Patient-Reported Outcomes in Subjects with Plaque Psoriasis Treated with Tapinarof Cream: Results from a Phase 2b, Randomized Parallel-Group Study

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SYNOPSIS

- Psoriasis is a chronic, immune-mediated disease characterized by scaly, erythematous, and pruritic plaques that can be painful and disfiguring[1]
- The burden of psoriasis is similar to other long-term conditions, such as congestive heart failure and chronic lung disease, and has a profound impact on mental health and wellbeing[2]
- Although multiple options are available for the treatment of plaque psoriasis, there is a need for efficacious 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 and atopic dermatitis
- This 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
- The primary analysis showed that tapinarof cream was efficacious and well tolerated in adult subjects with psoriasis and may represent an effective option in the topical treatment of the disease[1]

OBJECTIVES

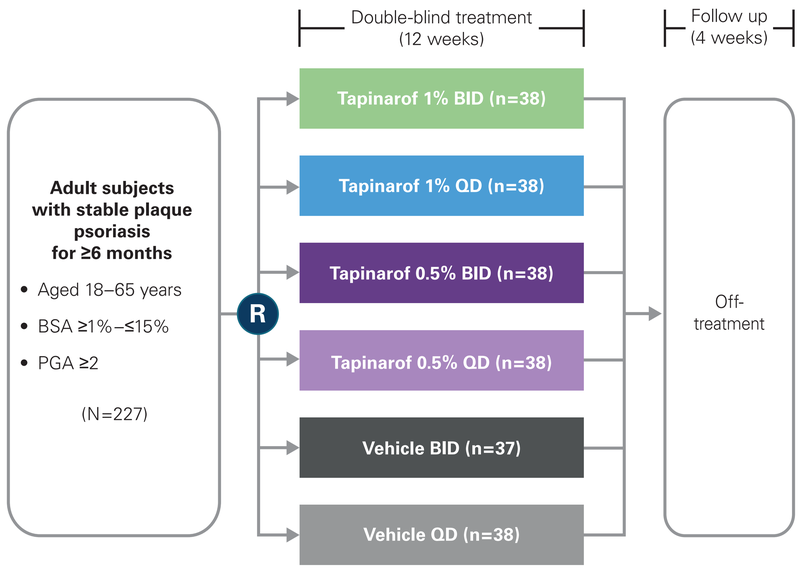
- To present the patient-reported outcomes from the Phase 2b study in subjects with psoriasis following treatment with topical tapinarof cream, including subject global impression of overall severity of psoriasis symptoms, overall severity of pruritus symptoms, and impact of symptoms on subject-reported health outcomes as assessed by the Psoriasis Symptom Diary (PSD)

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



BID, twice daily; BSA, body surface area; PGA, Physician Global Assessment; QD, once daily.

Study Outcomes and Statistical Analysis

- The primary endpoint was 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[3]
- Subject-reported outcomes assessed in this study included subject global impression of change in overall severity of psoriasis symptoms and of pruritus symptoms from baseline to Week 12, and change over time in daily PSD scores
  - Subjects were asked to rate the overall severity of their psoriasis symptoms and of their pruritus symptoms at baseline on a scale of 1 'mild' to 4 'very severe'
  - The change in overall severity of psoriasis symptoms and pruritus symptoms from baseline to Week 12 was rated by subjects from 1 'very improved' to 7 'very worse'
  - The PSD consisted of the 16 questions in the established version, plus six additional questions to assess the severity and bother of skin flaking, dryness, and bleeding
  - Each question asked about how severe and how bothersome signs and symptoms were to the subject within the last 24-hour period and subjects rated their daily scores from 0 'absent' to 10 'worst imaginable'
- Incidence, frequency, and nature of adverse events (AEs) and serious AEs were collected from the start of study treatment until end of study visit at Week 16
- No formal hypothesis tests were planned

