Safety and Tolerability of Fixed Combination Halobetasol Propionate 0.01% and Tazarotene 0.045% (HP/TAZ) Lotion in Patients With Moderate-to-Severe Plaque Psoriasis: Results From a 1-Year, Open-Label Study

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SYNOPSIS

- Topical corticosteroids are the mainstay of psoriasis treatment, particularly for mild disease,[1] though topical treatments as part of combination therapy for moderate-to-severe psoriasis is becoming increasingly common
- However, continuous use of topicals may be limited due to application-site adverse events (AEs)[1]
- Recent phase 3 clinical data have demonstrated efficacy and tolerability of a fixed combination lotion containing halobetasol propionate 0.01% and tazarotene 0.045% (HP/TAZ; Duobrii® Ortho Dermatologics, Bridgewater, NJ) in patients with moderate-to-severe localized plaque psoriasis[2,3]

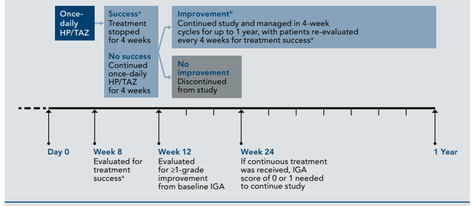
OBJECTIVE

- To investigate AEs and local skin reactions following long-term use of HP/TAZ lotion

METHODS

- This was a 1-year multicenter, open-label study (NCT02462083) in patients with moderate-to-severe plaque psoriasis
- Participants were treated with HP/TAZ lotion once-daily for 8 weeks and intermittently as needed in 4-week intervals (**Figure 1**)
  - At week 8, treatment was stopped for participants that achieved treatment success; those who did not reach treatment success were treated for 4 additional weeks
  - All participants were re-evaluated at week 12; those demonstrating ≥1-grade improvement in baseline Investigator's Global Assessment (IGA) continued the study and were subsequently managed in 4-week cycles, either treated with HP/TAZ lotion once-daily if they had not achieved treatment success or receiving no treatment until the next evaluation if they had achieved treatment success
- Maximum continuous exposure was 24 weeks

FIGURE 1. **Open-Label Study Design**



Maximum continuous exposure was 24 weeks.
[a]Treatment success defined as score of 0 or 1 on IGA.
[b]Improvement defined as ≥1-grade improvement from baseline IGA.
HP/TAZ, halobetasol propionate 0.01%/tazarotene 0.045%; IGA, Investigator's Global Assessment.

RESULTS

Participants and Exposure

- A total of 550 participants were included in the safety population
  - Mean age was 51.9 years (range: 19 to 87 years); 65.6% were male and 86.0% were white
  - Baseline IGA was moderate (3; 86.5%) or severe (4; 13.5%); median affected Body Surface Area was 5%
- Median amount of study drug used was 256.5 g, median length of exposure was 172 days, and median number of applications was 164

Treatment-Emergent Adverse Events

- Over half of participants experienced treatment-emergent adverse events (TEAEs) during the year-long study, primarily during the first 12 weeks (**Table 1**)
  - Most TEAEs were mild or moderate
  - None of the serious adverse events (SAEs) were related to treatment
- The most common TEAEs related to study drug were application site reactions (**Table 1**)

TABLE 1. **Treatment-Emergent Adverse Event Summary (Safety Population)**

	0-12 Weeks (n=527)	>12-24 Weeks (n=392)	>24-36 Weeks (n=239)	>36 Weeks-EOS (n=219)	Total (N=550)
Number of TEAEs, No.	395	194	98	71	758
Participants with ≥1 TEAE, n (%)	223 (42.3)	130 (33.2)	61 (25.5)	43 (19.6)	314 (57.1)
Discontinued study drug due to TEAE, n (%)	30 (5.7)	9 (2.3)	2 (0.8)	0	41 (7.5)
Participants with ≥1 SAE,[a] n (%)	6 (1.1)	5 (1.3)	5 (2.1)	2 (0.9)	18 (3.3)
Treatment-related TEAE, n (%)	120 (22.8)	43 (11.0)	18 (7.5)	8 (3.7)	161 (29.3)
TEAEs by severity, n (%)					
Mild	99 (18.8)	67 (17.1)	28 (11.7)	22 (10.0)	122 (22.2)
Moderate	101 (19.2)	55 (14.0)	26 (10.9)	16 (7.3)	151 (27.5)
Severe	23 (4.4)	8 (2.0)	7 (2.9)	5 (2.3)	41 (7.5)
Most common treatment-related TEAEs,[b] n (%)					
Application site dermatitis	38 (7.2)	20 (5.1)	6 (2.5)	2 (0.9)	56 (10.2)
Application site pruritus	22 (4.2)	6 (1.5)	4 (1.7)	2 (0.9)	33 (6.0)
Application site pain	24 (4.6)	2 (0.5)	1 (0.4)	1 (0.5)	28 (5.1)
Application site irritation	10 (1.9)	4 (1.0)	3 (1.3)	1 (0.5)	13 (2.4)

[a]None of the SAEs were deemed related to treatment; [b]In >2% of total participants.
EOS, end of study; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

