BACKGROUND

- Janus kinase 1 (JAK1) is a cytoplasmic tyrosine kinase that mediates signaling pathways activated by various cytokines.
- Various cytokine pathways relevant to the pathophysiology of atopic dermatitis (AD) signal via JAK1, including interleukin (IL)-2, IL-4, IL-13, IL-22, IL-31, and thymic stromal lymphopoietin, thereby mediating type 2 helper T-cell differentiation and itch through downstream effects.
- Abrocitinib is an oral once-daily JAK1 selective inhibitor under investigation for the treatment of AD.

METHODS

Study Design and Endpoints
- JADE MONO-1 was a multicenter, international, randomized, double-blind, placebo-controlled, monotherapy, phase 3 study.
- Patients aged ≥12 years with moderate to severe AD (Investigator’s Global Assessment (IGA) ≥3; Eczema Area and Severity Index (EASI) score ≥16; affected percentage of body surface area ≥10, and Peak Pururu Number Rating Scale (PP-NRS), used with permission of Regeneron Pharmaceuticals, Inc. and Sanofi) score ≥4 were randomly assigned (2:2:1) to receive once-daily oral abrocitinib 200 mg, abrocitinib 100 mg, or placebo for 12 weeks.

Key Assessments
- Co-primary endpoints:
  - Proportion of patients achieving IGA response (clear or almost clear) with ≥2-grade improvement from baseline at week 12
  - Proportion of patients achieving EASI ≥75 improvement from baseline (EASI-75) at week 12

Secondary endpoints (not multiplicity controlled):
- Proportion of patients achieving PP-NRS response (≥4-point improvement from baseline) at weeks 2, 4, and 12
- Other secondary endpoints
  - Safety was assessed via adverse event (AE) and laboratory monitoring.

Efficacy
- At week 12, significantly more abrocitinib-treated (200 mg and 100 mg) placebo patients achieved IGA response (Figure 2A).
- Differences in IGA response rates compared with placebo for abrocitinib 200 mg and 100 mg were 26.0% (95% CI, 26.2–45.7; P <0.0001) and 15.8% (95% CI, 6.8–24.8; P <0.0001), respectively.
- At week 12, significantly more abrocitinib-treated (200 mg and 100 mg) than placebo-treated patients achieved EASI-75 response (Figure 2B).
- Differences in EASI-75 response rates compared with placebo for abrocitinib 200 mg and 100 mg were 51.0% (95% CI, 40.5–61.5; P <0.0001) and 27.9% (95% CI, 17.4–38.3; P <0.0001), respectively.
- Proportions of patients achieving IGA or EASI-75 responses were higher with abrocitinib treatment at weeks 2, 4, and 8 and then increased through week 12 (Figure 2).

RESULTS

Patient Disposition, Demographics, and Baseline Disease Characteristics
- Most patients in all treatment arms completed the study (Figure 1).
- Demographics and baseline disease characteristics were balanced across treatment arms (Table 1).

Table 1. Demographics and Baseline Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo (N=77)</th>
<th>Abrocitinib 200 mg (N=154)</th>
<th>Abrocitinib 100 mg (N=156)</th>
<th>Total (N=387)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>31.5 (14.4)</td>
<td>31.3 (14.2)</td>
<td>31.7 (14.0)</td>
<td>31.5 (14.4)</td>
</tr>
<tr>
<td>Male, %</td>
<td>69 (70.7)</td>
<td>66 (42.9)</td>
<td>72 (46.0)</td>
<td>68 (40.1)</td>
</tr>
<tr>
<td>sunscreen use, %</td>
<td>45.6%</td>
<td>57.2%</td>
<td>58.8%</td>
<td>54.1%</td>
</tr>
</tbody>
</table>

- Clinical laboratory evaluations:
  - Hemoglobin, neutrophils, and lymphocytes showed no clinically significant changes.
  - Platelet counts reached a nadir at week 4 and trended toward baseline thereafter despite continued therapy.
  - Dose-related changes in lipid levels were observed (~10% increase in low-density lipoprotein and ~20% increase in high-density lipoprotein).

Table 2. Summary of Adverse Events

<table>
<thead>
<tr>
<th>AE, % (n)</th>
<th>Placebo (N=77)</th>
<th>Abrocitinib 200 mg (N=154)</th>
<th>Abrocitinib 100 mg (N=156)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abrocitinib</td>
<td>57.4% (44)</td>
<td>44.8% (69)</td>
<td>45.6% (71)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>3.9% (3)</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Discontinuation because of AEs</td>
<td>7.1% (5)</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Venous thromboembolism</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Death</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- Abrocitinib 200 mg or 100 mg once-daily significantly improved signs and symptoms of moderate to severe AD compared with placebo in adolescent and adult patients.
- Abrocitinib was well tolerated and showed an acceptable short-term safety profile.
- Abrocitinib represents a novel oral therapy for adult and adolescent patients with moderate to severe AD.

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