Efficacy of Tapinarof Cream 1% Once Daily for the Treatment of Mild to Severe Intertriginous Plaque Psoriasis

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INTRODUCTION

- Topical agents are a mainstay of treatment in patients with mild, moderate, and severe psoriasis[1,2]
- Topical corticosteroids (TCS), while efficacious for the treatment of psoriasis, are associated with adverse events (AEs), including acne, rosacea, perioral dermatitis, facial erythema, hirsutism, skin thinning and atrophy, ecchymosis, striae, in addition to the risk of systemic AEs, which can limit their use[3]
- Due to the risks associated with TCSs, treatment is often applied intermittently. Furthermore, multiple TCSs with differing potencies may be required to treat psoriasis in different locations on the body, especially sensitive areas[4]
- Plaque psoriasis commonly affects intertriginous areas; this is also called inverse psoriasis
  - Affected areas, such as the groin or genitals, are prone to AEs due to the presence of thin skin and direct occlusion, potentially increasing the likelihood of treatment absorption[5]
- There remains a need for efficacious non-steroidal topical therapies for psoriasis that have minimal systemic absorption, no risk of systemic AEs, and can be used without restrictions relating to duration or extent of use, or site of application, including in intertriginous areas
- Tapinarof cream 1% (VTAMA®, Dermavant Sciences, Inc.) is a non-steroidal, topical aryl hydrocarbon receptor agonist approved for the treatment of plaque psoriasis in adults, with no warnings, contraindications, drug–drug interactions, or restrictions on location, extent, or duration of use[6]
- In the phase 3 PSOARING trial program (N=1,025), tapinarof cream 1% once daily (QD) was efficacious and well tolerated for the treatment of plaque psoriasis for up to 52 weeks, including in intertriginous and sensitive skin areas[7]
  - 227 patients with plaque psoriasis in intertriginous area, including axillae, gluteal cleft, inframammary areas, genitalia, and skin folds, reported favorable tolerability with tapinarof use.[8] Efficacy data specific to intertriginous areas were not captured in the phase 3 PSOARING trial program

OBJECTIVE

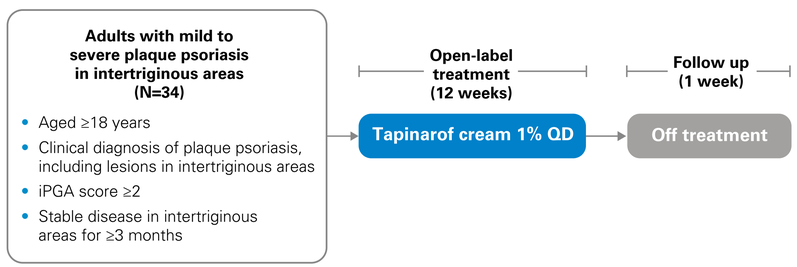
- To investigate the real-world efficacy and safety from the phase 4, 12-week, open-label trial of tapinarof cream 1% QD for the treatment of adults with mild to severe plaque psoriasis in intertriginous areas

MATERIALS AND METHODS

Trial Design

- In this phase 4, open-label multicenter trial, adults with mild to severe plaque psoriasis in intertriginous areas received tapinarof cream 1% QD for 12 weeks, followed by 1 week of follow up (NCT05680740) (**Figure 1**)

Figure 1. Intertriginous Plaque Psoriasis Trial Design



iPGA, intertriginous Physician Global Assessment; QD, once daily.

Endpoints and Statistical Analysis

- The primary efficacy endpoint was intertriginous Physician Global Assessment (iPGA) response at Week 12, defined as the proportion of patients with an iPGA score of clear (0) or almost clear (1) and ≥2-grade improvement from baseline at Week 12
- Additional efficacy endpoints included time to achieve an iPGA response, and achievement of complete disease clearance (iPGA score of 0) by visit
- A Static Physician's Global Assessment of Genitalia (sPGA-G) response was defined as the proportion of patients with a baseline score ≥2, who achieve a score of clear (0) or minimal (1) with a ≥2-grade improvement from baseline
- Local tolerability was evaluated using investigator-assessed Local Tolerability Scale (LTS) and LTS-external genitalia scores by visit
  - The LTS is evaluated on a 5-point scale of 0 (no irritation) to 4 (very severe) for dryness, erythema, and peeling
- Change in Peak Pruritus Numerical Rating Scale (PP-NRS) score for intertriginous areas was assessed by visit (Weeks 1, 2, 4, 6, 8, and 12)
  - The PP-NRS is evaluated on an 11-point scale, where 0 indicates "no itch" and 10 indicates "worst imaginable itch" within the last 24 hours
- Safety assessments included incidence, frequency, and duration of treatment-emergent adverse events (TEAEs)

