Efficacy of Tapinarof Cream by Body Region in Subjects With Plaque Psoriasis in a Phase 2b Randomized Controlled Study

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INTRODUCTION

- Psoriasis is a chronic, immune-mediated disease characterized by scaly, erythematous, and pruritic plaques that can be painful and disfiguring[1]
- Plaque localization can impact quality of life, and response to treatment may also vary by body region[2]
- Although multiple options are available for the treatment of plaque psoriasis, there is a need for effective topical therapies that can be used without body surface area (BSA) restrictions or concerns for the duration of treatment
- Tapinarof is a therapeutic aryl hydrocarbon receptor modulating agent (TAMA) under investigation for the treatment of psoriasis (NCT03956355 & NCT03983980) and atopic dermatitis
- This previously conducted phase 2b dose-finding study (NCT02564042) was designed to assess the efficacy and safety of tapinarof cream in subjects with plaque psoriasis[3,4]
- This analysis was conducted to explore whether the efficacy and safety of tapinarof varied across body regions

OBJECTIVES

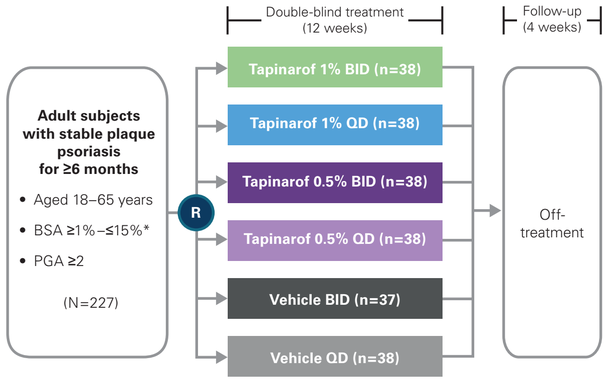
- To report efficacy outcomes by mean change in Psoriasis Area and Severity Index (PASI) from baseline, overall and by body region

METHODS

Study Design

- In this multicenter (United States, Canada, and Japan), phase 2b, double-blind, vehicle-controlled, randomized study, adult subjects with psoriasis were randomized 1:1:1:1:1:1 to receive tapinarof cream 0.5% or 1% once (QD) or twice daily (BID) or vehicle QD or BID for 12 weeks and followed up for 4 more weeks (**Figure 1**)

Figure 1. Study Design



*Excluding scalp. BID, twice daily; BSA, body surface area; PGA, Physician Global Assessment; QD, once daily; R, randomized.

Study Outcomes and Statistical Analysis

- The primary endpoint was Physician Global Assessment (PGA) response rate at Week 12, defined as the proportion of subjects with a PGA score of clear (0) or almost clear (1) and ≥2-grade improvement in PGA score from baseline to Week 12[3]
- Additional *post-hoc* efficacy analyses reported here include mean change in PASI from baseline overall and by body region (upper extremities, lower extremities, head/neck, and trunk)
- Incidence, frequency, and nature of adverse events (AEs) and serious AEs were collected from the start of study treatment until the end-of-study visit at Week 16

RESULTS

Subject Disposition

- A total of 227 subjects (of 290 screened) were randomized (intent-to-treat population), and of those randomized, 175 subjects (77%) completed the study, including the Week 16 follow-up visit

Baseline Characteristics

- Mean demographic and baseline characteristics were comparable across groups (**Table 1**)
- Mean PASI score at baseline was 8.8 (standard deviation 4.5)
- PGA category at baseline:
  - 15% had a PGA of 2 (mild)
  - 80% had a PGA of 3 (moderate)
  - 5% had a PGA of 4 (severe)