FIGURE 2. **Local Skin Reactions Over Time, By Severity (Safety Population)**

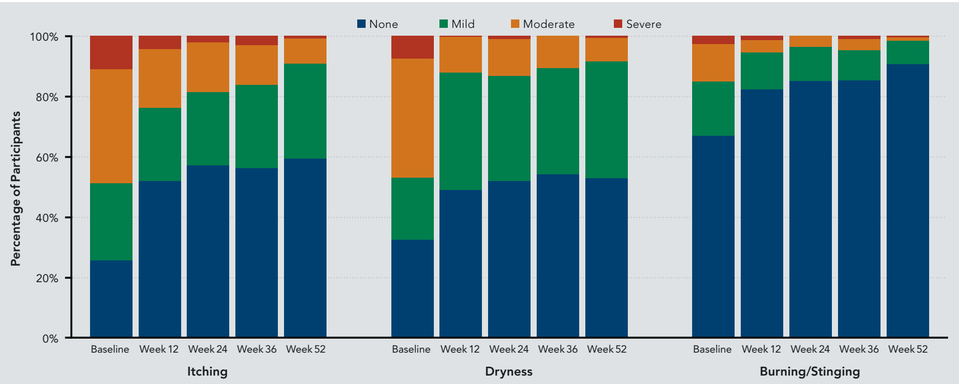
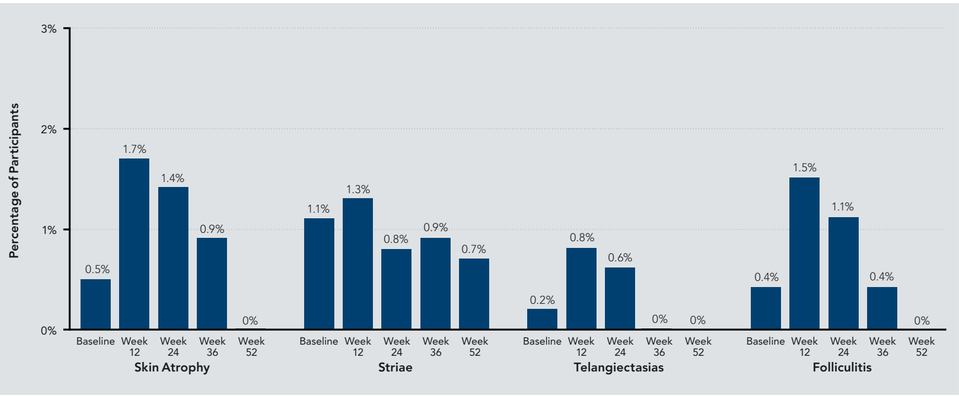


FIGURE 3. **Incidence of Local Skin Reactions Over Time (Safety Population)**



Skin Reactions

- Select local signs/symptoms showed marked improvements in severity of itching, dryness, and burning/stinging over the study course; greatest improvement was for itching (**Figure 2**)
- Incidence of treatment-emergent Grade 3 local skin reactions was 22.2% for itching, 6.9% for dryness, and 9.8% for burning/stinging
- Incidence of other local skin reactions are shown in **Figure 3**
  - Incidence peaked at 2.3% for skin atrophy (week 8), 2.7% for folliculitis (week 8), and 1.5% for striae and telangiectasias (week 28)
- Local skin reactions most frequently reported as AEs were application site folliculitis (14 participants [2.5%]; 1 discontinued) and application site atrophy (4 participants [0.7%]; 1 discontinued); no participant reported striae or telangiectasias AEs
- Most local skin reactions were transient and resolved prior to end of dosing

CONCLUSIONS

- No clinically meaningful trends in local skin reactions were observed following long-term use of a fixed combination HP 0.01%/TAZ 0.045% lotion
- The types of TEAEs were consistent with those of a corticosteroid and retinoid product, but occurred at lower-than-anticipated frequencies, suggesting a favorable long-term safety profile for HP/TAZ lotion

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AUTHOR DISCLOSURES

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Dr. Jeffery Sugarman is a consultant for Ortho Dermatologics, Bausch Health, Regeneron, Sanofi, and Pfizer.
Dr. David M Pariser has served as consultant to Atacama Therapeutics, Bickel Biotechnology, Biofrontera AG, Celgene, Dermira, LEO, Regeneron, Sanofi, TDM SurgiTech, TheraVida, and Ortho Dermatologics; investigator for Abbott Laboratories, Almirall, Amgen, AOBiome, Asana Biosciences, Bickel Biotechnology, Celgene, Dermavant, Dermira, Eli Lilly, LEO, Menlo Therapeutics, Merck & Co., Novartis, Novo Nordisk A/S, Ortho Dermatologics, Pfizer, Regeneron, and Stiefel; on advisory board for Pfizer; and on the data monitoring board for BMS.
Dr. Jerry Bagel is an investigator and speaker for Ortho Dermatologics.
Dr. Tina Lin is an employee of Ortho Dermatologics and may hold stock and/or stock options in its parent company.
Dr. Robert Israel is an employee of Bausch Health US, LLC and may hold stock and/or stock options in its parent company.

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