RESULTS

Subject Characteristics

- A total of 227 subjects (of the 290 subjects originally screened) were randomized into the study at 17 sites in the United States, 12 sites in Canada, and 11 sites in Japan (intent-to-treat analysis population)
- Of those randomized, 175 subjects (77%) completed the study including the Week 16 follow-up visit
- Overall, mean demographic and baseline characteristics were comparable across treatment groups (**Table 1**)
- Most subjects (80%) had a baseline PGA category of 3 (moderate) and a baseline mean Psoriasis Area and Severity Index (PASI) score of 8.8 (standard deviation 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 score, 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 score, 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)

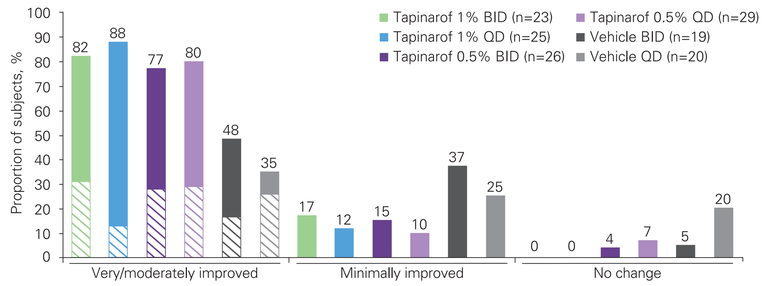
*Characteristics provided for the mITT analysis population (n=196); †Mean scores based on a scale of 0 'absent' to 10 'worst imaginable'. Demographics (age, sex and weight) provided for the safety analysis population (n=227). The mITT analysis population included subjects in the ITT population minus the subjects from one site due to protocol violation. 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.

- Primary endpoint: PGA response rates (defined as PGA score 0 or 1 and ≥2-grade improvement) at Week 12 were higher 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[3]

Subject Impressions

- At baseline, 88% of subjects rated their psoriasis symptoms as moderate or severe across all treatment groups: 43–61% rated as moderate and 28–44% rated as severe
- At Week 12, a greater proportion of subjects in the tapinarof cream groups (82–88% in the 1% groups and 77–80% in the 0.5% groups) rated the overall severity of their psoriasis symptoms as 'very/moderately improved' compared with 35–48% in the vehicle groups (**Figure 2a**)

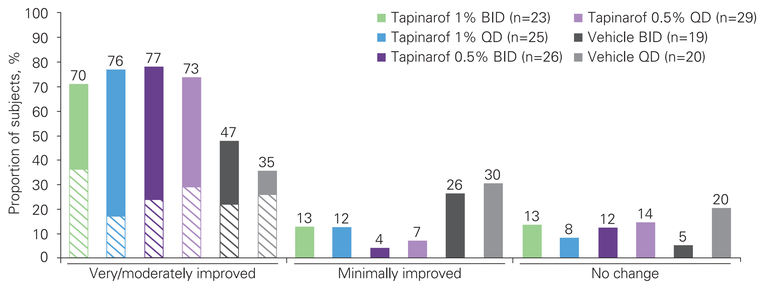
Figure 2a. Subject Impression of Change in Severity of Psoriasis Symptoms at Week 12



Results derived from the mITT analysis population including subjects in the ITT population minus the subjects from one site due to protocol violation (n=196). N is number of subjects with available results at Week 12. Hatched portion of bar corresponds to proportion of subjects with 'moderately improved' symptoms. BID, twice daily; ITT, intent-to-treat; mITT, modified intent-to-treat; QD, once daily.

- At Week 12, a greater proportion of subjects in the tapinarof cream groups (70–76% in the 1% groups and 73–77% in the 0.5% groups) rated the overall severity of their pruritus symptoms as 'very/moderately improved' compared with 35–47% in the vehicle groups (**Figure 2b**)

Figure 2b. Subject Impression of Change in Severity of Pruritus Symptoms at Week 12



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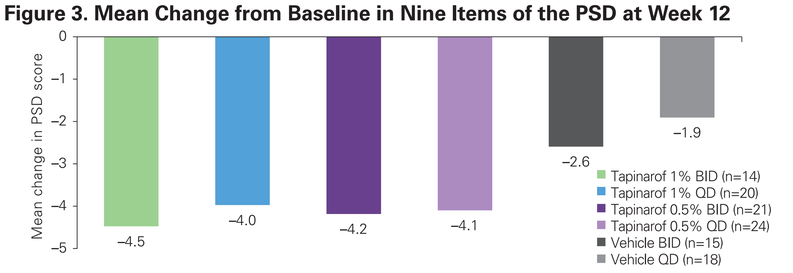
Severity of Psoriasis Symptoms (PSD)

