Tapinarof Cream for the Treatment of Plaque Psoriasis: Efficacy and Safety by Baseline Disease Characteristics and Skin Type in a Phase 2b Randomized 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]
- 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 cream is a therapeutic aryl hydrocarbon receptor modulating agent (TAMA) under investigation for the treatment of psoriasis (ClinicalTrials.gov ID: NCT03956355) and atopic dermatitis
- This previously conducted phase 2b dose-finding study (ClinicalTrials.gov ID: NCT02564042) was designed to assess the efficacy and safety of tapinarof cream in subjects with plaque psoriasis[2,3]
- Factors related to disease characteristics and skin type may influence clinical outcomes in psoriasis[4,5]
- This *post-hoc* analysis was conducted to explore whether the efficacy and safety of tapinarof cream varied across subgroups by baseline disease characteristics and skin type

OBJECTIVE

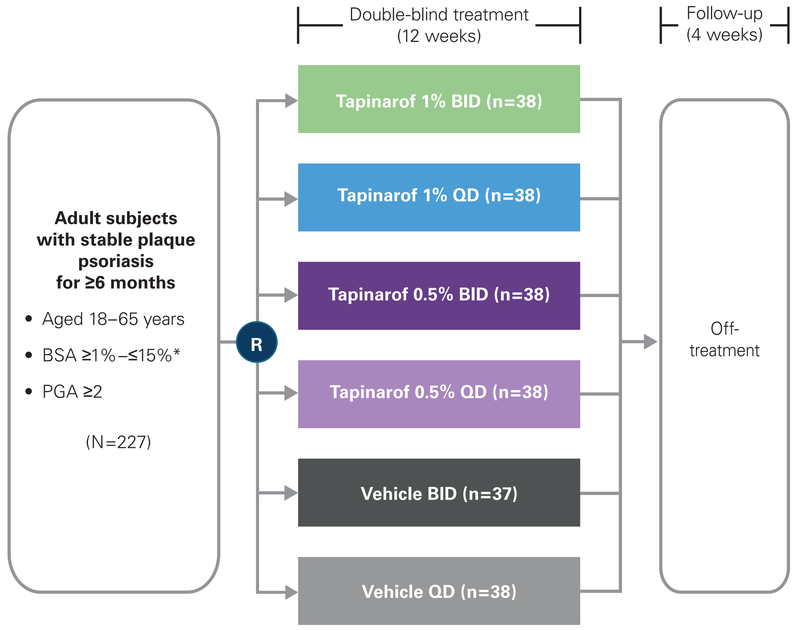
- To evaluate the efficacy and safety of tapinarof through *post-hoc* analysis from a phase 2b study in subjects with plaque psoriasis stratified by baseline disease characteristics, including % BSA affected, duration of psoriasis, and Fitzpatrick skin type

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.

Study Outcomes and Statistical Analysis

- The primary endpoint was Physician Global Assessment (PGA) response rates at Week 12, defined as the proportion of subjects with a PGA score of clear or almost clear (0 or 1) and ≥2-grade improvement in PGA score from baseline to Week 12[2]
- Additional *post-hoc* efficacy analyses reported here include PGA response rates at Week 12, stratified by the following baseline disease characteristics and skin type:
  - Baseline % BSA affected: 1 to <10% and ≥10%
  - Baseline duration of psoriasis: 6 months to <5 years, 5 years to <10 years, and ≥10 years
  - Fitzpatrick skin type: Fitzpatrick skin type I and II, Fitzpatrick skin type III and IV, and Fitzpatrick skin type V and VI
- 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 Characteristics

- A total of 227 subjects (of the 290 subjects originally screened) were randomized (intent-to-treat population) and of those randomized, 175 subjects (77%) completed the study, including the Week 16 follow-up visit
- Mean demographic and baseline characteristics were comparable across treatment groups (**Table 1**)
- Overall, 15% of subjects had a baseline PGA category of 2 (mild), 80% had a PGA category of 3 (moderate), and 5% had a PGA category of 4 (severe)
- Baseline mean Psoriasis Area and Severity Index score was 8.8 (standard deviation [SD] 4.5)

Table 1. Baseline Subject Demographics and Characteristics

	Tapinarof 1% cream		Tapinarof 0.5% cream		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)
Mean duration of psoriasis, years (SD)	15.7 (14.1)	16.6 (12.9)	17.9 (14.1)	16.6 (13.3)	18.1 (15.0)	16.0 (12.4)
Fitzpatrick skin type I, n (%)	2 (6)	3 (9)	1 (3)	2 (6)	1 (3)	1 (3)
Fitzpatrick skin type II, n (%)	8 (24)	7 (20)	10 (31)	6 (19)	5 (17)	13 (39)
Fitzpatrick skin type III, n (%)	17 (50)	14 (40)	6 (19)	13 (41)	11 (37)	11 (33)
Fitzpatrick skin type IV, n (%)	2 (6)	7 (20)	7 (22)	7 (22)	7 (23)	5 (15)
Fitzpatrick skin type V, n (%)	5 (15)	3 (9)	5 (16)	4 (13)	5 (17)	3 (9)
Fitzpatrick skin type VI, n (%)	0	1 (3)	3 (9)	0	1 (3)	0

Baseline disease 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 an NRS 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; NRS, numeric rating scale; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily; SD, standard deviation.