RESULTS

Baseline Patient Demographics and Disease Characteristics

- Overall, 34 patients were enrolled at seven sites in the US (**Table 1**)
  - 85.3% of patients (n=29/34) completed treatment; 82.4% of patients (n=28/34) completed the trial (Week 13)
  - Mean age was 54.1 years, and 58.8% were male
  - Most patients (64.7%) had a baseline iPGA score of 3 (moderate)

Table 1. Baseline Demographics and Disease Characteristics

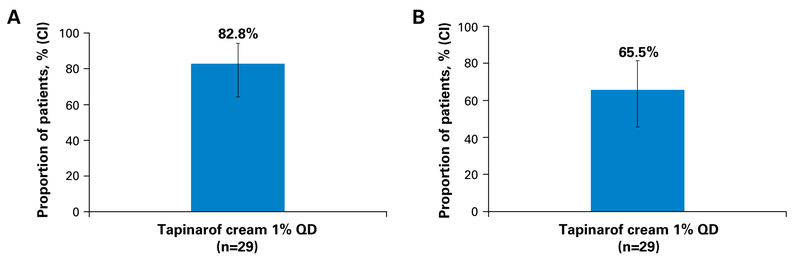
	Tapinarof cream 1% QD (N=34)
Age, years, mean (SD)	54.1 (15.9)
Male, n (%)	20 (58.8)
iPGA, n (%)	
2 – Mild	10 (29.4)
3 – Moderate	22 (64.7)
4 – Severe	2 (5.9)
sPGA-G, n (%)	
1 – Minimal	1 (25.0)
2 – Mild	1 (25.0)
3 – Moderate	2 (50.0)

iPGA, intertriginous Physician Global Assessment; QD, once daily; SD, standard deviation; sPGA-G, Static Physician's Global Assessment of Genitalia.

Achievement of iPGA Response, Complete Disease Clearance, and sPGA-G Response

- 82.8% of patients (n=24/29) achieved an iPGA response with tapinarof cream at Week 12 (**Figure 2A**); a response was seen as early as Week 2
- Median time to achieve an iPGA response was approximately 6 weeks (45 days)
- 65.5% (n=19/29) of patients achieved complete disease clearance (iPGA score of 0 [clear]) with tapinarof cream at Week 12 (**Figure 2B**), and achievement was observed as early as Week 2 with a median time to iPGA=0 of approximately 8 weeks (58 days)
  - Completely clear intertriginous skin [iPGA=0] was maintained in 64.3% of patients to Week 13, after tapinarof treatment was completed at Week 12
- 100% (n=3/3) of patients with intertriginous psoriasis in the genital area achieved an sPGA-G response at Week 4 and maintained through Week 12 (n=2/2)
  - sPGA-G response was demonstrated as early as Week 2

Figure 2. Proportion of Patients who Achieved (A) an iPGA Response* and (B) Complete Disease Clearance (iPGA=0) at Week 12

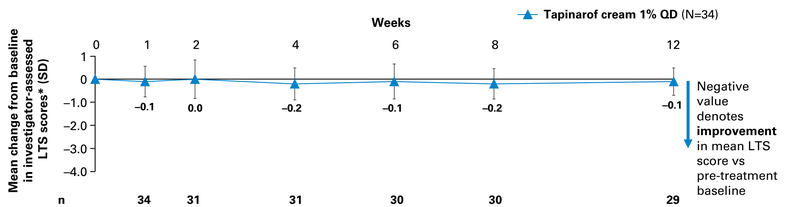


95% CI calculated using Clopper Pearson method.
*iPGA score of clear (0) or almost clear (1) and ≥2-grade improvement from baseline at Week 12.
CI, confidence interval; iPGA, intertriginous Physician Global Assessment; QD, once daily.

