Tapinarof Cream 1% Once Daily for Plaque Psoriasis: Pooled Efficacy from Three Phase 3 Trials

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INTRODUCTION

- Tapinarof (VTAMA®; Dermavant Sciences, Inc., USA) is a first-in-class, non-steroidal, topical, aryl hydrocarbon receptor agonist approved by the Food and Drug Administration for the treatment of plaque psoriasis in adults, and under investigation for the treatment of plaque psoriasis in children down to 2 years of age, and for atopic dermatitis (AD) in adults and children down to 2 years of age[1]
- 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)[2]
  - Efficacy continued to improve beyond the 12-week trials in PSOARING 3 (NCT04053387), the long-term extension (LTE) trial, with a high rate of complete disease clearance (Physician Global Assessment [PGA]=0; 40.9%), ~4-month remittive effect off therapy, and durability of response on therapy for up to 52 weeks[3]
- Data from the two phase 3 trials and the LTE trial have been pooled to evaluate the combined efficacy and safety of tapinarof cream 1% QD

OBJECTIVE

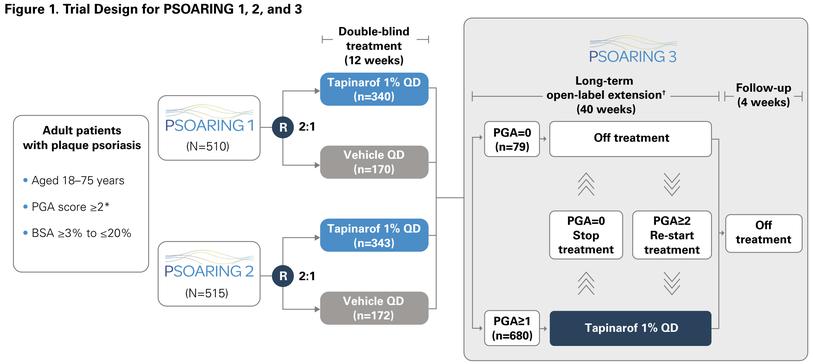
- To assess the efficacy and safety of tapinarof cream 1% QD using pooled data from three phase 3 trials, under conditions of continuous or intermittent treatment for up to 1 year

METHODS

Trial Design

- The pooled efficacy analyses included all patients in the PSOARING 1, 2, and 3 trials (**Figure 1**) who had a baseline PGA score of ≥2 before tapinarof treatment
- These patients included the following:
  - Patients randomized to tapinarof cream 1% QD in the PSOARING 1 and 2 trials who may or may not have continued into the LTE trial
  - Patients randomized to vehicle in the PSOARING 1 and 2 trials who continued into the LTE trial, and had a PGA score of ≥2 (mild or worse) before receiving treatment with tapinarof cream 1% QD in the LTE trial
- In PSOARING 3, patients were treated with tapinarof cream 1% QD based on individual patient PGA score:
  - Patients who entered with a PGA score of ≥1 received tapinarof cream until complete disease clearance was achieved (PGA=0)
  - Patients 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 score of 0 was achieved

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



*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 treatment period.
BSA, body surface area; LTE, long-term extension; PGA, Physician Global Assessment; QD, once daily; R, randomized.

Endpoints and Statistical Analysis

- Safety: Adverse events (AEs), laboratory values, vital signs, and physical exams
- Efficacy endpoints:
  - Proportions of patients who achieved a PGA score of 0 (clear) or 1 (almost clear), and ≥1-grade improvement in PGA score at any time point
  - Proportions of patients who achieved a 75% improvement in Psoriasis Area and Severity Index score (PASI75), and a 90% improvement in Psoriasis Area and Severity Index score (PASI90) at any time point
- Time-to-event parameters were summarized using the Kaplan–Meier product limit method, using observed cases

RESULTS

Baseline Patient Demographics and Disease Characteristics

- Overall, 915 eligible patients were included in the pooled efficacy analyses (**Table 1**)
- Overall, patients' 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
- At baseline, 78.1% had a PGA score of 3 (moderate), mean PASI score was 8.7, and mean body surface area affected was 7.8%

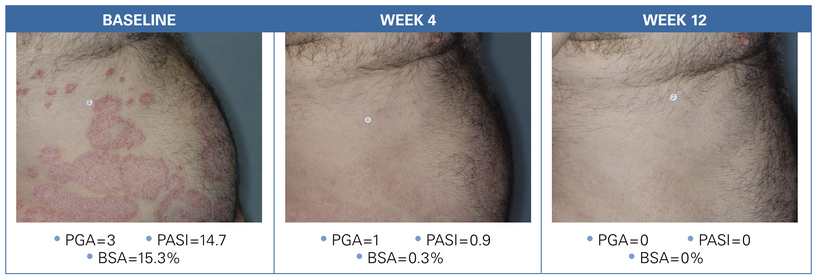
Table 1. Baseline Disease Characteristics in Pooled Analyses

	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.

