Rapid Improvements in Itch with Tapinarof Cream 1% Once Daily in Two Phase 3 Trials in Adults with Mild to Severe Plaque Psoriasis

Leon Kircik,[1] Matthew Zirwas,[2] Shawn G. Kwatra,[3] G. Michael Lewitt,[4] Holly Glover,[5] Tomas Chao,[6] Philip M. Brown,[7] David S. Rubenstein,[7] Anna M. Tallman[7]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Bexley Dermatology, Bexley, OH, USA; [3]Johns Hopkins University School of Medicine, Baltimore, MD, USA; [4]Illinois Dermatology Institute, Chicago, IL, USA; [5]Dermatology and Skin Cancer Surgery Center, Waxahachie, TX, USA; [6]Atlanta North Dermatology, Woodstock, GA, USA; [7]Dermavant Sciences, Inc., Morrisville, NC, USA

BACKGROUND

- Itch affects 60–90% of patients with psoriasis; it may be severe, with a significant negative impact on health-related quality of life (HR-QoL)[1–4]
  - Itch can negatively affect physical activity, sleep, and psychological well-being
- In the Multinational Assessment of Psoriasis and Psoriatic Arthritis (MAPP) survey that included 1,005 US patients, many patients reported itch as the most important factor contributing to disease severity; however, physicians generally considered itch to be less important[5]
- Tapinarof (VTAMA®; Dermavant Sciences, Inc.) is a first-in-class, non-steroidal, topical, aryl hydrocarbon receptor (AhR) agonist approved by the Food and Drug Administration for the treatment of plaque psoriasis in adults,[6] and under investigation for the treatment of psoriasis in children down to 2 years of age and for atopic dermatitis in adults and children down to 2 years of age
  - Tapinarof cream 1% once daily (QD) demonstrated statistically significant efficacy versus vehicle and was well tolerated in adults with mild to severe plaque psoriasis in two 12-week, pivotal phase 3 trials, PSOARING 1 (NCT03956355) and PSOARING 2 (NCT03983980)[7]
- Several patient-reported methods of assessing the impact of itch were utilized in the pivotal trials:
  - The Peak Pruritus Numeric Rating Scale (PP-NRS) measures maximal itch symptoms, scored on an 11-point scale, where 0=no itch and 10=worst imaginable itch[8]
  - The Dermatology Life Quality Index (DLQI) is a 10-item questionnaire that evaluates the impact of psoriasis symptoms on QoL; itch item 1 (evaluating itch, soreness, painfulness, or stinging) is scored on a 4-point scale rating the impact of itch on QoL, where 0=not at all and 3=very much[9]
  - The Psoriasis Symptom Diary (PSD) assesses the severity, bother, and functional impact of psoriasis symptoms; items 1 (itching severity) and 2 (bothered by itching) are rated on an 11-point scale, where 0=absent and 10=worst imaginable[10]

OBJECTIVE

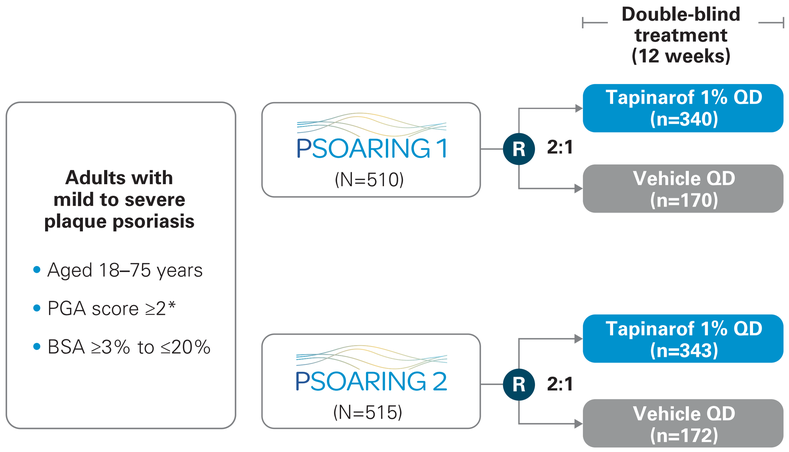
- To present patient-reported itch outcomes from the PSOARING 1 and PSOARING 2 clinical trials

