Efficacy, Safety, and Tolerability of a Halobetasol 0.01%/Tazarotene 0.045% Fixed Combination in the Treatment of Severe Plaque Psoriasis: Post Hoc Analysis of Two Phase 3 Randomized Controlled Trials

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SYNOPSIS

- Psoriasis is a chronic, immune-mediated disease that can have frequent exacerbations and remissions[1,2]
- The use of topical therapy is a key component in the management of almost all psoriasis patients[3]
- Topicals are considered first-line therapy for mild disease[3] and are having an increasing role in moderate-to-severe psoriasis as an integral part of combination therapy

OBJECTIVE

- To investigate the efficacy, safety, and tolerability of a once-daily application of a fixed combination halobetasol propionate 0.01% and tazarotene 0.045% (HP/TAZ; Duobrii™ Ortho Dermatologics, Bridgewater, NJ) lotion compared with its vehicle in patients with severe localized plaque psoriasis

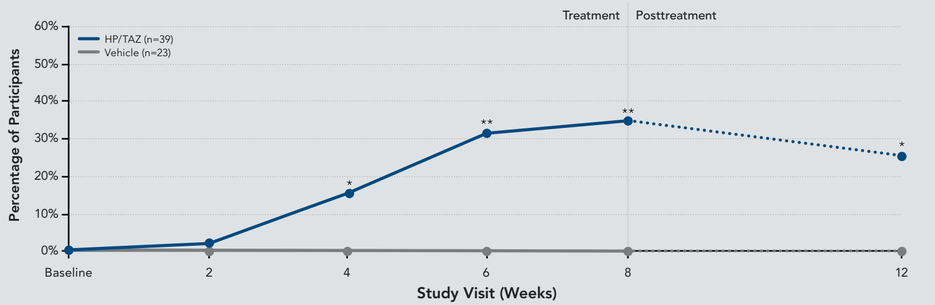
METHODS

- In two phase 3, multicenter, double-blind, vehicle-controlled studies (NCT02462070 and NCT02462122), patients were randomized (2:1) to receive HP/TAZ or vehicle once-daily for 8 weeks, with a 4-week posttreatment follow-up[4]
  - In these studies, CeraVe®hydrating cleanser and CeraVe®moisturizing lotion (L'Oreal, NY) were provided as needed for optimal moisturization/cleaning of the skin
- Data from these studies were pooled and analyzed post hoc in participants with severe psoriasis (Investigator Global Assessment [IGA] of 4 and Body Surface Area [BSA] of 3%–12%)
- Efficacy assessments included treatment success (≥2-grade improvement from baseline in IGA score and a score of 'clear' or 'almost clear' [primary endpoint]), impact on individual signs of psoriasis (erythema, plaque elevation, and scaling) at the target lesion, mean change in BSA and IGAxBSA, and the proportion of patients achieving a clinically meaningful response (≥50% improvement in IGAxBSA)
- Safety and treatment-emergent adverse events (TEAEs) were evaluated throughout the study

