Tapinarof Cream 1% Once Daily for Plaque Psoriasis: Efficacy by Baseline Disease Characteristics and Demographics in Two Pivotal Phase 3 Trials

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SYNOPSIS

- Tapinarof is a first-in-class, non-steroidal, topical therapeutic aryl hydrocarbon receptor modulating agent (TAMA) in development for the treatment of psoriasis and atopic dermatitis
- In two identical, randomized, double-blind phase 3 trials, PSOARING 1 and PSOARING 2, tapinarof cream 1% once daily (QD) demonstrated highly statistically significant efficacy versus vehicle at 12 weeks and was well tolerated in adults with mild-to-severe plaque psoriasis[1]

OBJECTIVE

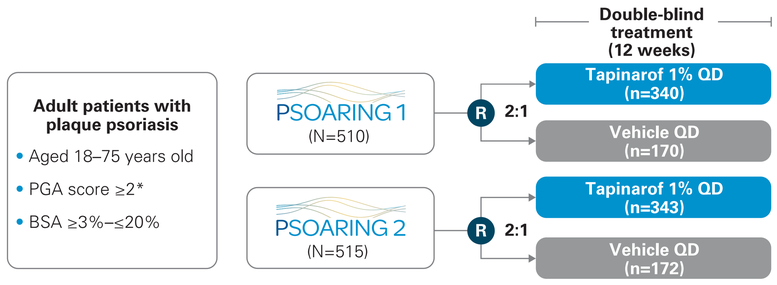
- To present results for the pivotal phase 3 primary efficacy endpoint (proportion of patients who achieved a Physician Global Assessment [PGA] response at Week 12) by baseline disease characteristics and demographics using pooled data from PSOARING 1 and PSOARING 2

METHODS

Study Design

- Patients with mild-to-severe plaque psoriasis were randomly assigned 2:1 to receive tapinarof cream 1% QD or vehicle QD for 12 weeks in two identical, phase 3, multicenter (US and Canada), double-blind, vehicle-controlled trials (**Figure 1**)
- Following the double-blind period, patients could enroll in a separate open-label, long-term extension study for an additional 40 weeks of treatment, or complete a follow-up visit 4 weeks after the end of treatment (Week 16)

Figure 1. Study Design



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

Endpoints and Statistical Analysis

- The primary endpoint was PGA response at Week 12, defined as the proportion of patients with a PGA score of 0 (clear) or 1 (almost clear) and ≥2-grade improvement in PGA score from baseline to Week 12
- The incidence, frequency, and nature of adverse events (AEs) and serious AEs were monitored from the start of study treatment until the end-of-study visit
- The pooled analyses used multiple imputation for the intention-to-treat (ITT) populations in PSOARING 1 and 2
- Tapinarof cream 1% QD and vehicle groups were compared within each subgroup for the primary endpoint using 95% confidence intervals for the relative risk calculated using Cochran-Mantel-Haenszel analyses stratified by baseline PGA score

RESULTS

Patient Disposition and Baseline Characteristics

- The pooled analysis population included 1,025 patients randomized to tapinarof cream 1% QD (n=683) or vehicle QD (n=342) in PSOARING 1 and 2 (ITT population)
- Baseline disease characteristics and demographics in the pooled population were comparable across treatment groups (**Table 1**)
- Overall, at baseline, 82% had a PGA score of 3 (moderate), 57% had psoriasis for >10 years, and 26% had ≥10% body surface area (BSA) affected

Table 1. Baseline Patient Demographics and Disease Characteristics (Pooled PSOARING 1 and 2)

	Tapinarof 1% QD (n=683)	Vehicle QD (n=342)
Age <65 years, n (%)	584 (85.5)	302 (88.3)
Male, n (%)	401 (58.7)	188 (55.0)
Race, n (%)		
Caucasian	586 (85.8)	284 (83.0)
Asian	46 (6.7)	25 (7.3)
Black/African American	30 (4.4)	17 (5.0)
American Indian or Alaska Native	2 (0.3)	2 (0.6)
Native Hawaiian or Other Pacific Islander	1 (0.1)	1 (0.3)
Other*	13 (1.9)	10 (2.9)