METHODS

Trial Design

- Adults with mild to severe plaque psoriasis enrolled in PSOARING 1 or PSOARING 2 were randomized 2:1 to tapinarof 1% QD or vehicle QD for 12 weeks (**Figure 1**)

Figure 1. PSOARING 1 and 2 Trial 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 proportion of patients achieving a PP-NRS score of 0 or 1, indicating an itch-free state, was compared between treatment groups at baseline and Weeks 2, 4, 8, and 12 using the Cochran-Mantel-Haenszel analysis stratified by baseline Physician Global Assessment (PGA) score
- PP-NRS total score and PSD items 1 and 2 scores were assessed for improvement from baseline at Weeks 2, 4, 8, and 12
- DLQI item 1 score was assessed for improvement from baseline at Weeks 4 and 12
- Continuous variables were analyzed using an analysis of covariance, with randomized treatment as a factor, baseline PGA score as a covariate, and baseline value as a continuous covariate
  - Treatment effect is presented as a least squares mean difference

RESULTS

Baseline Patient Demographics and Disease Characteristics

- The analyses included 683 tapinarof-treated and 342 vehicle-treated patients (**Table 1**)
  - Mean PP-NRS, DLQI, and PSD total scores and PSD items 1 and 2 scores were similar across treatment groups in PSOARING 1 and 2

Table 1. Baseline Patient Demographics and Disease Characteristics

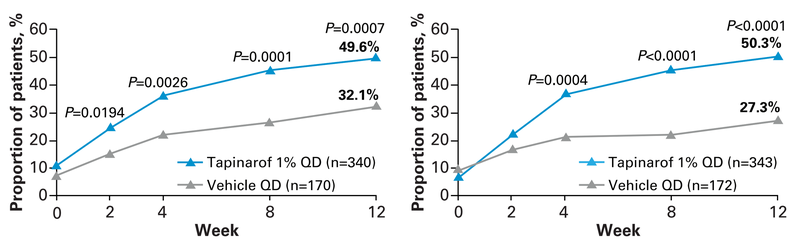
	PSOARING 1		PSOARING 2	
	Tapinarof 1% QD (n=340)	Vehicle QD (n=170)	Tapinarof 1% QD (n=343)	Vehicle QD (n=172)
Age, years, mean (SD)	49.8 (13.7)	49.1 (13.3)	50.0 (13.1)	50.0 (13.7)
Male, n (%)	213 (62.6)	86 (50.6)	188 (54.8)	102 (59.3)
Weight, kg, mean (SD)	91.7 (24.6)	92.8 (22.7)	92.9 (24.3)	89.6 (19.9)
BMI, kg/m2, mean (SD)	31.4 (7.8)	32.5 (7.6)	31.8 (7.7)	30.7 (6.3)
PP-NRS total score, mean (SD)	5.7 (2.9)	6.1 (2.8)	5.9 (2.7)	6.1 (2.8)
Score of 0 or 1, n (%)	36 (10.6)	13 (7.6)	24 (7.0)	15 (8.7)
DLQI total score, mean (SD)	8.2 (5.8)	8.7 (5.9)	8.5 (5.9)	8.6 (5.9)
Item 1, mean (SD)	1.8 (0.9)	1.9 (0.8)	1.8 (0.8)	1.9 (0.8)
PSD total score, mean (SD)	73.1 (41.2)	74.9 (43.0)	74.0 (38.4)	76.0 (41.2)
Item 1, mean (SD)	5.6 (2.7)	5.9 (2.7)	5.8 (2.6)	6.0 (2.8)
Item 2, mean (SD)	5.5 (2.9)	5.7 (3.0)	5.6 (2.8)	5.7 (3.0)

Intention-to-treat population.
BMI, body mass index; DLQI, Dermatology Life Quality Index; PP-NRS, Peak Pruritus Numeric Rating Scale; PSD, Psoriasis Symptom Diary; QD, once daily; SD, standard deviation.

