Treat-to-Target Outcomes and Measures of Treatment Success in Three Phase 3 Trials of Tapinarof Cream 1% Once Daily for Mild to Severe Plaque Psoriasis

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INTRODUCTION

- Treat-to-target strategies are used in several chronic diseases to improve outcomes[1]
- Treatment goals for psoriasis have been recommended by the US National Psoriasis Foundation (e.g., achieving a percent body surface area [%BSA] affected of ≤1.0% at 3 months) and the European S3-Guidelines on the Systemic Treatment of Psoriasis (e.g., achieving a ≥75% decrease in Psoriasis Area and Severity Index [PASI75] within 3–4 months)[1,2]
- Analyses of a large cohort of patients treated with systemic or biologic therapies (British Association of Dermatologists Biologics and Immunomodulators Register) have shown that achieving an absolute PASI total score of ≤2 corresponded to achievement of a 90% decrease in PASI score (PASI90)[3]
- In clinical practice, many patients fail to meet treatment targets, and current topical treatments alone are generally insufficiently efficacious[4,5]
  - Even with use of approved systemic agents, alone or in combination, a global study found that 57% of patients with moderate to severe plaque psoriasis had not achieved clear/almost clear skin on current therapy[6]
- In addition, most topical therapies approved by the Food and Drug Administration (FDA) for psoriasis are restricted to ≤12 weeks of continuous use (e.g., ≤8 weeks for corticosteroids or calcipotriene, and ≤12 weeks for retinoids)[7]
- Tapinarof (VTAMA®; Dermavant Sciences, Inc., USA) is a first-in-class, non-steroidal, topical, aryl hydrocarbon receptor agonist approved by the FDA for the treatment of plaque psoriasis in adults, and under investigation for the treatment of psoriasis in children down to 2 years of age and for atopic dermatitis in adults and children down to 2 years of age[8]
- Tapinarof cream 1% once daily (QD) demonstrated statistically significant efficacy versus vehicle and was well tolerated in adults with mild to severe plaque psoriasis in two identical, 12-week, pivotal phase 3 trials, PSOARING 1 (NCT03956355) and PSOARING 2 (NCT03983980)[9,10]
  - Physician Global Assessment (PGA) response (PGA=0 or 1 and a ≥2-grade improvement from baseline by Week 12) was achieved by 35.4% and 40.2% of the tapinarof-treated patients versus 6.0% and 6.3% of vehicle-treated patients, respectively (both *P*<0.0001)
  - PASI75 was achieved by 36.1% and 47.6% of the tapinarof-treated patients versus 10.2% and 6.9% of vehicle-treated patients by Week 12, respectively (both *P*<0.0001)
- In PSOARING 3 (NCT04053387), the long-term extension trial in which patients received intermittent or continuous tapinarof treatment, efficacy continued to improve beyond the 12-week trials, with a 40.9% rate of complete disease clearance (PGA=0), ~4-month remittive effect off therapy, and durability of response on therapy of up to 52 weeks[11]

OBJECTIVE

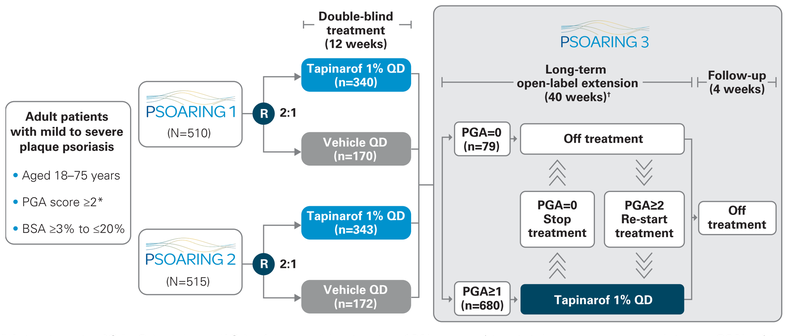
- To present analyses of treat-to-target outcomes for patients treated with tapinarof cream 1% QD in the PSOARING trials, including more-aggressive targets of the proportion of patients achieving an absolute PASI total score of ≤1, ≤2, or ≤3, or a %BSA affected of ≤1% or ≤0.5%