Table 1. Baseline Subject Demographics and Characteristics

	Tapinarof cream 1%		Tapinarof cream 0.5%		Vehicle	
	BID (n=38)	QD (n=38)	BID (n=38)	QD (n=38)	BID (n=37)	QD (n=38)
Mean age, years (SD)	45.9 (11.9)	48.5 (10.6)	49.6 (10.9)	48.7 (9.7)	46.7 (12.6)	46.4 (10.2)
Male sex, n (%)	26 (68)	26 (68)	24 (63)	25 (66)	23 (62)	29 (76)
Mean weight, kg (SD)	85.6 (22.5)	86.7 (22.6)	88.6 (27.4)	89.3 (23.1)	87.8 (28.3)	91.6 (21.6)
PGA, mean (SD)	2.9 (0.4)	2.7 (0.5)	3.0 (0.5)	2.9 (0.4)	3.0 (0.3)	2.8 (0.4)
PASI, mean (SD)	10.6 (5.0)	8.5 (3.6)	8.2 (4.5)	7.9 (4.8)	9.0 (4.3)	8.7 (4.4)
% BSA affected, mean (SD)	8.2 (4.5)	6.5 (3.3)	7.2 (4.5)	6.1 (4.3)	6.6 (3.6)	7.0 (4.6)
Pruritus score, mean (SD)*	5.6 (2.6)	4.4 (2.9)	6.2 (2.2)	4.5 (2.6)	5.5 (2.8)	4.9 (2.4)

Characteristics provided for the mITT population (n=196), which included subjects in the ITT population minus the subjects from one site due to protocol violation. Demographics (age, sex, and weight) provided for the safety population (n=227). *Mean scores based on a numeric rating scale of 0 'absent' to 10 'worst imaginable'; data provided for subjects with available results (n=32, 35, 30, 32, 29, and 32, respectively).
BID, twice daily; BSA, body surface area; ITT, intent-to-treat; mITT, modified intent-to-treat; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily; SD, standard deviation.

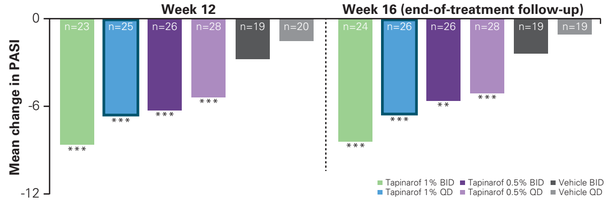
PGA Response Rates

- Primary endpoint: PGA response rates (defined as PGA score 0 or 1 and ≥2-grade improvement) at Week 12 were significantly higher (at 0.05 significance level) in the tapinarof cream groups than the vehicle groups (65% [1% BID], 56% [1% QD], 46% [0.5% BID], and 36% [0.5% QD] vs 11% [vehicle BID] and 5% [vehicle QD]) and were maintained for 4 weeks after the end-of-study treatment in all active treatment groups, except for the 0.5% BID group[3]

Mean Change in PASI

- Mean PASI improvements at Week 12 were significantly greater in all tapinarof groups vs vehicle groups (all $P<0.001$): –8.70 (1% BID), –6.62 (1% QD), –6.30 (0.5% BID), and –5.41 (0.5% QD) vs –2.77 (vehicle BID) and –1.54 (vehicle QD); significant improvements were maintained in all tapinarof groups for 4 weeks after the last application through Week 16 (**Figure 2**)

Figure 2. Mean Change in PASI from Baseline

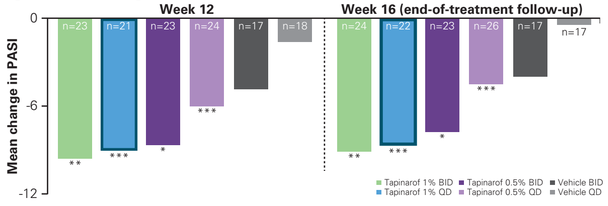


n is number of subjects with available results at Weeks 12 and 16. Difference vs vehicle was statistically significant at **$P<0.01$, ***$P<0.001$.
BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily.

Mean Change in PASI by Body Region

- **Upper extremities**: Mean PASI improvements in the upper extremities at Week 12 were significantly greater in all tapinarof groups vs vehicle groups: –9.65 (1% BID; $P=0.001$), –9.05 (1% QD; $P<0.001$), –8.70 (0.5% BID; $P=0.011$), and –6.04 (0.5% QD; $P<0.001$) vs –4.88 (vehicle BID) and –1.61 (vehicle QD); significant improvements were maintained in all tapinarof groups for 4 weeks after the last application through Week 16 (**Figure 3**)

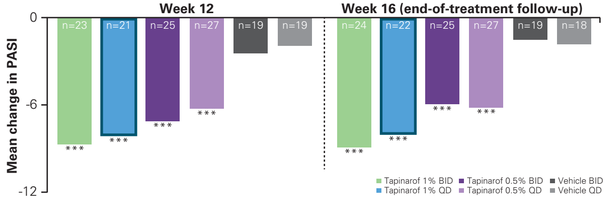
Figure 3. Mean Change in PASI from Baseline in the Upper Extremities



n is number of subjects with available results at Weeks 12 and 16. Difference vs vehicle was statistically significant at *$P<0.05$, **$P<0.01$, ***$P<0.001$.
BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily.

