Tapinarof Cream 1% Once Daily for Plaque Psoriasis: Improvements in Quality of Life and Clinical Efficacy in Two Pivotal Phase 3 Trials

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INTRODUCTION

- Psoriasis is a chronic, immune-mediated disease that substantially impacts quality of life (QoL) through itching, pain, and disfigurement[1]
- In addition to clinician-assessed efficacy endpoints, such as the Physician Global Assessment (PGA) and the Psoriasis Area and Severity Index (PASI), the importance of evaluating patient-reported outcomes (PROs) is increasingly recognized
  - More than 70% of patients have reported that psoriasis had a moderate to extremely high impact on their daily life[2]
  - Discordance between PROs and clinician-assessed outcomes has been observed for psoriasis[3,4]
- 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 psoriasis in children down to 2 years of age and for atopic dermatitis in adults and children down to 2 years of age[5]
- Tapinarof cream 1% once daily (QD) demonstrated highly 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)[6]
- Consistent with clinical efficacy as assessed by clinicians, tapinarof cream 1% QD demonstrated rapid, clinically meaningful, and highly statistically significant improvements in PROs compared with vehicle in PSOARING 1 and 2, including change in Dermatology Life Quality Index (DLQI) score from baseline to Week 12[7]

OBJECTIVE

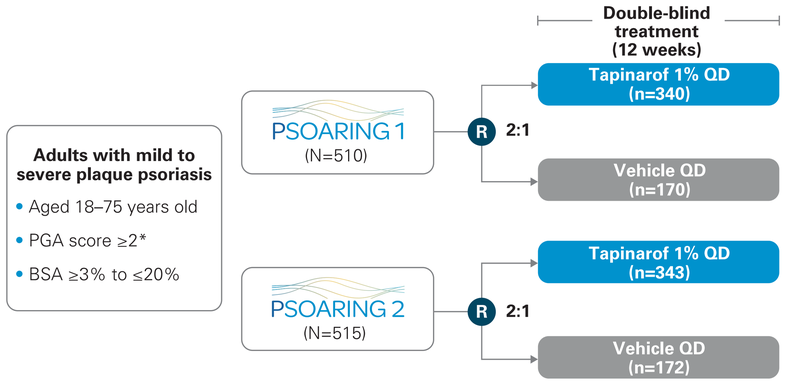
- To present further analyses of patient-reported and clinician-assessed outcomes for tapinarof cream 1% QD based on the DLQI, PGA, and PASI in PSOARING 1 and PSOARING 2

MATERIALS AND METHODS

Trial Design

- PSOARING 1 and PSOARING 2 were two identically designed, phase 3, multicenter (US and Canada), double-blind, vehicle-controlled, randomized trials in which patients with mild to severe plaque psoriasis were randomized to tapinarof cream 1% QD or vehicle QD for 12 weeks (**Figure 1**)

Figure 1. PSOARING 1 and PSOARING 2 Trial Design



*Patients with PGA=2 (mild) and PGA=4 (severe) were limited to ~10% each of the total randomized population; with ~80% of the total randomized population having a PGA=3 (moderate).
BSA, body surface area; PGA, Physician Global Assessment; QD, once daily; R, randomized.

Endpoints and Statistical Analysis

- The DLQI is a validated, dermatology-specific, 10-item patient questionnaire
  - Each item rates impact of disease on QoL on a 4-point scale from 0 (not at all) to 3 (very much)
  - Total scores range from 0 to 30, with lower scores indicating better health-related QoL (i.e., a lower impact of disease on QoL)
  - A total DLQI score of 0 or 1 indicates "no effect at all" of disease on QoL
  - A total DLQI score of 2–5 indicates a small effect, 6–10 a moderate effect, and >10 a very large effect on QoL[8]
- Efficacy assessments included PGA and PASI
- Spearman rank correlations were used to evaluate relationships between changes from baseline in efficacy (assessed using PGA and PASI) and changes from baseline in DLQI score at Week 12
- Analyses used observed cases and were based on the intention-to-treat population
- For the proportion of patients with DLQI of 0 or 1, *P* values for differences between tapinarof cream 1% QD and vehicle were calculated using Cochran-Mantel-Haenszel analyses and stratified by baseline PGA score. For the change in DLQI from baseline, *P* values were calculated using an analysis of covariance model with effects for treatment, baseline PGA score, and baseline DLQI

