remibrutinib 25 mg b.i.d. (n=44)</th>
<th>Remibrutinib 100 mg b.i.d. (n=45)</th>
<th>Placebo (n=43)</th>
<th>Total Randomized (n=311)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.5±16.0</td>
<td>44.0±16.5</td>
<td>45.2±13.4</td>
<td>46.1±15.2</td>
<td>47.4±14.6</td>
<td>44.9±13.8</td>
<td>45.1±15.2</td>
<td>45.0±14.9</td>
</tr>
<tr>
<td>Gender (female); n (%)</td>
<td>35 (79.5)</td>
<td>30 (68.2)</td>
<td>39 (83.0)</td>
<td>32 (72.7)</td>
<td>32 (72.7)</td>
<td>29 (64.4)</td>
<td>25 (58.1)</td>
<td>222 (71.4)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.4±19.4</td>
<td>79.0±20.2</td>
<td>76.7±14.7</td>
<td>78.4±16.8</td>
<td>77.1±19.9</td>
<td>78.9±19.3</td>
<td>78.4±16.5</td>
<td>78.1±18.0</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>
<td>12.7±6.2</td>
<td>12.9±6.6</td>
<td>10.8±6.7</td>
<td>13.4±7.9</td>
<td>12.8±6.9</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>
<td>29.8±6.7</td>
<td>29.3±7.9</td>
<td>29.3±6.0</td>
<td>27.6±7.6</td>
<td>29.6±7.1</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>
<td>4.9±5.5</td>
<td>3.8±4.5</td>
<td>4.5±5.2</td>
<td>3.6±4.8</td>
<td>4.9±6.2</td>
</tr>
<tr>
<td>Previous experience of angioedema (yes); n (%)</td>
<td>26 (59.1)</td>
<td>29 (65.9)</td>
<td>27 (57.4)</td>
<td>28 (63.6)</td>
<td>22 (50.0)</td>
<td>23 (51.1)</td>
<td>22 (51.2)</td>
<td>177 (56.9)</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD, unless stated otherwise. b.i.d., twice daily; CSU, chronic spontaneous urticaria; DLQI, Dermatology Life Quality Index; kg, kilogram; mg, milligrams; n, number of patients randomized to each arm; q.d., once daily; SD, standard deviation; UAS7, weekly Urticaria Activity Score.

Improvements in DLQI* scores from baseline to Week 4 and 12 were numerically greater in all remibrutinib groups vs. placebo.

Mean ± SD changes in DLQI scores from baseline to Week 4 and 12

* A decrease in DLQI score indicates an improvement in QoL.

b.i.d., twice daily; BL, baseline; DLQI, Dermatology Life Quality Index; mg, milligrams; q.d., once daily; QoL, quality of life; SD, standard deviation.

Proportions of patients achieving DLQI=0-1 at Week 4 and 12 were numerically greater in all remibrutinib groups vs. placebo.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Week 4 (%)</th>
<th>Week 12 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg q.d.</td>
<td>38.6</td>
<td>29.5</td>
</tr>
<tr>
<td>35 mg q.d.</td>
<td>29.5</td>
<td>40.9</td>
</tr>
<tr>
<td>100 mg q.d.</td>
<td>29.8</td>
<td>51.2</td>
</tr>
<tr>
<td>10 mg b.i.d.</td>
<td>29.5</td>
<td>53.5</td>
</tr>
<tr>
<td>25 mg b.i.d.</td>
<td>33.3</td>
<td>40.9</td>
</tr>
<tr>
<td>100 mg b.i.d.</td>
<td>35.6</td>
<td>38.3</td>
</tr>
<tr>
<td>Placebo</td>
<td>16.7</td>
<td>40.9</td>
</tr>
</tbody>
</table>

b.i.d., twice daily; DLQI, Dermatology Life Quality Index; mg, milligrams; q.d., once daily.
Conclusions

- Compared to placebo, all remibrutinib doses provided marked improvements in DLQI as early as Week 4, which were maintained at Week 12.

- These findings are consistent with the previously reported results of remibrutinib treatment on UAS7¹.

DLQI, Dermatology Life Quality Index; UAS7, weekly Urticaria Activity Score.