Achieving an Itch-free State as Measured by PP-NRS Score of 0 or 1 at Weeks 2, 4, 8, and 12

- Significance in achieving a PP-NRS score of 0 or 1 with tapinarof versus vehicle was demonstrated as early as Week 2 (first visit) in PSOARING 1 (P=0.0194) and Week 4 in PSOARING 2 (P=0.0004)
- A significantly higher proportion of tapinarof-treated patients versus vehicle achieved a PP-NRS score of 0 or 1 at Week 12: 49.6% vs 32.1% (P=0.0007) and 50.3% vs 27.3% (P<0.0001), respectively (**Figure 2**)

Figure 2. Rapid and Significant Achievement of an Itch-free State (PP-NRS Score of 0 or 1) with Tapinarof Cream 1% QD

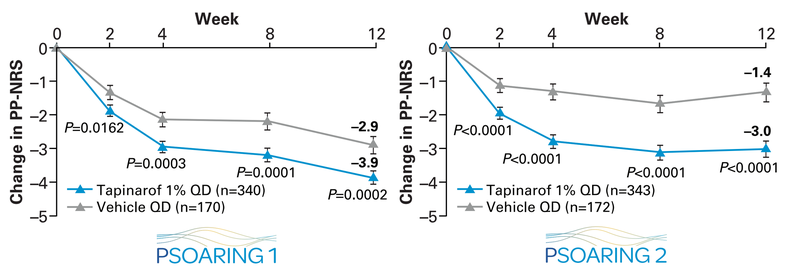


Intention-to-treat, observed cases
PP-NRS, Peak Pruritus Numeric Rating Scale; QD, once daily.

Mean Change in PP-NRS Score from Baseline at Weeks 2, 4, 8, and 12

- Itch assessed by PP-NRS was rapidly reduced with tapinarof versus vehicle, with significant improvements from Week 2 (P=0.0162 and P<0.0001), the earliest measured time point, in PSOARING 1 and 2, respectively
- Improvements from baseline reached –3.9 vs –2.9 (P=0.0002) and –3.0 vs –1.4 (P<0.0001) at Week 12 (**Figure 3**)

Figure 3. Early, Significant, and Continued Improvement in PP-NRS Score from Baseline

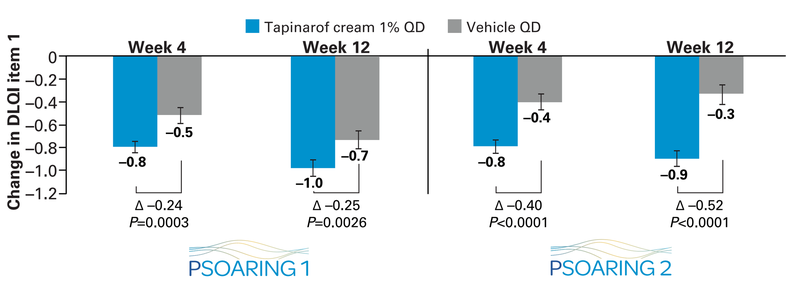


Intention-to-treat, observed cases. Least squares mean (standard error).
PP-NRS, Peak Pruritus Numeric Rating Scale; QD, once daily.

Mean Change in DLQI Item 1 Rating from Baseline at Weeks 4 and 12

- Significant improvements in DLQI itch item 1 were achieved by Week 4, the earliest measured time point, with tapinarof vs vehicle, with mean changes of –1.0 vs –0.7 (P=0.0026) and –0.9 vs –0.3 (P<0.0001) at Week 12, for PSOARING 1 and 2, respectively (**Figure 4**)

Figure 4. Significant Improvement in DLQI Itch Item 1* Rating from Baseline at Weeks 4 and 12

