Efficacy and Safety of Ruxolitinib Cream for the Treatment of Atopic Dermatitis: Results From Two Phase 3, Randomized, Double-Blind Studies

Kim Papp, MD, PhD, Jack C. Szepietowski, MD, PhD, Leon Kiricik, MD, Darryl Toth, MD, Michael E. Kilgowski, MD, PhD, MBA, May Venturanza, MD, Kang Sun, PhD, Eric Simpson, MD

Background
- Atopic dermatitis (AD) is a chronic, inflammatory skin disease that greatly impacts patients’ quality of life.
- Juncykinase (JAK) inhibitors modulate inflammatory cytokines involved in the pathogenesis of AD and may also directly modulate itch.
- Ruxolitinib (RUX) is a potent, selective inhibitor of JAK1 and JAK2.

In a phase 2 study (NCT03011892), RUX cream provided dose-dependent efficacy in patients with AD, with no notable adverse events.

Objectives
- To report efficacy and safety of RUX cream in patients with AD in two phase 3 studies.

Methods

Patients and Study Design
- Eligible patients were aged ≥12 years with AD for ≥2 years, an Investigator’s Global Assessment (IGA) score of 2 or 3, and 3% to 20% affected body surface area.
- Exclusion criteria included immunocompromised status, use of AD systemic therapies during the washout period and during the study, use of other topical anti-itch medications, and use of immunosuppressants within 8 weeks of the washout period and during the study, and any serious dermatological condition that could interfere with study conduct, interpretation of data, or patients’ well-being.

TRuE-AD1 and TRuE-AD2 had identical study designs (Figure 1):
- In both studies, patients were randomized (2:1:1) to either of 2 RUX cream dose regimens (0.75%, 1.5%) BID or vehicle cream for a period of double-blind treatment.
- Patients on RUX cream could subsequently continue treatment for 44 weeks; patients randomized to vehicle were re-randomized 1:1 to either RUX cream regimen.

Assessments
- The primary endpoint was the proportion of patients achieving IGA-TS success (IGA-TS, score of 0 or 1 with improvement of ≥75% in Eczema Area and Severity Index score from baseline) at Week 8.
- The main secondary endpoints were the proportion of patients achieving ≥75% improvement in Eczema Area and Severity Index score from baseline (EASI-75) and the proportion of patients with a ≥4-point improvement in itch numerical rating scale (NRS) score from baseline.

Statistical Analyses
- All efficacy analyses were conducted by log-rank regression using the intent-to-treat population.
- All secondary endpoints were analyzed using descriptive statistics.
- The efficiency population consisted of all patients for TRuE-AD1 (all randomized patients) and all patients for TRuE-AD2 (vehicle, n=118; 0.75%, RUX, n=231; 1.5%, RUX, n=236).
- All patients who applied the study cream at least once (i.e., all randomized patients) were included in the safety population in both studies.

Results
- In TRuE-AD1, 317 patients were randomized, and 598 (88.4%) completed treatment in the vehicle-controlled group.
- In TRuE-AD2, 318 patients were randomized, and 561 (90.6%) completed treatment in the vehicle-controlled group.

Table 1. Patient Demographics and Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Vehicle (n=317)</th>
<th>0.75% RUX (n=156)</th>
<th>1.5% RUX (n=161)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), y</td>
<td>32.0 (17.6–72.8)</td>
<td>32.0 (17.6–72.8)</td>
<td>32.0 (17.6–72.8)</td>
</tr>
<tr>
<td>Female, %</td>
<td>57.0 (41.1–75.0)</td>
<td>57.0 (41.1–75.0)</td>
<td>57.0 (41.1–75.0)</td>
</tr>
<tr>
<td>White</td>
<td>70.5 (57.4–83.3)</td>
<td>70.5 (57.4–83.3)</td>
<td>70.5 (57.4–83.3)</td>
</tr>
<tr>
<td>Black</td>
<td>12.0 (5.6–23.0)</td>
<td>12.0 (5.6–23.0)</td>
<td>12.0 (5.6–23.0)</td>
</tr>
<tr>
<td>Other</td>
<td>17.5 (11.9–25.0)</td>
<td>17.5 (11.9–25.0)</td>
<td>17.5 (11.9–25.0)</td>
</tr>
<tr>
<td>Region</td>
<td>North America</td>
<td>90.0 (78.8–100.0)</td>
<td>90.0 (78.8–100.0)</td>
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<tr>
<td>European</td>
<td>10.0 (21.2–88.9)</td>
<td>10.0 (21.2–88.9)</td>
<td>10.0 (21.2–88.9)</td>
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<tr>
<td>Baseline IGA score</td>
<td>5.4 (3.5–7.5)</td>
<td>5.4 (3.5–7.5)</td>
<td>5.4 (3.5–7.5)</td>
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<tr>
<td>Baseline EASI score</td>
<td>26.0 (9.0–45.0)</td>
<td>26.0 (9.0–45.0)</td>
<td>26.0 (9.0–45.0)</td>
</tr>
</tbody>
</table>

Efficacy
- Significantly more patients treated with RUX cream versus vehicle demonstrated IGA-TS (primary endpoint) responses were time- and dose-dependent (Figure 3).
- Significantly more patients treated with RUX cream achieved EASI-75 vs vehicle; responses were time- and dose-dependent (Figure 4).
- Both strengths of RUX cream showed greater improvement in mean percentage change in EASI scores vs vehicle; statistical significance was observed at Week 2 and later (Figure 4).
- Significantly greater itch reductions in itch NRS scores were observed within 12 hours of the first application of RUX cream (1.5%, P<0.001; Figure 5).

Safety
- RUX cream was well tolerated and not associated with clinically significant application site reactions (Table 2).

Conclusions
- Ruxolitinib cream showed superior efficacy vs vehicle in IGA-TS, EASI-75, and 24-point reduction in itch NRS score in these two phase 3 studies.
- Application of ruxolitinib cream brought about rapid (within 12 hours of initiation of therapy), substantial, and sustained reduction in itch.

- Ruxolitinib cream demonstrated a dual mode of action: antipruritic and anti-inflammatory.
- No notable safety findings (either local or systemic) were associated with treatment, including on sensitive skin areas.
- The successful outcomes of TRuE-AD1 and TRuE-AD2 support the potential of ruxolitinib cream as an effective and well-tolerated topical treatment for patients with AD.

Disclosures
- The authors have disclosed all potential conflicts of interest. For a complete list of disclosures, please see the supplemental material.

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