Table 1. (Cont)

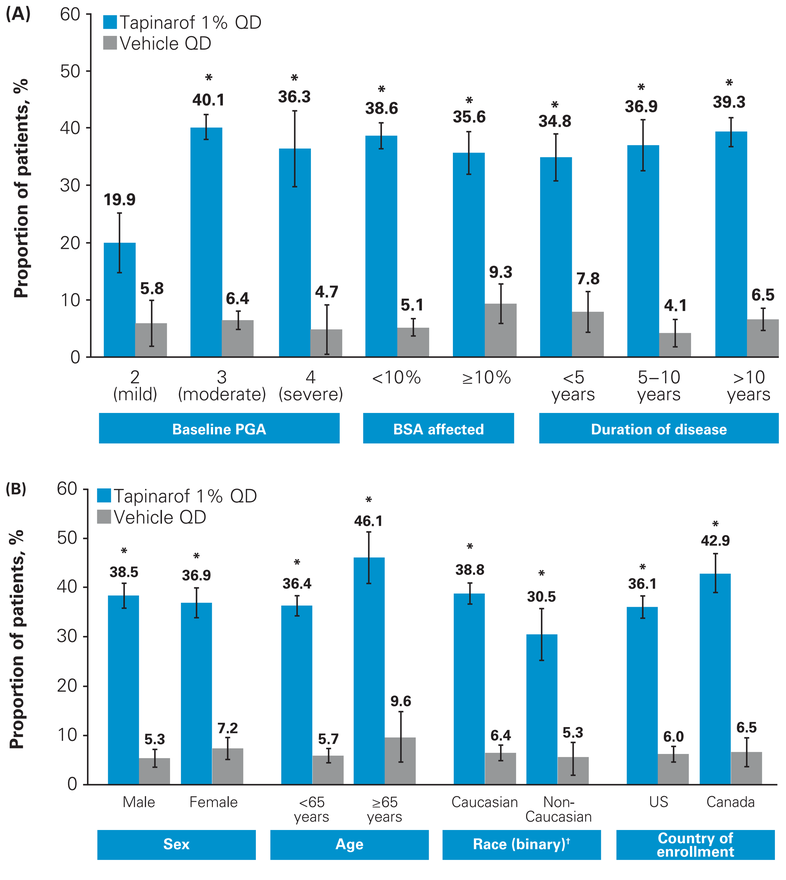
Country of enrollment, n (%)		
US	514 (75.3)	262 (76.6)
Canada	169 (24.7)	80 (23.4)
PGA, n (%)		
2 – Mild	67 (9.8)	36 (10.5)
3 – Moderate	559 (81.8)	277 (81.0)
4 – Severe	57 (8.3)	29 (8.5)
BSA affected, n (%)		
<10%	505 (73.9)	257 (75.1)
≥10%	178 (26.1)	85 (24.9)
Duration of disease, n (%)		
<5 years	154 (22.5)	73 (21.3)
5–10 years	128 (18.7)	89 (26.0)
>10 years	401 (58.7)	180 (52.6)

*Includes patients with multiple races reported. ITT population.
BSA, body surface area; ITT, intention-to-treat; PGA, Physician Global Assessment; QD, once daily.

PGA Response by Baseline Disease Characteristics and Demographics

- The primary endpoint (PGA of 0 or 1 and ≥2-grade improvement at Week 12) was met; PGA response rates were highly statistically significant in the tapinarof cream 1% QD group versus the vehicle group in both PSOARING 1 and 2: 35.4% vs 6.0% (P<0.0001) and 40.2% vs 6.3% (P<0.0001), respectively[1]
- The efficacy of tapinarof cream was consistent across subgroups, regardless of baseline disease characteristics such as PGA score, %BSA affected, and duration of disease, and demographics such as sex, age, race, country of enrollment (**Figure 2**)
- Notably, based upon the definition of PGA response requiring achievement of PGA=0 or 1 with ≥2-grade improvement, mild patients had to achieve complete disease clearance (PGA=0) and severe patients had to improve a minimum of 3 points, to be responders