RESULTS

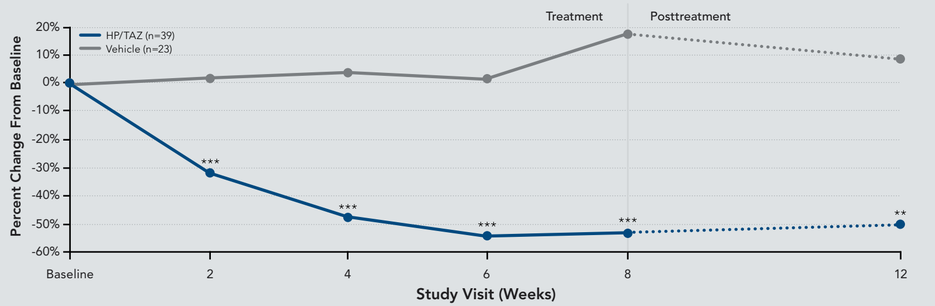
- A total of 62 participants with severe psoriasis (IGA 4; mean BSA 7.4%) were included in this analysis
- By Week 8, 34.8% of participants achieved treatment success with HP/TAZ compared with 0% on vehicle (*P*=0.004; **Figure 1**)
- HP/TAZ lotion was also significantly superior in reducing psoriasis signs and symptoms and reducing BSA
  - At Week 8, significantly more HP/TAZ-treated participants achieved ≥2-grade improvement in erythema (47.4%), plaque elevation (66.4%), and scaling (65.4%) compared with vehicle (14.0% [*P*=0.016], 14.8% [*P*<0.001], and 14.7% [*P*<0.001], respectively)
  - Participants treated with HP/TAZ lotion achieved a 32.8% mean reduction from baseline in BSA, compared with a 39.6% increase with vehicle (*P*=0.013)
- HP/TAZ lotion demonstrated significantly greater reduction in IGAxBSA compared to vehicle from Week 2 onward (*P*<0.001; **Figure 2**)
  - By Week 8, the mean reduction in IGAxBSA in HP/TAZ-treated participants was 52.9% compared with a mean increase of 17.5% in vehicle-treated participants (*P*<0.001)
  - Most participants treated with HP/TAZ lotion achieved a clinically meaningful response (IGAxBSA-50)

FIGURE 1: Percentage of Participants With Severe Psoriasis Achieving Treatment Success[a] by Study Visit (ITT Population; Pooled Data)



*P<0.05 vs vehicle; **P<0.01 vs vehicle.
[a]Treatment success was defined as ≥2-grade improvement from baseline in IGA score and a score of 'clear' or 'almost clear'.
HP/TAZ, halobetasol propionate 0.01% and tazarotene 0.045%; IGA, Investigator Global Assessment; ITT, intent-to-treat.

FIGURE 2: Mean Percent Change in IGAxBSA by Study Visit in Participants With Severe Psoriasis (ITT Population; Pooled Data)



**P<0.01 vs vehicle; ***P<0.001 vs vehicle.
BSA, body surface area; HP/TAZ, halobetasol propionate 0.01% and tazarotene 0.045%; IGA, Investigator Global Assessment; ITT, intent-to-treat.

- One participant (2.6%) treated with HP/TAZ lotion discontinued due to AEs
- The most frequently reported treatment-related TEAEs with HP/TAZ were application site pain (7.9%), contact dermatitis (5.3%) and pruritus (5.3%; **Table 1**)

TABLE 1: Summary of Treatment-Emergent Adverse Events in Participants with Severe Psoriasis Through Week 8 (Safety Population; Pooled Data)

n (%)	HP/TAZ Lotion (n=38)	Vehicle Lotion (n=23)
Participants reporting any TEAEs	18 (47.4)	8 (34.8)
Participants reporting any SAEs	0	0
Deaths	0	0
Participants discontinuing due to TEAEs	1 (2.6)	1 (4.3)
Severity of TEAEs		
Mild	8 (21.1)	2 (8.7)
Moderate	9 (23.7)	5 (21.7)
Severe	1 (2.6)	1 (4.3)
Relationship to study drug		
Related	8 (21.1)	3 (13.0)
Unrelated	10 (26.3)	5 (21.7)
Treatment-related TEAEs reported in ≥2% of participants		
Application site pain	3 (7.9)	0
Pruritis	2 (5.3)	1 (4.3)
Contact dermatitis	2 (5.3)	0
Rash	1 (2.6)	0
Skin atrophy	1 (2.6)	0
Skin lesion	1 (2.6)	0
Telangiectasia	1 (2.6)	0
Wound secretion	1 (2.6)	0
Skin irritation	0	1 (4.3)
Peripheral swelling	0	1 (4.3)
Pain in extremity	0	1 (4.3)
Burning sensation	0	1 (4.3)

HP/TAZ, halobetasol propionate 0.01% and tazarotene 0.045%; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSION

- In patients with severe localized plaque psoriasis, HP/TAZ lotion provides rapid and sustained efficacy with good tolerability and safety over 8 weeks of once-daily use

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AUTHOR DISCLOSURES

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