- **Lower extremities**: Mean PASI improvements in the lower extremities at Week 12 were significantly greater in all tapinarof groups vs vehicle groups (all $P<0.001$): –8.74 (1% BID), –8.19 (1% QD), –7.16 (0.5% BID), and –6.33 (0.5% QD) vs –2.47 (vehicle BID) and –2.0 (vehicle QD); significant improvements were maintained in all tapinarof groups for 4 weeks after the last application through Week 16 (**Figure 4**)

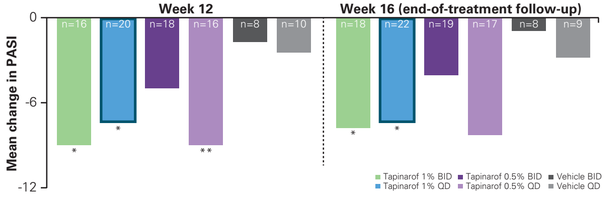
Figure 4. Mean Change in PASI from Baseline in the Lower Extremities



n is number of subjects with available results at Weeks 12 and 16. Difference vs vehicle was statistically significant at ***$P<0.001$. BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily.

- **Head/neck**: Mean PASI improvements in the head/neck at Week 12 were significantly greater in all tapinarof groups vs vehicle groups, except for the 0.5% BID group: –9.0 (1% BID; $P=0.023$), –7.40 (1% QD; $P=0.019$), –5.0 (0.5% BID; $P=0.149$), and –9.0 (0.5% QD; $P=0.007$) vs –1.75 (vehicle BID) and –2.5 (vehicle QD); significant improvements were maintained in the 1% tapinarof groups for 4 weeks after the last application through Week 16 (**Figure 5**)

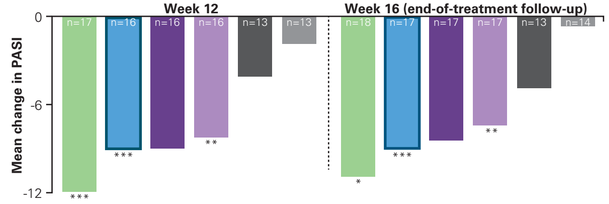
Figure 5. Mean Change in PASI from Baseline in the Head/Neck



n is number of subjects with available results at Weeks 12 and 16. Difference vs vehicle was statistically significant at *$P<0.05$, **$P<0.01$.
BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily.

- **Trunk**: Mean PASI improvements in the trunk at Week 12 were significantly greater in all tapinarof groups vs vehicle groups, except for the 0.5% BID group: –11.94 (1% BID; $P<0.001$), –9.13 (1% QD; $P<0.001$), –9.0 (0.5% BID; $P=0.052$), and –8.25 (0.5% QD; $P=0.001$) vs –4.08 (vehicle BID) and –1.85 (vehicle QD); significant improvements were maintained in all tapinarof groups, except for 0.5% BID, for 4 weeks after the last application through Week 16 (**Figure 6**)

Figure 6. Mean Change in PASI from Baseline in the Trunk



n is number of subjects with available results at Weeks 12 and 16. Difference vs vehicle was statistically significant at *$P<0.05$, **$P<0.01$, ***$P<0.001$.
BID, twice daily; PASI, Psoriasis Area and Severity Index; QD, once daily.

Safety

- Tapinarof cream was generally well tolerated[3]
- Treatment-emergent AEs (TEAEs) were mostly mild to moderate in severity
- The most common treatment-related TEAEs were folliculitis (10% tapinarof vs 1% vehicle), contact dermatitis (3%; all tapinarof), and headache (1%; all tapinarof)

CONCLUSIONS

- Tapinarof cream demonstrated consistent and durable efficacy across body regions as measured by mean change in PASI from baseline to Week 12, which was maintained for 4 weeks after last application of study treatment
- These findings support previously reported efficacy and safety outcomes[3,4]
- A phase 3 clinical trial program of tapinarof cream 1% QD in psoriasis, consisting of two studies PSOARING 1 (NCT03956355) and PSOARING 2 (NCT03983980) has completed. The long-term extension study PSOARING 3 (NCT04053387) is ongoing

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