RESULTS

Baseline Patient Disease Characteristics

- The analyses included 683 tapinarof-treated patients and 342 vehicle-treated patients (**Table 1**)
- At baseline, 79.2%–83.9% of patients had a PGA score of 3 (moderate), and mean PASI was 8.9–9.1 in PSOARING 1 and 2, respectively
- Mean DLQI score was 8.2–8.7 across treatment groups and trials
  - Only 5.6%–7.6% of patients had a DLQI of 0 or 1, indicating no impact of disease on QoL

Table 1. Baseline Demographics and Disease Characteristics in PSOARING 1 and PSOARING 2

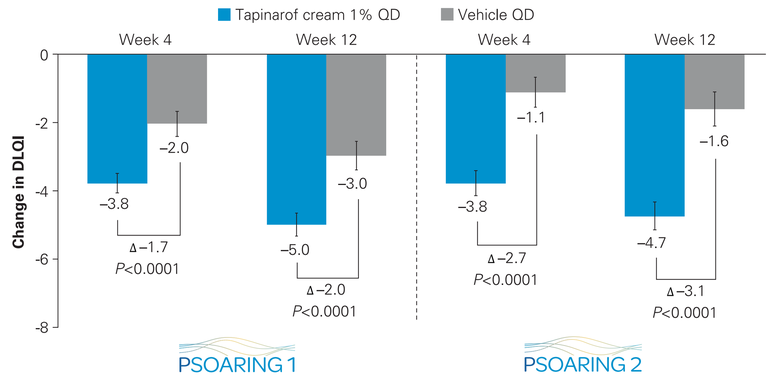
	PSOARING 1		PSOARING 2	
	Tapinarof cream 1% QD (n=340)	Vehicle QD (n=170)	Tapinarof cream 1% QD (n=343)	Vehicle QD (n=172)
Age, years, mean (SD)	49.8 (13.7)	49.1 (13.3)	50.0 (13.1)	50.0 (13.7)
Male, n (%)	213 (62.6)	86 (50.6)	188 (54.8)	102 (59.3)
Weight, kg, mean (SD)	91.7 (24.6)	92.8 (22.7)	92.9 (24.3)	89.6 (19.9)
BMI, kg/m^2, mean (SD)	31.4 (7.8)	32.5 (7.6)	31.8 (7.7)	30.7 (6.3)
PGA, n (%)				
2 – Mild	39 (11.5)	21 (12.4)	28 (8.2)	15 (8.7)
3 – Moderate	271 (79.7)	133 (78.2)	288 (84.0)	144 (83.7)
4 – Severe	30 (8.8)	16 (9.4)	27 (7.9)	13 (7.6)
PASI, mean (SD)	8.7 (4.0)	9.2 (4.4)	9.1 (3.7)	9.3 (4.0)
BSA affected, %, mean (SD)	7.8 (4.6)	8.2 (5.1)	7.8 (4.4)	7.3 (4.1)
DLQI, mean (SD)*	8.2 (5.8)	8.7 (5.9)	8.5 (5.9)	8.6 (5.9)
DLQI of 0 or 1, n (%)*	25 (7.4)	13 (7.6)	19 (5.6)	10 (5.8)

*Baseline DLQI data was missing for three patients in the tapinarof groups (two in PSOARING 1; one in PSOARING 2).
BMI, body mass index; BSA, body surface area; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily; SD, standard deviation.

Change in DLQI from Baseline to Week 12

- Significant improvements in mean DLQI were achieved by Week 4, the earliest evaluation time point; improvement continued through Week 12 in the tapinarof cream 1% QD versus vehicle groups in PSOARING 1 and 2: –5.0 vs –3.0 and –4.7 vs –1.6 (both *P*<0.0001), respectively (**Figure 2**)

Figure 2. Change in DLQI at Week 4 and Week 12



ITT population, OC. Least squares mean (SE).
DLQI, Dermatology Life Quality Index; ITT, intention-to-treat; OC, observed cases; QD, once daily; SE, standard error.