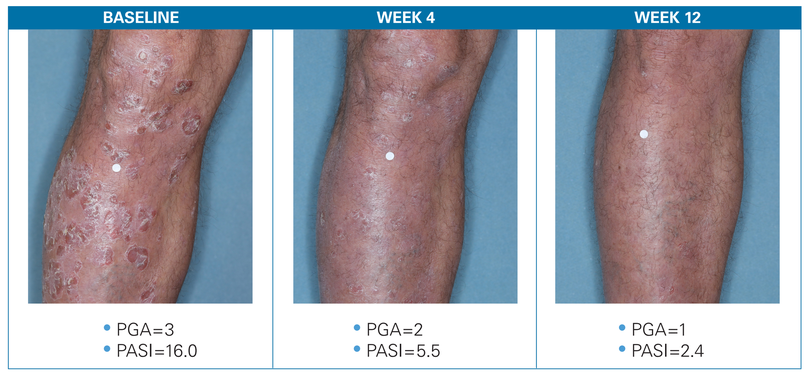
Figure 2. PGA Response at Week 12 by Baseline Disease Characteristics (A) and Demographics (B) (Pooled PSOARING 1 and 2)



*Lower limit of the 95% CI for the relative risk >1, indicating a significantly higher probability of PGA response with tapinarof compared with vehicle. Relative risk and associated 95% CIs were calculated using Cochran-Mantel-Haenszel analyses, stratified by baseline PGA score. Relative risk indicates the probability of PGA response occurring in the tapinarof group versus the probability of PGA response occurring in the vehicle group. †Non-Caucasian category includes Asian, Black/African American, American Indian or Alaska Native, Native Hawaiian, or Other Pacific Islander, and Other and has been grouped due to small patient numbers.
ITT, MI. Mean proportion (SE). PGA response defined as a PGA score of 0 (clear) or 1 (almost clear) with ≥2-grade improvement from baseline. BSA, body surface area; CI, confidence interval; ITT, intention-to-treat; MI, multiple imputation; PGA, Physician Global Assessment; QD, once daily; SE, standard error.

- **Figure 3** displays photographs of the clinical response of a patient treated with tapinarof cream who achieved the primary and secondary efficacy endpoints at Week 12

Figure 3. Clinical Response of a Patient with Plaque Psoriasis who Achieved Primary and Secondary Efficacy Endpoints at Week 12



PGA and PASI are global efficacy assessments. Example of one representative target lesion of one tapinarof-treated patient from PSOARING 1 clinical trial. Individual results may vary.
PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.

Safety

- Treatment-emergent AEs (TEAEs) were mostly mild to moderate in severity, with a low rate of study discontinuation (5.6% in PSOARING 1 and 5.8% in PSOARING 2)
- The most common TEAEs overall were folliculitis (20.2% tapinarof vs 0.9% vehicle), nasopharyngitis (5.7% tapinarof vs 4.4% vehicle), and contact dermatitis (4.8% tapinarof vs 0.3% vehicle)
- Although conclusions cannot be drawn due to the small number of patients in some subgroups, the frequency and type of AEs appeared to be generally comparable across subgroups and consistent with those observed in the overall population

CONCLUSIONS

- Tapinarof cream 1% QD was consistently efficacious and well tolerated irrespective of baseline PGA score, BSA affected, duration of psoriasis, sex, age, race, or country of enrollment (US or Canada)
- Due to the small number of patients in some subgroups, limitations exist regarding the ability to draw definitive conclusions from the subgroup analysis
- The consistent efficacy and tolerability in all subgroups support the potential use of tapinarof cream across a broad spectrum of disease severity and patient demographics
- A long-term extension trial (PSOARING 3) of intermittent treatment with tapinarof cream 1% QD based on PGA score demonstrated continued efficacy following the 12-week pivotal trials and an ~4-month remittive effect off therapy[2]
- Tapinarof cream 1% QD has potential to be the first topical psoriasis treatment with a novel mechanism of action in over 20 years

REFERENCES

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