Tapinarof Cream 1% Once Daily: Disease Control Off Treatment and Minimal Disease Activity Through End of Remittive Period in a 1-year Trial

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BACKGROUND

- Psoriasis is a chronic, recurrent, inflammatory skin disease that significantly impacts health-related quality of life (HR-QoL)[1,2]
- Topical therapies remain the mainstay of treatment, regardless of disease severity; however, there are often limitations on duration of use[3]
  - In addition, efficacy may not be sustained after withdrawal of treatment, and rebound may be seen with some agents, particularly corticosteroids[4,5]
- Therefore, there is a need for durable efficacious topical therapies that can be used without restrictions on duration, site, and extent of use, or concerns due to long-term adverse effects or local intolerance
- Tapinarof (VTAMA®; Dermavant Sciences, Inc.) 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,[6] and is 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
- 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)[7]
- In the long-term extension trial, PSOARING 3, tapinarof cream 1% QD demonstrated an ~4-month remittive effect off therapy (maintenance of Physician Global Assessment [PGA]=0 or 1), a high rate (41%) of complete disease clearance (PGA=0), and durability on therapy for up to 52 weeks[8]

OBJECTIVE

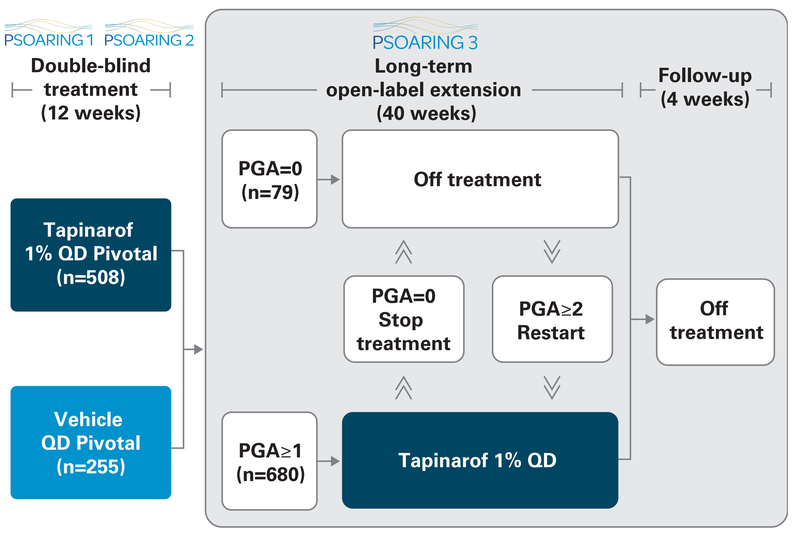
- To characterize disease activity and HR-QoL at the end of the off-therapy remittive period in PSOARING 3, across multiple objective and patient-reported parameters

MATERIALS AND METHODS

PSOARING Program Trial Design

- In PSOARING 1 and PSOARING 2, adults with mild to severe plaque psoriasis were assigned to tapinarof 1% cream or vehicle cream QD for 12 weeks
  - Entry criteria included a baseline PGA score of 2 (mild) to 4 (severe), and a percentage body surface area (%BSA) affected of 3–20%
- Patients completing PSOARING 1 and 2 were eligible to enroll in PSOARING 3 for up to 40 weeks of open-label treatment with tapinarof cream 1% QD, followed by 4 weeks of follow-up (**Figure 1**)
- In PSOARING 3, patients were treated with tapinarof based on their individual PGA score
  - Patients who entered with a PGA score of ≥1 received tapinarof until complete disease clearance was achieved, defined as a PGA score of 0
  - Patients who entered with, or achieved, a PGA score of 0 discontinued treatment and were observed for disease signs and symptoms to evaluate the off-treatment 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 was restarted and continued until a PGA score of 0 (clear) was achieved when treatment was discontinued again
  - The protocol-defined "remittive period" was therefore the duration of time off therapy from achieving a PGA score of 0 to any subsequent disease worsening (PGA score ≥2) and restarting therapy

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



Four patients (3 previously assigned to tapinarof, 1 previously assigned to vehicle) did not have a baseline PGA and are listed as missing.
PGA, Physician Global Assessment; QD, once daily.