- **Figure 2** displays clinical response for a patient with plaque psoriasis treated with tapinarof cream 1% QD, whose improvement exceeded the PGA, PASI75, and PASI90 endpoints by Week 4

Figure 2. Clinical Response of a Patient with Plaque Psoriasis Treated with Tapinarof Cream 1% QD

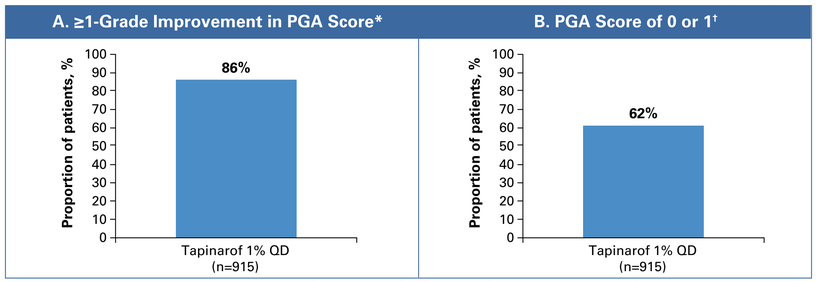


Example of one representative target lesion of one patient treated with tapinarof cream 1% QD from the PSOARING 2 clinical trial. Individual results may vary.
BSA, body surface area; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily.

PGA Score Outcomes

- The proportion of patients with a ≥1-grade improvement in PGA score increased over time: 77.4% of patients at Week 12 and 80.9% at Week 52, even with intermittent therapy
- The proportion of patients with a PGA score of 0 or 1 increased over time: 42.3% of patients at Week 12 and 47.5% at Week 52, even with intermittent therapy
- 86.1% of patients (n=788) achieved a ≥1-grade improvement in PGA score at any visit (**Figure 3A**)
- 62.0% of patients (n=567) achieved a PGA score of 0 or 1 at any visit (**Figure 3B**)

Figure 3. Proportion of Patients Achieving a ≥1-Grade Improvement in PGA Score and a PGA Score of 0 or 1 at any time point

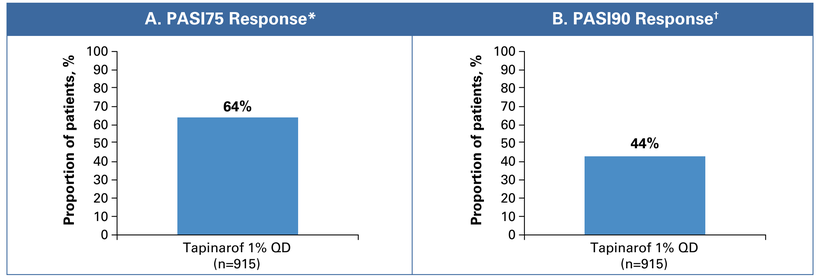


*Median time to a ≥1-grade improvement in PGA score was 29 (95% CI, 29.0–31.0) days. †Median time to a PGA score of 0 or 1 was 112 (95% CI, 92.0–115.0) days.
ITT population, OC.
CI, confidence interval; ITT, intention-to-treat; OC, observed cases; PGA, Physician Global Assessment; QD, once daily.

Achieving PASI75 and PASI90 Responses

- The proportion of patients achieving a PASI75 response increased over time; this was achieved by 44.1% of patients at Week 12 and 55.1% at Week 52, even with intermittent therapy
- The proportion of patients achieving a PASI90 response increased over time; this was achieved by 20.8% of patients at Week 12 and 32.6% at Week 52, even with intermittent therapy
- 63.5% of patients (n=581) achieved a PASI75 response at any visit (**Figure 4A**)
- 44.2% of patients (n=404) achieved a PASI90 response at any visit (**Figure 4B**)

Figure 4. Proportion of Patients Achieving PASI75 and PASI90 Responses at any time point



*Median time to a PASI75 response was 111 (95% CI, 89–113) days. †Median time to a PASI90 response was 225 (95% CI, 197–252) days.
ITT population, OC.
CI, confidence interval; ITT, intention-to-treat; OC, observed cases; PASI75, ≥75% improvement in Psoriasis Area and Severity Index score; PASI90, ≥90% improvement in Psoriasis Area and Severity Index score; QD, once daily.

Safety

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

CONCLUSIONS

- These pooled analyses from the three phase 3 trials further demonstrated the efficacy and safety of tapinarof cream 1% QD to treat mild to severe plaque psoriasis under conditions of continuous or intermittent treatment for up to 1 year
- Efficacy increased over time through 52 weeks across multiple endpoints, even with intermittent therapy
- Safety outcomes were consistent with the individual phase 3 trials
- These analyses provide additional, robust evidence that tapinarof cream 1% QD represents a first-in-class, non-steroidal, topical therapy for patients with plaque psoriasis that is effective and well tolerated with long-term use, including on intertriginous and sensitive skin areas

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