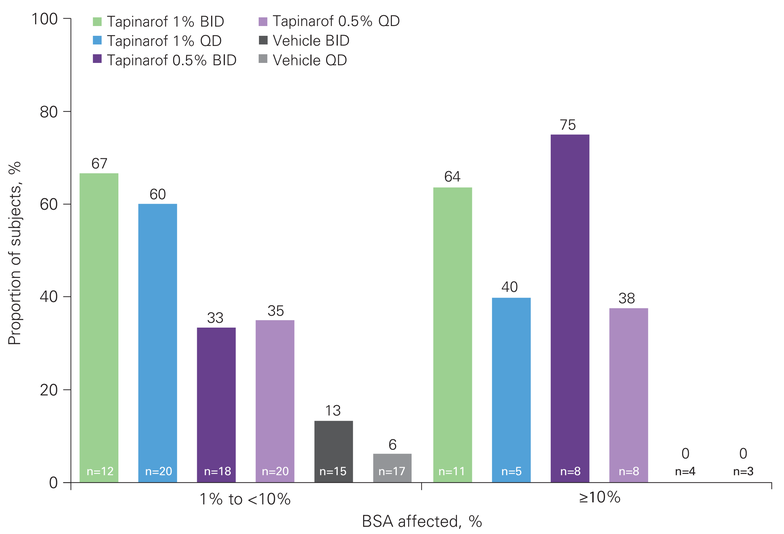
PGA Response Rates

- 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], 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[2]

PGA Response Rates by Baseline % BSA Affected

- PGA response rates at Week 12 were higher in tapinarof cream groups than vehicle groups, regardless of baseline % BSA affected (**Figure 2**)
  - 1 to <10% BSA affected (n=102): 67% (1% BID), 60% (1% QD), 33% (0.5% BID), and 35% (0.5% QD) vs 13% (vehicle BID) and 6% (vehicle QD)
  - ≥10% BSA affected (n=39): 64% (1% BID), 40% (1% QD), 75% (0.5% BID), and 38% (0.5% QD) vs 0% (vehicle BID) and 0% (vehicle QD)

Figure 2. Proportion of Subjects Who Achieved PGA Response* at Week 12 by % BSA Affected at Baseline

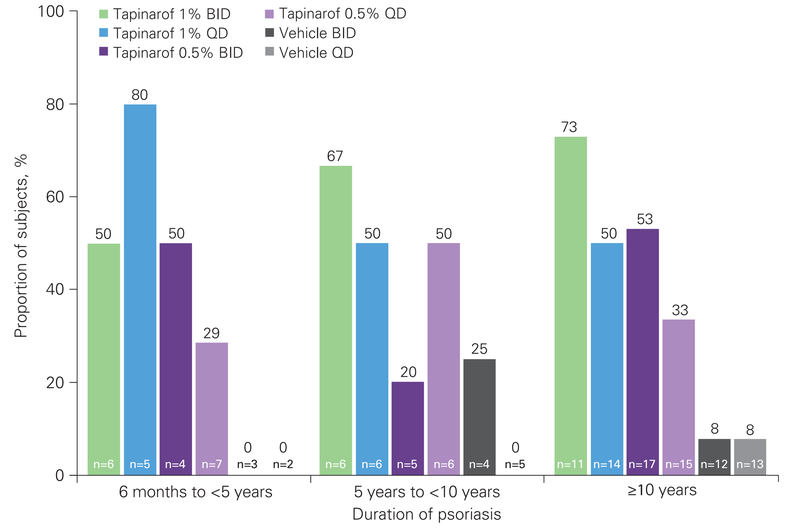


n is number of subjects with available results at Week 12. *Defined as PGA score 0 or 1 (clear or almost clear) and ≥2-grade improvement from baseline. BID, twice daily; BSA, body surface area; PGA, Physician Global Assessment, QD, once daily.