Statistical Analysis

- This post hoc analysis of patients at the end of the first remittive period was based on observed cases in the intention-to-treat population

Endpoints

- Proportion of patients with a PGA score of 2 (mild), 3 (moderate), or 4 (severe)
- Mean Psoriasis Area and Severity Index (PASI) score, where a score of <5 indicates mild, 5–10 moderate, and >10 severe disease[9]
- Mean %BSA affected, where <3% indicates mild, 3–10% moderate, and >10% severe disease
- Mean Dermatology Life Quality Index (DLQI) score, where patients rate items for impact on HR-QoL. Total scores range from 0–30, with lower scores indicating better dermatology-specific HR-QoL, and a score of 0 or 1 representing no effect on HR-QoL[10]

RESULTS

Baseline Patient Demographics and Disease Characteristics

- 91.6% (n=763) of eligible patients completing PSOARING 1 and 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 12-week pivotal trials
- Patients previously randomized to tapinarof cream 1% QD (Tapinarof→Tapinarof) in the pivotal trials had lower baseline disease scores in PSOARING 3 than patients previously randomized to vehicle QD (Vehicle→Tapinarof), reflecting the significant efficacy of tapinarof in the pivotal trials
- In PSOARING 3, the mean total duration of the remittive effect was approximately 4 months (130 days; standard deviation, 89 days; n=312)

Table 1. PSOARING 3 Baseline Patient Demographics and Disease Characteristics

	Overall (N=763)	Tapinarof→Tapinarof* (n=508)	Vehicle→Tapinarof* (n=255)
Age, years, mean (SD)	50.7 (12.9)	50.5 (12.9)	51.0 (12.9)
Male, n (%)	448 (58.7)	304 (59.8)	144 (56.5)
Weight, kg, mean (SD)	92.4 (23.9)	92.6 (25.1)	92.1 (21.3)
BMI, kg/m^2, mean (SD)	31.7 (7.7)	31.6 (8.1)	31.8 (7.0)
PGA, n (%)†			
0 – Clear	79 (10.4)	74 (14.6)	5 (2.0)
1 – Almost clear	161 (21.1)	144 (28.3)	17 (6.7)
2 – Mild	247 (32.4)	187 (36.8)	60 (23.5)
3 – Moderate	249 (32.6)	93 (18.3)	156 (61.2)
4 – Severe	23 (3.0)	7 (1.4)	16 (6.3)
PASI, mean (SD)†	4.8 (4.7)	3.3 (3.5)	7.7 (5.4)
BSA affected, %, mean (SD)†	4.7 (5.6)	3.3 (4.7)	7.3 (6.2)
DLQI, mean (SD)	4.3 (5.1)‡	3.3 (4.3)§	6.2 (6.0)¶

*Tapinarof→Tapinarof and Vehicle→Tapinarof: Patients previously assigned to tapinarof or vehicle, respectively, in the pivotal trials who enrolled in PSOARING 3. †Four patients (3 previously assigned to tapinarof, 1 previously assigned to vehicle) did not have a baseline PGA, PASI, and BSA value and are listed as missing. ‡n=757. §n=504. ¶n=253. Intention-to-treat population.

BMI, body mass index; BSA, body surface area; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; SD, standard deviation.

Durable Efficacy and Minimal Disease Activity Across Multiple Objective and Patient-reported Measures Through the End of the Remittive Period