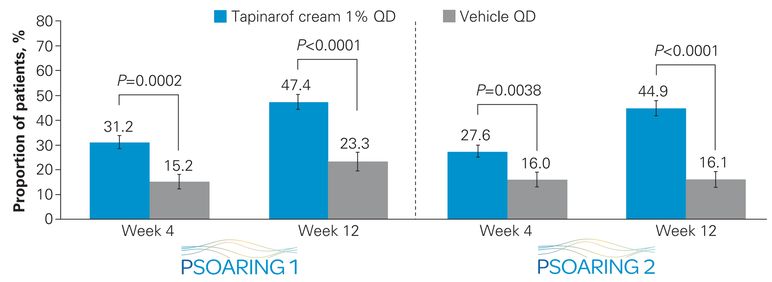
Correlation Between DLQI and PGA or PASI

- Improvements from baseline in DLQI and PGA at Week 12 in the tapinarof cream groups were statistically positively correlated in both PSOARING 1 and 2 (Spearman correlation: 0.28 and 0.29 [both *P*<0.0001]), respectively
- Improvements from baseline in DLQI and PASI at Week 12 in the tapinarof cream groups were also statistically positively correlated in both PSOARING 1 and 2 (Spearman correlation: 0.28 and 0.40 [both *P*<0.0001]), respectively

Proportion of Patients with DLQI of 0 or 1

- The proportion of patients achieving a DLQI of 0 or 1, indicating no effect of psoriasis on QoL, was significantly higher in the tapinarof cream versus vehicle groups at Week 12 in PSOARING 1 and 2: 47.4% vs 23.3% and 44.9% vs 16.1% (both *P*<0.0001), respectively (**Figure 3**)
- Statistically significant improvements in the proportion of patients achieving a DLQI of 0 or 1 with tapinarof cream versus vehicle were observed as early as Week 4 in both trials

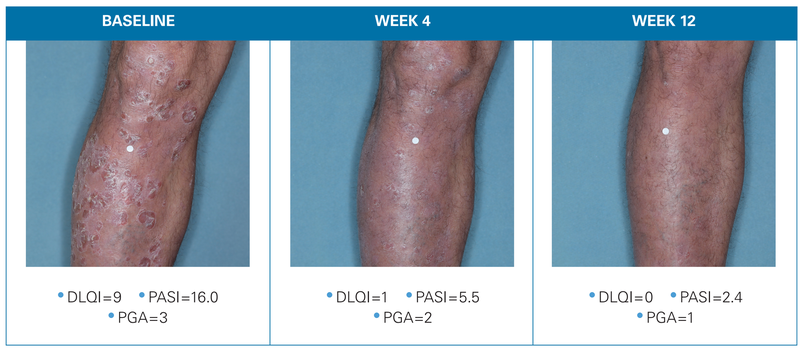
Figure 3. Proportion of Patients with DLQI of 0 or 1



ITT population, OC.
DLQI, Dermatology Life Quality Index; ITT, intention-to-treat; OC, observed cases; QD, once daily.

- **Figure 4** shows a patient treated with tapinarof cream 1% QD monotherapy who achieved DLQI=1 by Week 4, and showed further improvement to DLQI=0 at Week 12, as well as achieving the trial primary and secondary endpoints

Figure 4. Improvement in DLQI, PASI, and PGA in 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 the PSOARING 1 clinical trial. Individual results may vary.
DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.

CONCLUSIONS

- Tapinarof cream 1% QD demonstrated rapid, clinically meaningful, and statistically significant improvements in investigator-assessed objective efficacy measures and patient-reported QoL
- In addition to overall improvement in total DLQI, a large proportion (45%–47%) of patients treated with tapinarof achieved a DLQI of 0 or 1 (no negative effects of psoriasis on their QoL) by Week 12, with a significant improvement observed as early as Week 4
- Agreement between investigator assessments of efficacy and patient-reported QoL with tapinarof cream 1% QD provides additional confirmation of the clinically meaningful improvements in psoriasis demonstrated across these trials[4]
- The correlations between improvements in DLQI and investigator-assessed efficacy suggest that, beyond clinical improvements captured by the PGA and PASI, other important factors, such as mental/emotional well-being and satisfaction with treatment, may contribute to the considerable QoL improvements observed

REFERENCES

1. Feldman SR, et al. *Am Health Drug Benefits*. 2016;9:504. 2. Feldman SR, et al. *Cutis*. 2013;92:258–263. 3. Carr E, et al. *JAMA Dermatol*. 2021;157:413–420. 4. Griffiths C, et al. *J Eur Acad Dermatol Venereol*. 2018;32:1523–1529. 5. Dermavant Sciences. VTAMA (tapinarof) cream, 1%: US prescribing information. 2022. https://www.vtama.com/docs/DMVT_VTAMA_PI.pdf. Accessed 22 July 2022. 6. Lebwohl MG, et al. *N Engl J Med*. 2021;385(24):2219–2229. 7. Bissonnette R, et al. Poster presented at: American Academy of Dermatology; March 19-23, 2021. 8. Hongbo Y, et al. *J Invest Derm*. 2005;125:659–664.

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