PGA Response Rates by Baseline Duration of Psoriasis

- PGA response rates at Week 12 were higher in tapinarof cream groups than in vehicle groups, regardless of baseline duration of psoriasis, except for the 0.5% BID treatment group in the 5 years to <10 years subgroup (**Figure 3**)
  - 6 months to <5 years (n=27): 50% (1% BID), 80% (1% QD), 50% (0.5% BID), and 29% (0.5% QD) vs 0% (vehicle BID) and 0% (vehicle QD)
  - 5 years to <10 years (n=32): 67% (1% BID), 50% (1% QD), 20% (0.5% BID), and 50% (0.5% QD) vs 25% (vehicle BID) and 0% (vehicle QD)
  - ≥10 years (n=82): 73% (1% BID), 50% (1% QD), 53% (0.5% BID), and 33% (0.5% QD) vs 8% (vehicle BID) and 8% (vehicle QD)

Figure 3. Proportion of Subjects Who Achieved PGA Response* at Week 12 by Duration of Psoriasis at Baseline

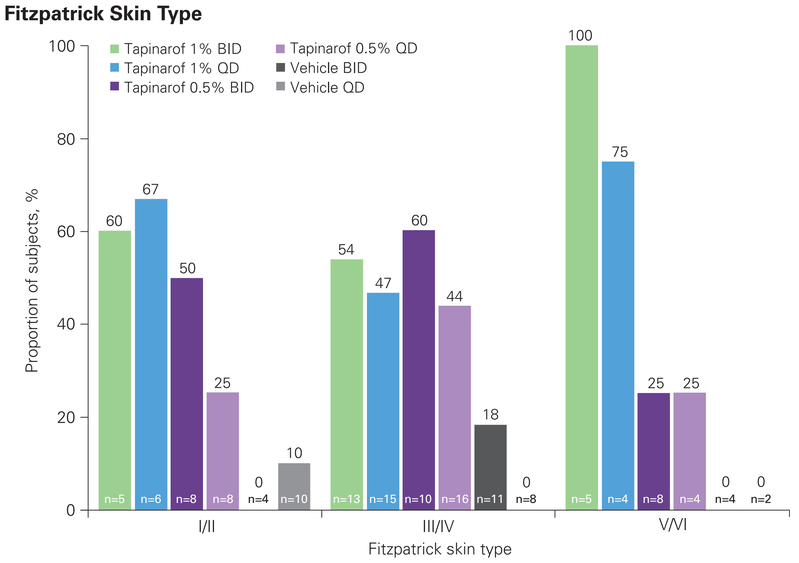


n is number of subjects with available results at Week 12. *Defined as PGA score 0 or 1 (clear or almost clear) and ≥2-grade improvement from baseline. BID, twice daily; PGA, Physician Global Assessment, QD, once daily.

PGA Response Rates by Fitzpatrick Skin Type

- PGA response rates at Week 12 were higher in tapinarof cream groups than vehicle groups, regardless of Fitzpatrick skin type (**Figure 4**)
  - Fitzpatrick skin type I/II (n=41): 60% (1% BID), 67% (1% QD), 50% (0.5% BID), and 25% (0.5% QD) vs 0% (vehicle BID) and 10% (vehicle QD)
  - Fitzpatrick skin type III/IV (n=73): 54% (1% BID), 47% (1% QD), 60% (0.5% BID), and 44% (0.5% QD) vs 18% (vehicle BID) and 0% (vehicle QD)
  - Fitzpatrick skin type V/VI (n=27): 100% (1% BID), 75% (1% QD), 25% (0.5% BID), and 25% (0.5% QD) vs 0% (vehicle BID) and 0% (vehicle QD)

Figure 4. Proportion of Subjects Who Achieved PGA Response* at Week 12 by Fitzpatrick Skin Type



n is number of subjects with available results at Week 12. *Defined as PGA score 0 or 1 (clear or almost clear) and ≥2-grade improvement from baseline. BID, twice daily; PGA, Physician Global Assessment, QD, once daily.

Safety

- 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)
- Incidence and type of AEs were generally comparable across subgroups and consistent with those observed in the overall population

CONCLUSIONS

- Overall, tapinarof cream was efficacious and well tolerated regardless of baseline % BSA affected, psoriasis duration, and Fitzpatrick skin type
- Higher PGA response rates at Week 12 were observed in the 1% QD tapinarof cream group vs vehicle across all subgroups
- These findings support the previously reported efficacy and safety outcomes of the overall population[2,3]
- A phase 3 study of tapinarof cream 1% QD in psoriasis is ongoing

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ACKNOWLEDGMENTS

The authors thank the participating investigators, patients and their families, and colleagues involved in the conduct of the study. Editorial and medical writing support under the guidance of the authors was provided by ApotheCom, UK, and was funded by Dermavant Sciences, Inc. in accordance with Good Publication Practice (GPP3) guidelines (*Ann Intern Med.* 2015;163:461–464).

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