SYNOPSIS

In two 12-week pivotal phase 3 trials, PSOARING 1 (NCT03956335) and PSOARING 2 (NCT03983980), tapinarof cream 1% once daily (QD) demonstrated highly statistically and clinically significant efficacy versus vehicle and was well tolerated in adults with active plaque psoriasis.

Tapinarof cream 1% QD also demonstrated maintenance of efficacy for 4 weeks after treatment discontinuation in a 12-week phase 2b trial, warranting further investigation of a potential remittive effect.

OBJECTIVE

To present the results of PSOARING 3 (NCT04053387), a long-term extension designed to assess the safety, efficacy, duration of response, tolerability, and duration of remittive effect of tapinarof during re-treated intermittent treatment, based on patient Physical Global Assessment (PGA) score.

METHODS

Study Design

Patients completing PSOARING 1 and PSOARING 2 were eligible to enroll in PSOARING 3 for 40 weeks of open-label treatment with tapinarof cream 1% QD, followed by four weeks of follow-up (Figure 1).

In PSOARING 3, patients were treated with tapinarof 1% QD based on individual patient PGA score:

- Patients who entered with a PGA score of ≥1 received tapinarof 1% QD until complete disease clearance was achieved, as defined by a PGA score of 0.
- Patients who entered with, or achieved, a PGA score of 0 discontinued treatment and were observed for remittive effect, defined as maintenance of a PGA score of 0 (clear) or 1 (almost clear), while off therapy.

If disease worsening occurred, defined as a PGA score ≥2, tapinarof 1% QD was started and continued until a PGA score of 0 (clear) was achieved.

RESULTS

Complete Disease Clearance (PGA of 0)

Overall, 40.9% (312/763) of patients achieved complete disease clearance at least once during the study; this included 233 patients who entered the study with a PGA of ≥2, and 79 patients who entered with a PGA of 0 (Figure 2a).

Response Among Patients Entering With a PGA of ≥2

Overall, 58.2% (303/519) of patients entering the study with a PGA of ≥2 achieved a PGA of 0 (clear) or 1 (almost clear) at least once during the study (Figure 2b).

Remittive Effect: Time To First Worsening Among Patients Entering With a PGA of 0 (n=79)

The duration of remittive effect (Kaplan-Meier estimated median, 95% confidence interval) for off therapy for patients who entered the study with a PGA of 0 (clear) was 115.0 (95% CI, 85.0-168.0) days (Figure 3).

Maintenance of a PGA of 0 (Clear) or 1 (Almost Clear) While Off Therapy

A high rate of complete disease clearance (40.9%) and a remittive effect of approximately 4 months off therapy was demonstrated with tapinarof 1% QD, with no tachyphylaxis observed for up to 52 weeks.

Safety

As previously reported, there were no new safety signals on the long-term safety trial and AEs were consistent with previous studies.

CONCLUSIONS

Tapinarof cream 1% QD provided sustained improvement in efficacy endpoints with long-term intermittent use.

A high rate of complete disease clearance (40.9%) and a remittive effect of approximately 4 months off therapy was demonstrated with tapinarof 1% QD, with no tachyphylaxis observed for up to 52 weeks.

Tapinarof cream 1% QD was well tolerated with long-term use and had a safety profile consistent with previous studies.