MATERIALS AND METHODS

Trial Design

- Pooled efficacy analyses included all patients who had a baseline PGA score of ≥2 (mild or worse) before tapinarof cream 1% QD treatment in the PSOARING trials (**Figure 1**)
- This included:
  - Patients assigned to vehicle in PSOARING 1 and 2 who received tapinarof in PSOARING 3
  - Patients who received intermittent or continuous tapinarof treatment in PSOARING 3 based on their PGA score (where those who entered with, or achieved, a PGA score of 0 discontinued treatment and were observed for remittive effect [maintenance of PGA=0 or 1] while off therapy; if disease worsening occurred [PGA≥2], tapinarof cream was restarted and continued until a PGA=0 was achieved)

Figure 1. PSOARING 1, 2, and 3 Trial Design



*Patients with PGA=2 (mild) and PGA=4 (severe) limited to ~10% each of the total randomized population; ~80% of the total randomized population with PGA=3 (moderate). †Patients electing not to participate in the LTE trial had a follow-up visit 4 weeks after completion of the treatment period.
BSA, body surface area; LTE, long-term extension; PGA, Physician Global Assessment; QD, once daily; R, randomized.

Endpoints and Statistical Analysis

- Proportion of patients who achieved a PASI total score of ≤3, ≤2, or ≤1
- Proportion of patients who achieved a %BSA affected of ≤1.0% or ≤0.5%
- Efficacy analyses were based on pooled data from observed cases; time-to-event analyses were based on Kaplan–Meier estimates
- The safety population included all patients who received tapinarof in the PSOARING trials

RESULTS

Baseline Patient Demographics and Disease Characteristics

- Overall, 915 eligible patients were included in the pooled efficacy analyses (**Table 1**)
- Mean age was 50.2 years, 58.7% were male, mean weight was 92.2 kg, and mean body mass index was 31.6 kg/m^2
- 78.1% had a PGA score of 3 (moderate), mean PASI score was 8.7, and mean BSA affected was 7.8%

Table 1. Baseline Disease Characteristics (Pooled Analysis)

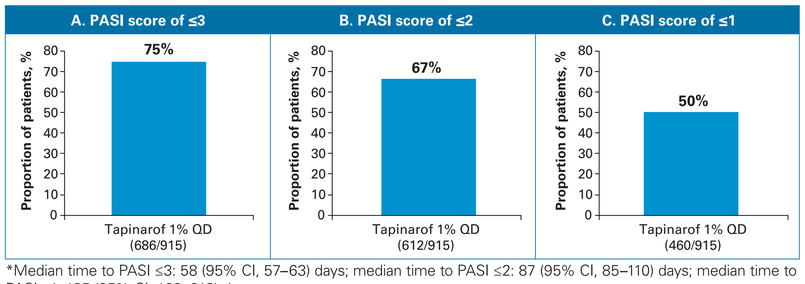
	Tapinarof cream 1% QD (n=915)
PGA, n (%)	
2 – Mild	127 (13.9)
3 – Moderate	715 (78.1)
4 – Severe	73 (8.0)
PASI, mean (SD)	8.7 (4.2)
BSA affected, %, mean (SD)	7.8 (5.0)

BSA, body surface area; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily; SD, standard deviation.

Achievement of Absolute PASI Total Score of ≤3, ≤2, or ≤1

- PASI scores of ≤3, ≤2, and ≤1 were achieved by 75.0% (n=686), 66.9% (n=612), and 50.3% (n=460) of patients, respectively (**Figure 2**)
- The median time to target (95% confidence interval [CI]) was 58 (57–63) days, 87 (85–110) days, and 185 (169–218) days for achieving PASI ≤3, ≤2, and ≤1, respectively

Figure 2. Proportion of Patients Achieving Absolute PASI Treatment Targets (Total Score of ≤3, ≤2, or ≤1)*



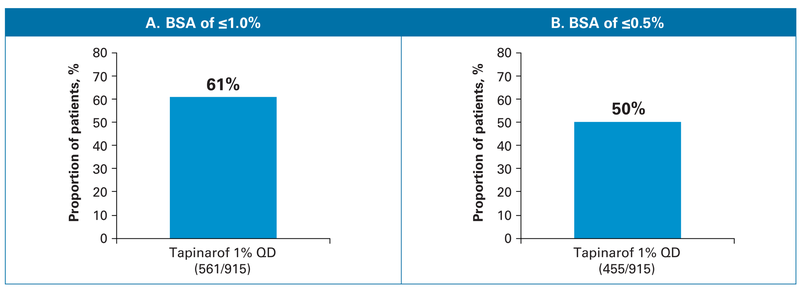
*Median time to PASI ≤3: 58 (95% CI, 57–63) days; median time to PASI ≤2: 87 (95% CI, 85–110) days; median time to PASI ≤1: 185 (95% CI, 169–218) days.