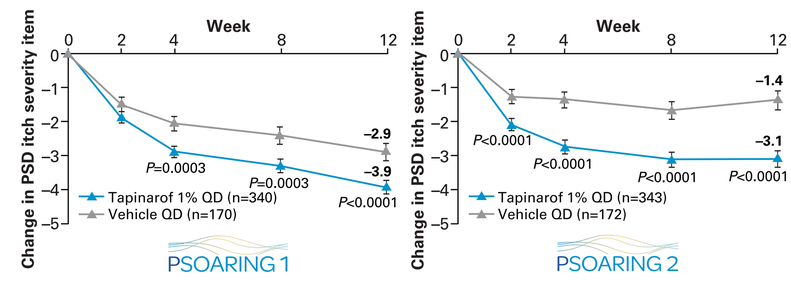


*DLQI item 1 evaluates itch, soreness, painfulness, or stinging.
Intention to treat, observed cases. Least squares mean (standard error).
DLQI, Dermatology Life Quality Index; QD, once daily.

Mean Change in PSD Itch Severity Item Rating from Baseline at Weeks 2, 4, 8, and 12

- Itch severity was rapidly reduced with tapinarof versus vehicle with statistically significant improvements as early as Week 4 in PSOARING 1 (P=0.0003) and Week 2 (P<0.0001) in PSOARING 2
- Severity decreased by –3.9 vs –2.9 and –3.1 vs –1.4 (both P<0.0001) from baseline at Week 12 in PSOARING 1 and 2, respectively (**Figure 5**)

Figure 5. Early and Sustained Improvement in PSD Itch Severity Item Rating from Baseline at Weeks 2, 4, 8, and 12

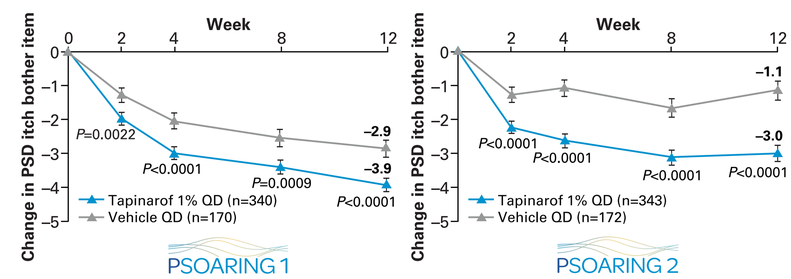


Intention-to-treat, observed cases. Least squares mean (standard error).
PSD, Psoriasis Symptom Diary; QD, once daily.

Mean Change in PSD Itch Bother Item Rating from Baseline at Weeks 2, 4, 8, and 12

- Patients reported significantly less bothersome itch symptoms with tapinarof versus vehicle by Week 2 (P=0.0022 and P<0.0001) in PSOARING 1 and 2, respectively
- Improvements with tapinarof were significant versus vehicle at all evaluations, reaching changes of –3.9 vs –2.9 and –3.0 vs –1.1 (both P<0.0001) from baseline at Week 12 in PSOARING 1 and 2, respectively (**Figure 6**)

Figure 6. Rapid and Significant Improvement in PSD Itch Bother Item Rating from Baseline at Weeks 2, 4, 8, and 12



Intention-to-treat, observed cases. Least squares mean (standard error).
PSD, Psoriasis Symptom Diary; QD, once daily.

Safety

- Treatment-emergent adverse events (TEAEs) were mostly mild to moderate and discontinuations due to TEAEs were low

CONCLUSIONS

- Tapinarof cream 1% QD demonstrated rapid, clinically meaningful, and statistically significant improvements in itch across multiple outcome measures, from the earliest visit at Week 2 through Week 12, in the phase 3 pivotal trials
- Significantly more tapinarof-treated patients achieved an itch-free state of PP-NRS=0 or 1 compared with vehicle-treated patients
- Tapinarof cream 1% QD is a well-tolerated treatment option for patients with mild to severe plaque psoriasis, including when applied to sensitive and intertriginous skin areas[11]
- Achieving an itch-free state is an essential target for decreasing the burden of disease and improving HR-QoL for patients with plaque psoriasis