REFERENCES

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Table 1. PSOARING 3 Baseline Patient Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (n=763)</th>
<th>Tapinarof – Tapinarof* (n=508)</th>
<th>Vehicle – Tapinarof* (n=255)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years, mean (SD)</strong></td>
<td>50.7 (12.88)</td>
<td>50.5 (12.87)</td>
<td>51.0 (12.93)</td>
</tr>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>448 (58.7)</td>
<td>430 (84.6)</td>
<td>14 (56.5)</td>
</tr>
<tr>
<td><strong>Weight, kg, mean (SD)</strong></td>
<td>92.4 (23.90)</td>
<td>92.6 (25.13)</td>
<td>92.1 (21.28)</td>
</tr>
<tr>
<td><strong>BMI, kg/m², mean (SD)</strong></td>
<td>31.7 (7.71)</td>
<td>31.6 (8.07)</td>
<td>31.8 (6.97)</td>
</tr>
<tr>
<td><strong>PGA, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 – Clear</td>
<td>79 (10.4)</td>
<td>74 (14.6)</td>
<td>5 (2.0)</td>
</tr>
<tr>
<td>1 – Almost Clear</td>
<td>161 (21.1)</td>
<td>144 (28.3)</td>
<td>17 (6.7)</td>
</tr>
<tr>
<td>2 – Mild</td>
<td>247 (32.4)</td>
<td>187 (36.8)</td>
<td>60 (23.5)</td>
</tr>
<tr>
<td>3 – Severe</td>
<td>249 (32.6)</td>
<td>93 (18.3)</td>
<td>156 (61.2)</td>
</tr>
<tr>
<td>4 – Severe</td>
<td>23 (3.0)</td>
<td>7 (1.4)</td>
<td>16 (6.3)</td>
</tr>
<tr>
<td><strong>PSAI, mean (SD)</strong></td>
<td>4.8 (4.72)</td>
<td>3.3 (3.53)</td>
<td>7.5 (3.97)</td>
</tr>
<tr>
<td><strong>BSA affected, %, mean (SD)</strong></td>
<td>4.7 (4.60)</td>
<td>3.3 (4.74)</td>
<td>73.6 (2.10)</td>
</tr>
</tbody>
</table>

*Tapinarof—Tapinarof patients previously assigned to tapinarof in the pivotal trials who enrolled in PSOARING 3; Vehicle—Tapinarof patients previously assigned to the vehicle trials who enrolled in PSOARING 3.

**ITT population: LOCF, IIT, intention-to-treat; LOCF, last observation carried forward; PGA, Physician Global Assessment.

Endpoints and Statistical Analysis

Safety: Adverse events (AEs), laboratory values, vital signs and physical exams

Efficacy:

- Complete Disease Clearance: Proportion of patients achieving PGA of 0 (clear) at least once during the trial

- Remittive Effect: Duration of efficacy maintenance defined as PGA of 0 (clear) or 1 (almost clear) while off therapy after achieving complete disease clearance (PGA=0)

- Response: Proportion of patients who entered the trial with a PGA≥2 and achieved a PGA of 0 (clear) or 1 (almost clear) at least once during the trial

- Durability of Response: absence of tachyphylaxis: Maintenance of efficacy while on treatment, defined as the proportion of patients who achieved a PGA score of 0 or 1 at least once during the trial, and trends in Psoriasis Area and Severity Index (PASI) score and percentage of body surface area (%BSA) affected over time

Tolerability: Local tolerability using a patient-reported 5-point scale for burning, stinging and itching, and an investigator-assessed 5-point scale for dryness, erythema, and peeling

Efficacy analyses used observed case (OC) or last observation carried forward (LOCF) analysis that were based on the intent-to-treat (ITT) population

RESULTS

Baseline Patient Demographics and Disease Characteristics

Overall, 763 (91.6%) of eligible patients completing PSOARING 1 and PSOARING 2 opted to enroll in PSOARING 3.

Patient demographics and disease characteristics are summarized in Table 1, including baseline values by prior treatment arm in the pivotal trials.

Patients previously randomized to tapinarof 1% QD (Tapinarof—Tapinarof) had lower baseline disease scores compared to the vehicle group (Vehicle—Tapinarof), reflecting the significant efficacy of tapinarof in the pivotal studies – 14.6% (74/508) versus 2.0% (5/255) of patients had complete disease clearance (PGA of 0), and 85.2% (331/386) versus 30.2% (77/255) of patients had a PGA score of 1 (almost clear) or 2 (mild) in the tapinarof QD pivotal group (Tapinarof—Tapinarof) versus the vehicle QD pivotal group (Vehicle—Tapinarof) respectively.

Figure 1. PSOARING 3 Study Design

Figure 2a. Response Among Patients Entering With a PGA of ≥2

Figure 2b. Complete Disease Clearance (PGA=0) and Response Rates (PGA=0 or 1)

a. Complete disease clearance (PGA=0)

b. Response (PGA=0 or 1 among patients entering with a PGA of ≥2)

Figure 3. Duration of Remittive Effect Among Patients Entering With A PGA of 0 (n=79)

Overall, 58.2% (59/79) of patients who entered with a PGA of 0 (clear) achieved a PGA of 0 (clear) or 1 (almost clear) at least once during the study.

The duration of remittive effect (Kaplan-Meier estimated median, 95% confidence interval) for off therapy for patients who entered the study with a PGA of 0 (clear) was 115.0 (95% CI, 85.0-168.0) days.