Systemic exposure and safety profile of delgocitinib cream in adults with moderate to severe Chronic Hand Eczema in the Phase 3 DELTA 2 trial

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Objectives
• To examine systemic exposure of delgocitinib cream 20 mg/g in adults with moderate to severe Chronic Hand Eczema (CHE) in the randomized, double-blind, vehicle-controlled DELTA 2 trial
• To compare DELTA 2 systemic exposure with corresponding data from the randomized, double-blind, vehicle-controlled DELTA 1 trial

Results
In DELTA 2, the geometric mean plasma concentration of delgocitinib was 2.12, 0.20 and 0.12 ng/mL at Weeks 1, 4 and 8, respectively (Figure 1). The geometric mean (IC50) of delgocitinib in an IL-4 release assay (in vitro spiking of whole blood from healthy adults) was 17.2 ng/mL. In the Phase 1 trial, the lowest oral delgocitinib dose tested (1.5 mg; n=8) showed a peak systemic exposure (geometric mean Cmax) of 7.2 ng/mL (Table 1). No clinically meaningful changes in laboratory parameters versus cream vehicle were observed. No AEs of special interest were reported (eczema herpeticum, deep vein thrombosis, or pulmonary embolism). No malignancies, major adverse cardiovascular events or various thromboembolisms were reported in patients treated with delgocitinib cream. No changes or differences between the delgocitinib cream 20 mg/g and cream vehicle in laboratory parameters were assessed to be of clinical relevance (Figure 2).

Conclusions
• In the DELTA 2 trial, twice-daily application of delgocitinib cream 20 mg/g demonstrated
  – minimal systemic exposure in association with a favorable safety profile in patients with moderate to severe CHE treated for 16 weeks
  – no safety findings to support any causal relationship with systemic adverse events, with no AEs of special interest being reported
  – no clinically meaningful changes in laboratory parameters versus cream vehicle
• No systemic pharmacological effects are expected from twice-daily applications of delgocitinib cream 20 mg/g in patients with moderate to severe CHE

Table 1. Systemic exposure in the oral Phase 1 trial

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>n</th>
<th>AUC0-∞ (h*ng/mL)</th>
<th>Cmax (ng/mL)</th>
<th>tmax (h; median)</th>
<th>t1/2 (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>8</td>
<td>39.6</td>
<td>7.2</td>
<td>1.0</td>
<td>2.0</td>
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<tr>
<td>3</td>
<td>8</td>
<td>66.6</td>
<td>18.4</td>
<td>0.84</td>
<td>2.3</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>211.0</td>
<td>51.0</td>
<td>0.83</td>
<td>2.9</td>
</tr>
<tr>
<td>12</td>
<td>8</td>
<td>408.0</td>
<td>99.3</td>
<td>1.0</td>
<td>2.8</td>
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</tbody>
</table>

Figure 2. Mean (SD) change in laboratory parameters from baseline in DELTA 2

Figure 3. DELTA 2 trial design

Background
• The pathogenesis of CHE involves JAK-STAT signaling pathways.1,2
• The cream formulation of delgocitinib, a pan-JAK inhibitor, has been developed for topical treatment of CHE.

Methods
• The DELTA 2 pivotal Phase 3 clinical trial was randomized, double-blind and vehicle-controlled (Figure 3):
  – Adults (aged ≥18 years) with moderate to severe CHE were randomized 2:1 to twice-daily delgocitinib cream 20 mg/g (n=314) or cream vehicle (n=159) for 16 weeks followed by either 2-weeks safety follow up or transfer to a 26-week extension trial
  – Pharmacokinetic blood sampling was performed 2-h hours after delgocitinib cream application at Weeks 1, 4, 8 and 16.
  – LC/MS-based method with a lower limit of quantitation of 5 pg/mL
• In the Phase 1 trial (NCT05503279), single oral doses of delgocitinib 1.5, 3, 6, and 12 mg were tested in healthy volunteers (n=40) with sampling performed 30 minutes prior to administration and at 15 timepoints up to 24 hours post-administration.
  – IC50 of delgocitinib was assessed using an in vitro IL-4 release assay based on whole blood of healthy adults (n=4)

Table 2. Pharmacokinetic parameters following administration of delgocitinib cream in DELTA 2 trial

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>n</th>
<th>Mean (SD) Cmax (ng/mL)</th>
<th>Mean (SD) tmax (h)</th>
<th>Mean (SD) t1/2 (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>8</td>
<td>17.9 (10.7)</td>
<td>0.9 (0.4)</td>
<td>3.2 (2.0)</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>38.8 (25.9)</td>
<td>1.8 (0.9)</td>
<td>3.8 (2.3)</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>72.4 (50.7)</td>
<td>2.3 (1.2)</td>
<td>4.4 (2.5)</td>
</tr>
<tr>
<td>12</td>
<td>8</td>
<td>117.3 (91.0)</td>
<td>2.9 (1.5)</td>
<td>5.1 (3.0)</td>
</tr>
</tbody>
</table>

Acknowledgements
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