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ACKNOWLEDGMENTS

Trials funded by Dermavant Sciences, Inc. The authors thank the investigators, patients and their families, and colleagues involved in the conduct of the trials. L.K. has served as a consultant/speaker/investigator/advisory board member for Abbott Laboratories, AbbVie, Ablynx, Aclaris, Acambis, Allergan, Inc., Almirall, Amgen, Inc., Anacor Pharmaceuticals, Anaptys, Arcutis, Arena, Assos Pharma, Astellas Pharma US, Inc., Asubio, Bausch Health, Berlex Laboratories (Bayer HealthCare Pharmaceuticals), Biogen Idec, Biolife, Biopelle, BMS, Boehringer Ingelheim, Breckinridge Pharma, Cassiopea, Centocor, Inc., Cellceutix, Cipher, Coherus, Colbar, Combinatrix, Connetics Corporation, Coria, Dermavant Sciences, Inc., Dermira, Dermik Laboratories, Dow Pharmaceutical Sciences, Inc., Dr. Reddy's Lab, Dusa, Embil Pharmaceuticals, Eli Lilly, EOS, Exeltis, Ferndale Laboratories, Inc., Foamix, Ferrer, Galderma, Genentech, Inc., GlaxoSmithKline, Glenmark, Health Point, Ltd, Idera, Incyte, Intendis, Innocutis, Innovail, Isdin, Johnson & Johnson, Kyowa Kirin, Laboratory Skin Care Inc., LEO Pharma, L'Oreal, 3M, Maruho, Medical International Technologies, Merck, Medicis Pharmaceutical Corp., Merz, Nano Bio, Novartis AG, Nven Pharmaceuticals, Nucryst Pharmaceuticals Corp., Obagi, Onset, OrthoNeutrogena, PediaPharma, Pfizer, Promius, PuraCap, PharmaDerm, QLT, Inc., Quinnova, Quatrix, Regeneron, Sanofi, Serono (Merck Serono International SA), SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, Taro, TolerRx, Triax, UCB Pharma, Valeant Pharmaceuticals Intl., Warner-Chilcott, XenoPort, and ZAGE. M.Z. has served as an advisor/consultant/investigator/owner/speaker for AbbVie, All Free Clear, Amgen, Inc., Anaptys Bio, Arcutis, AsepticMD, Biocon, Cara, Concert, Dermavant Sciences, Inc., Edessa Biotech, Eli Lilly, EPI Health, Evelo Biosciences, Fitbit, Galderma, Genentech, Inc., Incyte, L'Oreal, LEO Pharma, Level-Ex, LUUM, Novartis, Oculus, Peloton, Pfizer, Regeneron, Sanofi, Sun, Trevi, UCB Pharma, and Vial. S.G.K. has served as an investigator/advisory board member/consultant for AbbVie, Aslan Pharmaceuticals, Arcutis Biotherapeutics, Castle Biosciences, Celldex Therapeutics, Galderma, Genzada Pharmaceuticals, Incyte, Johnson & Johnson, LEO Pharma, Novartis Pharmaceuticals Corporation, Pfizer, Regeneron Pharmaceuticals, and Sanofi. G.M.L. has served as a consultant/speaker/investigator/advisory board member for and/or has received grants from AbbVie, Amgen, Inc., Bristol Myers Squibb, Dermavant Sciences, Inc., DermTech, Eli Lilly, Galderma, LEO Phama, Janssen, Novan, Inc., Pfizer, Orthodermatologics, and UCB Biopharma. H.G. has served as a consultant/speaker/investigator/advisory board member of AbbVie, Almirall, Bristol Myers Squibb, Cassiopea, Dermavant Sciences, Inc., Eli Lilly, Galderma, Incyte, Isdin, LEO Pharma, Pfizer, and Sun Pharma. T.C. has served as an advisor and speaker for Dermavant Sciences, Inc. P.M.B., D.S.R., and A.M.T. are employees of Dermavant Sciences, Inc., with stock options. 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 (GPP) guidelines (*Ann Intern Med.* 2022;175:1298–1304).

Contact Dr Leon Kircik at wedoderm@yahoo.com.