Pooled Efficacy, Patient-Reported Outcomes, and Safety of Roflumilast Cream 0.15% From the INTEGUMENT-1 and INTEGUMENT-2 Phase 3 Clinical Trials of Adults and Children With Atopic Dermatitis

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease affecting quality of life, with itch being the most burdensome symptom.

Roflumilast cream 0.15% is a once-daily nonsteroidal formulation of roflumilast, a potent phosphodiesterase-4 (PDE-4) inhibitor.

Safety and local tolerability were favorable.

METHODS

INTEGUMENT-1 and INTEGUMENT-2 were identically designed, randomized, parallel-group, double-blind, vehicle-controlled, multi-center trials enrolling patients ≥6 years of age with mild to moderate AD (Validated Investigator

Patient safety was paramount, and all serious adverse events (SAEs) were review by an independent data monitoring board.

RESULTS

Baseline disease characteristics were consistent between treatment groups (Table 1), and patients were generally similar to vehicle.

Safety and local tolerability were similar across INTEGUMENT-1 and INTEGUMENT-2. 7 = strong reaction spreading beyond application site

Table 1. Patient Demographics and Baseline Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vehicle Cream (n=420)</th>
<th>Roflumilast Cream 0.15% QD (n=451)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race, n (%)</td>
<td>489 (55.3)</td>
<td>272 (60.0)</td>
<td>40% (10% to 70%)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td>489 (55.3)</td>
<td>272 (60.0)</td>
<td>40% (10% to 70%)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td>272 (60.0)</td>
<td>272 (60.0)</td>
<td>0% (−10% to 10%)</td>
</tr>
<tr>
<td>Age, n (%)</td>
<td>489 (55.3)</td>
<td>272 (60.0)</td>
<td>40% (10% to 70%)</td>
</tr>
<tr>
<td>Baseline AD severity</td>
<td>489 (55.3)</td>
<td>272 (60.0)</td>
<td>40% (10% to 70%)</td>
</tr>
<tr>
<td>Baseline AD extent</td>
<td>489 (55.3)</td>
<td>272 (60.0)</td>
<td>40% (10% to 70%)</td>
</tr>
<tr>
<td>Baseline AD intensity</td>
<td>489 (55.3)</td>
<td>272 (60.0)</td>
<td>40% (10% to 70%)</td>
</tr>
<tr>
<td>Baseline AD subjective symptoms</td>
<td>489 (55.3)</td>
<td>272 (60.0)</td>
<td>40% (10% to 70%)</td>
</tr>
</tbody>
</table>

Roflumilast Cream 0.15% QD

- Reduced Inflammation
- Improved Signs and Symptoms
- Improved Sleep
- Improved Quality of Life

CONCLUSION

- Once-daily, nonsteroidal roflumilast cream 0.15% provided significant improvement across multiple efficacy endpoints and PRS vs vehicle in patients with AD.
- Statistically significant improvement in itch was observed as early as 24 hours after first application of roflumilast cream 0.15% compared with vehicle.
- Patients treated with roflumilast achieved statistically significant greater improvements in PRS, including itch, sleep loss, and quality of life.
- Safety and local tolerability were favorable.

SAFETY AND LOCAL TOLERABILITY

- Incidence of treatment-emergent adverse events (AEs) was low in both treatment groups (Table 2).
- Local tolerability was similar for roflumilast cream and vehicle (Figure 7).
- 78% of patients reported no or mild sensation across both treatment groups at any time point.

Table 2. Safety

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vehicle Cream (n=420)</th>
<th>Roflumilast Cream 0.15% QD (n=451)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs, n (%)</td>
<td>489 (55.3)</td>
<td>272 (60.0)</td>
<td>40% (10% to 70%)</td>
</tr>
<tr>
<td>SAEs, n (%)</td>
<td>489 (55.3)</td>
<td>272 (60.0)</td>
<td>40% (10% to 70%)</td>
</tr>
<tr>
<td>Discontinuations due to AEs, n (%)</td>
<td>489 (55.3)</td>
<td>272 (60.0)</td>
<td>40% (10% to 70%)</td>
</tr>
</tbody>
</table>

REFERENCES


ACKNOWLEDGMENTS

- We thank the investigators and their patients for their participation in the trial. We are grateful to the project teams and the study site staff for their commitment.
- We are also thankful to the AbbVie team, led by Dr. Torsten Neckelmann, and funded by AbbVie Development.

DISCLOSURES

- Author contributions are as follows: YG and JH contributed equally to each manuscript. YG and JH are employees of AbbVie Development.