- Overall, there was a greater reduction from baseline in mean weekly PSD scores in the tapinarof cream groups than the vehicle groups
- Nine PSD items (2, 11, 12, 13, 14, 17, 18, 19, and 20 related to itching, scaling, flaking, dryness, and appearance) showed high mean severity scores (≥5) at baseline
  - By Week 12, scores from these items had reduced (improved) more in the tapinarof cream groups compared with the vehicle groups (**Figure 3**)

Figure 3. Mean Change from Baseline in Nine Items of the PSD at Week 12



Results derived from the mITT analysis population including subjects in the ITT population minus the subjects from one site due to protocol violation (n=196). N is number of subjects with available results at Week 12. BID, twice daily; ITT, intent-to-treat; mITT, modified intent-to-treat; PSD, Psoriasis Symptom Diary; QD, once daily.

Safety

- Overall, 46% (104/227) of subjects had treatment-emergent AEs (TEAEs): 56% in the tapinarof cream groups and 25% in the vehicle groups, and were mostly mild to moderate in severity
- The most frequently reported TEAE was folliculitis (**Table 2**)

Table 2. Safety Overview and Most Common TEAEs (Occurring in ≥5% of Subjects in Any Group)

Preferred term, n (%)	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)
Any TEAE	26 (68)	20 (53)	22 (58)	17 (45)	9 (24)	10 (26)
Treatment-related TEAEs	10 (26)	10 (26)	6 (16)	8 (21)	1 (3)	1 (3)
Serious TEAEs	1 (3)	3 (8)	3 (8)	0	0	0
Discontinuations due to TEAEs	5 (13)	5 (13)	4 (11)	1 (3)	0	1 (3)
TEAE by intensity						
Mild	10 (26)	8 (21)	11 (29)	12 (32)	5 (14)	8 (21)
Moderate	12 (32)	9 (24)	7 (18)	5 (13)	3 (8)	1 (3)
Severe	4 (11)	3 (8)	4 (11)	0	1 (3)	1 (3)
TEAEs occurring in ≥5% of subjects in any group						
Folliculitis	8 (21)	2 (5)	4 (11)	5 (13)	1 (3)	0
Dermatitis contact	4 (11)	4 (11)	1 (3)	3 (8)	0	0
Headache	4 (11)	1 (3)	0	1 (3)	1 (3)	1 (3)
Nasopharyngitis	1 (3)	0	4 (11)	2 (5)	0	2 (5)
Vomiting	0	0	3 (8)	0	1 (3)	0
Acne	2 (5)	0	1 (3)	0	0	0
Application-site dermatitis	1 (3)*	2 (5)	0	0	0	0
Miliaria	0	2 (5)	0	1 (3)	0	0
Dermatitis allergic	2 (5)	0	0	0	0	0
Urticaria	0	2 (5)	0	0	0	0

TEAE was defined as an AE that occurred on or after study treatment start date and on or before the last visit. *All TEAEs occurred once in each subject except 'application-site dermatitis', which occurred twice in a subject from the 1% BID group. AE, adverse event; BID, twice daily; QD, once daily; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- In all tapinarof cream groups, a greater proportion of subjects (77–88%) reported psoriasis signs and symptoms as 'very/moderately improved' after 12 weeks compared with the vehicle groups (35–48%)
- Similarly, a greater proportion of subjects in the tapinarof cream groups (70–77%) reported the overall severity of pruritus as 'very/moderately improved' after 12 weeks compared with the vehicle groups (35–47%)
- Overall, tapinarof cream was well tolerated and these results correspond to the previously reported clinical efficacy findings[3]
- Study findings demonstrated that tapinarof cream represents an important potential advance in topical medicine development, with beneficial effects on patient-reported outcomes in patients with psoriasis

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