Patient-Reported Outcomes in Subjects with Atopic Dermatitis Treated with Tapinarof Cream: Results from a Phase 2b, Randomized Parallel-Group Study

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SYNOPSIS

Atopic dermatitis (AD) is a chronic relapsing skin disease characterized by pruritus, burning sensations, xerosis, erythematous papules and plaques, exudation, crustung, and lichenification.

Patients with AD report an impact on sleep, quality of life, and psychosocial domains (social, academic, and occupational) due to persistent, intense pruritus, and the stigma associated with having visibly diseased skin.

The primary goal in the treatment of AD is to stabilize the disease and reduce the number of flares.

Tapinarof cream is a therapeutic aryl hydrocarbon receptor modulator agent (TAMRA) under investigation for the treatment of AD and psoriasis.

This Phase 2b dose-finding study (ClinicalTrials.gov ID: NCT02564055) was designed to assess the efficacy and safety of tapinarof cream in adolescents and adults with AD.

The primary analysis showed that tapinarof cream was efficacious and well tolerated in adolescents and adults with AD.

OBJECTIVES

To present patient-reported outcomes from the Phase 2b study in subjects with AD following treatment with topical tapinarof cream, including adolescent and adult impression of change in severity of AD symptoms and pruritus, changes in expanded Patient-Oriented Eczema Measure (POEM), and Daily Sign and Symptom Severity Diary scores.

METHODS

Study Design

In this multicenter (United States, Canada, and Japan), Phase 2b, double-blind, vehicle-controlled randomized study, subjects with AD were randomized 1:1:1:1:1 to receive tapinarof cream 0.5% or 1% once (QD) or twice daily (BID) or vehicle QD or BID for 12 weeks and followed up for 4 more weeks (Figure 1).

Study Outcomes and Statistical Analysis

The primary endpoint was the proportion of subjects with improvement in Investigator Global Assessment (IGA) score of clear or almost clear (0 or 1) and Q2-grade improvement in IGA score from baseline to Week 12.

Subject Impressions

At baseline, 86% of subjects rated their AD symptoms as moderate or severe across all treatment groups: 28–60% rated as moderate and 28–53% rated as severe.

At Week 12, a greater proportion of subjects in the tapinarof cream groups (81–89% in the 1% groups and 80–81% in the 0.5% groups) rated the overall severity of their pruritus symptoms as ‘very/moderately improved’ compared with 64–68% in the vehicle groups (Figure 2a).

Expanded POEM

At Week 12, improvements were observed in all tapinarof cream and vehicle-treated groups on all seven POEM items, except for the question relating to weeping or oozing for the 1% BID group.

The three additional items in the expanded POEM showed overall sleep quality improved across all treatment groups, with the largest improvements in the tapinarof cream groups.

For item 8 related to how many nights subjects woke up at least once because of AD, the number of subjects finding it difficult to fall (back) asleep after waking because of AD, the number of subjects finding it difficult or very difficult to fall (back) asleep were lower in all treatment groups at Week 12 compared with baseline, except for one subject in the vehicle BID group for item 10.

RESULTS

Subject Characteristics

A total of 247 subjects (of 363 subjects originally screened) were randomized into the three treatment groups (Table 1).

Overall, mean demographic and baseline characteristics were comparable across treatment groups (Table 1).

Most subjects (91%) had a baseline IGA score of 3 (moderate) and a baseline mean Eczema Area and Severity Index (EASI) score of 11.3 (standard deviation 6.0).

Primary endpoint: IGA response rates (defined as IGA score 0 or 1 and ≥2-grade improvement) at Week 12 were higher in the tapinarof cream groups than the vehicle groups (53% [1% BID], 46% [1% QD], 37% [0.5% BID], 34% [0.5% QD]) vs 24% [vehicle BID] and 28% [vehicle QD] and were maintained for 4 weeks after the end of study treatment (non-responder imputation method).

Table 1. Baseline Subject Demographics and Characteristics

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>N</th>
<th>Age, years (SD)</th>
<th>Sex, % (n)</th>
<th>IGA score, mean (SD)</th>
<th>EASI score, mean (SD)</th>
<th>BSA affected, %</th>
<th>Pruritus score, mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tapinarof 1% BID (n=43)</td>
<td>43</td>
<td>17 (10.1)</td>
<td>64 (27)</td>
<td>3.1 (0.3)</td>
<td>9.8 (5.2)</td>
<td>61 (26)</td>
<td>5.2 (3.3)</td>
</tr>
<tr>
<td>Tapinarof 0.5% QD (n=41)</td>
<td>41</td>
<td>17 (10.1)</td>
<td>64 (27)</td>
<td>3.1 (0.3)</td>
<td>9.8 (5.2)</td>
<td>61 (26)</td>
<td>5.2 (3.3)</td>
</tr>
<tr>
<td>Vehicle QD (n=28)</td>
<td>28</td>
<td>17 (10.1)</td>
<td>64 (27)</td>
<td>3.1 (0.3)</td>
<td>9.8 (5.2)</td>
<td>61 (26)</td>
<td>5.2 (3.3)</td>
</tr>
</tbody>
</table>

*Mean scores based on a numeric rating scale of 0 ‘absent’ to 10 ‘worst imaginable’. Data provided for the safety analysis population (n=247).

Subject Impressions

At baseline, 86% of subjects rated their AD symptoms as moderate or severe across all treatment groups: 28–60% rated as moderate and 28–53% rated as severe.

At Week 12, a greater proportion of subjects in the tapinarof cream groups (81–89% in the 1% groups and 80–81% in the 0.5% groups) rated the overall severity of their pruritus symptoms as ‘very/moderately improved’ compared with 64–68% in the vehicle groups.

Expanded POEM

At Week 12, improvements were observed in all tapinarof cream and vehicle-treated groups on all seven POEM items, except for the question relating to weeping or oozing for the 1% BID group.

The three additional items in the expanded POEM showed overall sleep quality improved across all treatment groups, with the largest improvements in the tapinarof cream groups.

For item 8 related to how many nights subjects woke up at least once because of AD, the number of subjects finding it difficult to fall (back) asleep after waking because of AD, the number of subjects finding it difficult or very difficult to fall (back) asleep were lower in all treatment groups at Week 12 compared with baseline, except for one subject in the vehicle BID group for item 10.

CONCLUSIONS

In all tapinarof cream groups, a greater proportion of subjects (81–91%) reported AD signs and symptoms as ‘very/moderately improved’ after 12 weeks compared with the vehicle groups (64–68%).

Similarly, a greater proportion of subjects in the tapinarof cream groups (78–87%) reported the overall severity of pruritus as ‘very/moderately improved’ after 12 weeks compared with the vehicle groups (47–64%).

Overall, tapinarof cream was well tolerated and these results correspond to the previously reported clinical efficacy findings.

Study findings demonstrated that tapinarof cream represents an important potential advance in topical medicine development, with beneficial effects on patient-reported outcomes in adolescents and adults with AD.

REFERENCES


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