The analysis population included patients receiving intermittent treatment with tapinarof, due to the forced-withdrawal design of PSOARING 3 (treatment withdrawal when patients achieved PGA=0). Pooled analysis, OC.
CI, confidence interval; OC, observed cases; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily.

Achievement of %BSA Affected of ≤1.0% or ≤0.5%

- The analyses indicated that 61.3% of patients (n=561) achieved %BSA of ≤1.0%, with a median time to target of 120 (95% CI, 113–141) days (**Figure 3A**)
  - In addition, 40% (95% CI, 37%–43%) achieved the guideline-recommended target[1] of %BSA of ≤1.0% at 3 months (90 days)
- %BSA of ≤0.5% was achieved by 49.7% (n=455) of patients, with a median time to target of 199 (95% CI, 172–228) days (**Figure 3B**)

Figure 3. Proportion of Patients Achieving BSA Treatment Targets (≤1.0% or ≤0.5%)*



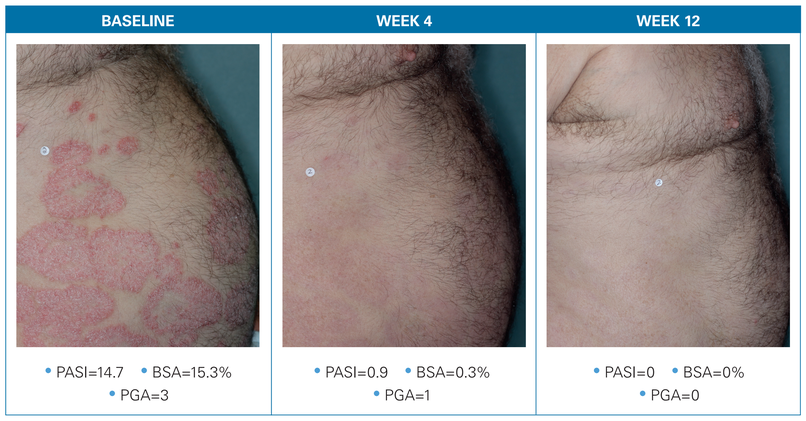
*Median time to BSA ≤1.0%: 120 (95% CI, 113–141) days; median time to BSA ≤0.5%: 199 (95% CI, 172–228) days.

The analysis population included patients receiving intermittent treatment with tapinarof, due to the forced-withdrawal design of PSOARING 3 (treatment withdrawal when patients achieved PGA=0). Pooled analysis, OC.
BSA, body surface area; CI, confidence interval; OC, observed cases; PGA, Physician Global Assessment; QD, once daily.

Absolute PASI ≤1 and %BSA of ≤0.5% Achieved by Week 4

- **Figure 4** shows the clinical response for a patient with plaque psoriasis treated with tapinarof cream 1% QD, whose improvement by Week 4 exceeded the absolute PASI, %BSA, and PGA endpoints

Figure 4. Total PASI, BSA, and PGA Scores at Baseline, Week 4, and Week 12 in a Patient with Moderate Plaque Psoriasis Treated with Tapinarof Cream 1% QD



PGA, PASI, and BSA are global efficacy assessments. Example of one representative target lesion of one tapinarof-treated patient from the PSOARING 2 clinical trial. Individual results may vary.

BSA, body surface area; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily.

Safety

- Treatment-emergent adverse events (TEAEs) were mostly mild to moderate
- The most common TEAEs (in ≥5% of patients) were folliculitis, contact dermatitis, and nasopharyngitis

CONCLUSIONS

- Tapinarof cream 1% QD was well tolerated and demonstrated rapid, clinically meaningful, and durable improvements in clinical efficacy in a high proportion of patients
- Treatment targets were achieved with tapinarof cream monotherapy, despite the challenges of meeting these goals with available systemic, biologic, topical, and combination therapies
- The aggressive target of ≤1% BSA affected was achieved by 40% of tapinarof-treated patients within ~3 months; attainment continued to increase over time, with 50% of patients achieving this target at ~4 months
- These findings support continuing tapinarof treatment beyond 3 months for patients who are experiencing improvement but not yet meeting the ≤1% BSA affected treatment target advocated by the National Psoriasis Foundation[12]
- An absolute PASI total score of ≤2 was achieved by 67% of tapinarof-treated patients; this is a treatment target that has been shown to correspond to a PASI90 response[3]
- These analyses may have underestimated the percentage of patients who achieved treatment targets, due to the unique forced-withdrawal design of PSOARING 3 that resulted in intermittent rather than continuous treatment

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