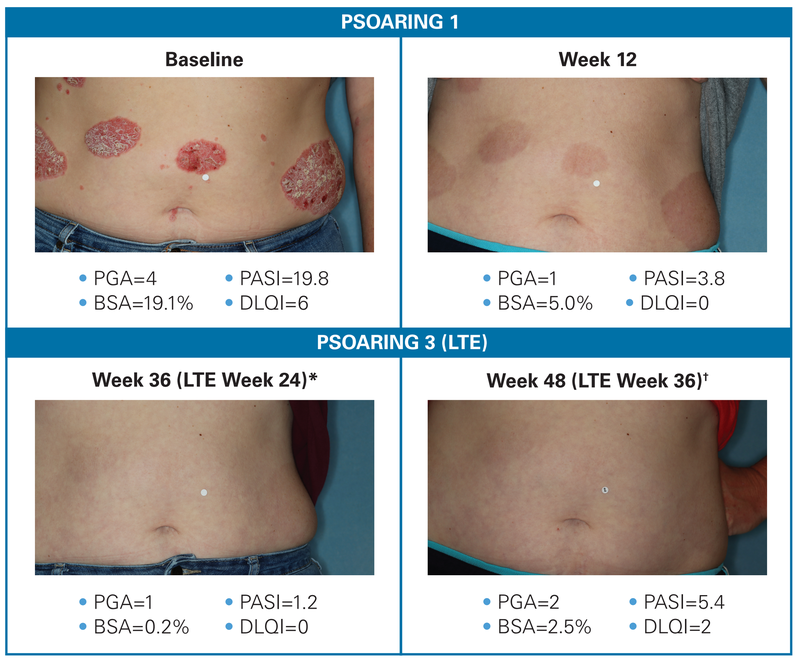
PGA Scores

- A large majority of patients (83%; n=166/199) had a PGA score of 2 (mild) at the end of the remittive period, 16% had a PGA score of 3 (moderate), and 1% had a PGA score of 4 (severe), demonstrating that efficacy was maintained through the off-therapy remittive period, with minimal disease activity and no evidence of symptom rebound or rapid worsening

PASI, %BSA Affected, and DLQI Scores

- Minimal disease activity was confirmed on multiple measures of disease severity and HR-QoL, with no evidence of symptom rebound or rapid worsening at the end of the off-therapy remittive period
  - **Mean PASI was 2.6** (standard deviation [SD] ±1.5) compared with baseline values of 8.9 (4.1) and 9.1 (3.8) in the pivotal trials and 4.8 (4.7) at baseline in PSOARING 3
  - **Mean %BSA affected was 1.5** (±2.0) compared with baseline values of 7.9 (4.8) and 7.6 (4.3) in the pivotal trials and 4.7 (5.6) at baseline in PSOARING 3
  - **Mean DLQI was 1.6** (±2.5) compared with baseline values of 8.4 (5.8) and 8.5 (5.9) in the pivotal trials and 4.3 (5.1) at baseline in PSOARING 3
- **Figure 2** displays improvements in clinical response in a patient with plaque psoriasis treated with tapinarof cream 1% QD, including a remittive period that persisted while off therapy for 6 months (24 weeks) during the PSOARING 3 LTE trial

Figure 2. Clinical Response Demonstrating Disease Control Through Remittive Effect in PSOARING 3 for a Patient with Plaque Psoriasis Treated with Tapinarof Cream 1% QD



PGA and PASI are global efficacy assessments. Example of one representative target lesion of one tapinarof-treated patient from PSOARING 1 and 3 clinical trials. Individual results may vary.
*LTE Week 24: Off treatment for 12 weeks (after achieving PGA=0 at LTE Week 12). †LTE Week 36: Off treatment for 24 weeks, with re-treatment at Week 36 due to disease worsening (PGA=2).

BSA, body surface area; DLQI, Dermatology Life Quality Index; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily.
Strober B, et al. *J Am Acad Dermatol.* 2022;87:800–6.

Safety

- There were no new safety signals during this long-term trial, and AEs were mostly mild or moderate, did not result in trial discontinuation, and were consistent with previous trials[7,8,11]

CONCLUSIONS

- In PSOARING 3, patients treated with tapinarof cream 1% QD who achieved a PGA score of 0 (completely clear) went on to experience an approximately 4-month remittive period of sustained disease control off therapy
- At the end of the protocol-defined remittive period, a high proportion of patients maintained minimal disease activity, as confirmed across multiple objective and patient-reported outcomes
  - More than 80% only had mild disease; patients reported only minimal impact on their HR-QoL
- These data confirm that patients treated with tapinarof cream 1% QD experienced durable protocol-defined remittive periods, with effective disease control off therapy
- As previously reported, in addition to the off-therapy disease control described here, tapinarof demonstrated high rates of complete disease clearance and durability on therapy for up to 52 weeks, and was well tolerated with no new safety signals during this long-term trial[6]

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