Investigator-assessed Local Tolerability

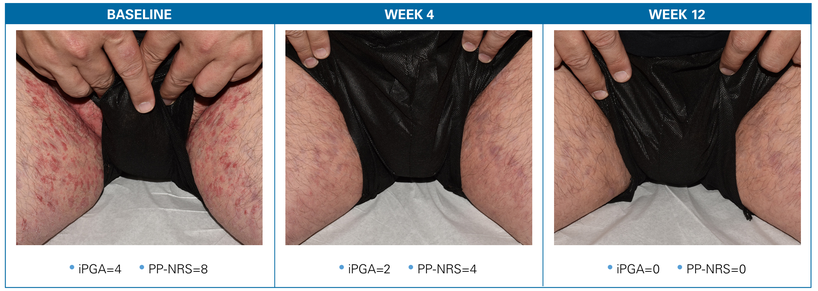
- Tapinarof cream was very well tolerated throughout the trial, and improvements from pre-treatment baseline scores were observed (**Figure 3**)
- The majority of patients had no irritation (LTS=0) at all visits for all intertriginous areas
- Additionally, for genitalia specifically, no irritation (LTS=0) was observed for most patients at all visits through Week 12

Figure 3. Tapinarof Cream 1% QD Demonstrated No Irritation Over 12 Weeks Plus Improvements from Pre-treatment Score for All Intertriginous Areas from Baseline



Week 0 is baseline, pre-treatment. Negative LTS scores indicate improvement.
*For all intertriginous areas. The LTS score is evaluated on a 5-point scale of 0 (no irritation) to 4 (very severe) for dryness, erythema, and peeling.
Intention-to-treat population.
LTS, local tolerability scale; QD, once daily; SD, standard deviation.

Figure 4. Complete Disease Clearance and Achievement of an Itch-free State in a Patient with Intertriginous Plaque Psoriasis and Pre-existing Irreversible Striae (Due to Previous TCS) Treated with Tapinarof Cream 1% QD



iPGA is a global efficacy assessment for psoriasis in all intertriginous areas. Example of one representative target lesion in a tapinarof-treated patient from the phase 4 intertriginous plaque psoriasis clinical trial. Individual results may vary.
iPGA, intertriginous Physician Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale; QD, once daily; TCS, topical corticosteroid.

Patient who Achieved Complete Disease Clearance (iPGA=0) at Week 12

- The patient in **Figure 4** had a 23-year history of plaque psoriasis and severe plaque psoriasis (iPGA=4) affecting the inguinal area at baseline. Due to previous TCS use, they also had pre-existing irreversible striae in the intertriginous skin. At Week 12, complete disease clearance (iPGA=0) was achieved
- Severe itch was reported by the patient at baseline (PP-NRS=8); reduction in itch surpassed the minimal clinically important ≥4-point improvement by Week 4, and continued to improve to a PP-NRS score of 0 (an itch-free state) at Week 12

Safety

- Most TEAEs were mild or moderate, and consistent with previous trials
- No atrophy, striae, telangiectasia, acne, rosacea, perioral dermatitis, facial erythema, hirsutism, skin thinning, ecchymosis, or withdrawal phenomena were reported in this phase 4 trial
- Only one patient discontinued from the trial due to an AE (contact dermatitis)

CONCLUSIONS

- Tapinarof cream 1% QD demonstrated rapid onset of clinically meaningful efficacy as early as Week 2 in patients with mild to severe plaque psoriasis, including in intertriginous areas and genitalia
- The primary endpoint of an iPGA response and the exploratory endpoint to achieve completely clear intertriginous skin were achieved by 82.8% and 65.5% of patients, respectively, at Week 12, and were maintained at Week 13, after treatment discontinuation
- Tapinarof was well tolerated; TEAEs were consistent with those seen in previous trials, and only one patient discontinued from the trial due to an AE
- Tapinarof cream 1% QD is a highly effective, non-steroidal topical treatment option for patients with mild to severe plaque psoriasis, with no restrictions on extent, duration, or location of use, including in sensitive and intertriginous areas

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