Halobetasol Propionate 0.01%/Tazarotene 0.045% Lotion for the Treatment of Plaque Psoriasis in Patients with Mild Scaling and Mild Plaque Elevation

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SYNOPSIS

- Combining tazarotene (TAZ) with a potent-to-superpotent topical corticosteroid, such as halobetasol propionate (HP), is recommended for the treatment of patients with mild-to-moderate psoriasis[1]
- The TAZ + HP combination may provide synergistic efficacy, increase the duration of remission, and reduce side effects of both HP and TAZ when used alone[1-3]
- A once-daily, fixed-combination HP 0.01%/TAZ 0.045% lotion (Duobrii,® Ortho Dermatologics) was developed utilizing polymeric emulsion technology, which allows for rapid and uniform distribution of HP and TAZ, humectants, and moisturizers on the skin
- HP/TAZ lotion has demonstrated efficacy and safety in patients with moderate-to-severe psoriasis,[4,5] including those with lower body surface area (BSA) involvement[6]

OBJECTIVE

- To evaluate efficacy and safety of HP 0.01%/TAZ 0.045% lotion in patients with either mild scaling or mild plaque elevation at baseline

METHODS

- In two phase 3, double-blind studies (NCT02462070, NCT02462122), adult participants were randomized 2:1 to HP/TAZ or vehicle lotion once daily for 8 weeks, with a 4-week posttreatment follow-up[4,5]
  - Participants were required to have an Investigator's Global Assessment (IGA) score of 3 (moderate) or 4 (severe) and affected BSA of 3 to 12% at baseline
  - In these studies, CeraVe® hydrating cleanser and CeraVe® moisturizing lotion (L'Oreal, NY) were provided as needed for optimal moisturization/cleaning of the skin
- Efficacy measures included treatment success (percentage of participants with ≥2-grade reduction in IGA score and a score of 0 [clear] or 1 [almost clear]), change in affected BSA, and percentage of participants with ≥2-grade improvements from baseline (success) in erythema, plaque elevation, and scaling
- Treatment-emergent adverse events (TEAEs) were evaluated
- Pooled, post hoc analyses were performed in subsets of patients with either mild scaling (score of 2) or mild plaque elevation (score of 2) at baseline

RESULTS

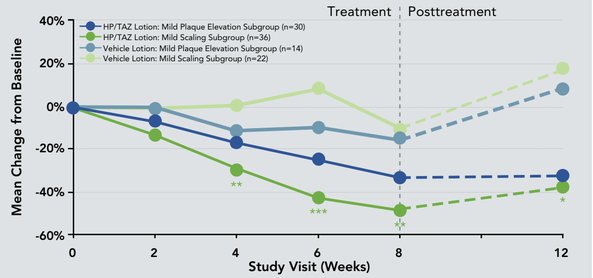
Demographics and Baseline Characteristics

- Of 418 study participants included in the overall population, 58 had mild scaling at baseline and 44 had mild plaque elevation at baseline
- Participant demographics and characteristics were generally similar across the groups, though there was a higher proportion of males in the mild scaling group and more participants in the mild scaling and plaque elevation groups had moderate IGA at baseline (**Table 1**)

Efficacy

- Compared with vehicle, HP/TAZ-treated participants in the mild scaling group had significantly greater reductions from baseline in affected BSA (**Figure 1**), higher rates of treatment success (**Figure 2**), and improvements in signs of psoriasis (**Figure 3**) at week 8
- Similar results were observed in the overall population (HP/TAZ vs vehicle at week 8: BSA reduction: -37.6% vs -3.1%; treatment success: 40.6% vs 9.9%; erythema success: 47.0% vs 14.5%; plaque elevation success: 59.6% vs 19.7%; scaling success: 61.2% vs 20.9% [P<0.001 for all])[5]
- In the mild plaque elevation group, those treated with HP/TAZ demonstrated significantly greater improvements in signs of psoriasis at week 8 versus vehicle (**Figure 3**)
  - A numerically higher treatment success rate was observed with HP/TAZ versus vehicle at week 8 in the mild plaque elevation group, with significance reached 4 weeks posttreatment (**Figure 2**)
  - Lack of statistical separation of HP/TAZ from vehicle for treatment success and BSA reduction may be partly attributed to the small population and/or favorable response to the vehicle formulation

FIGURE 1. BSA Reduction in Mild Plaque Elevation and Mild Scaling Subgroups (ITT Population, Pooled)



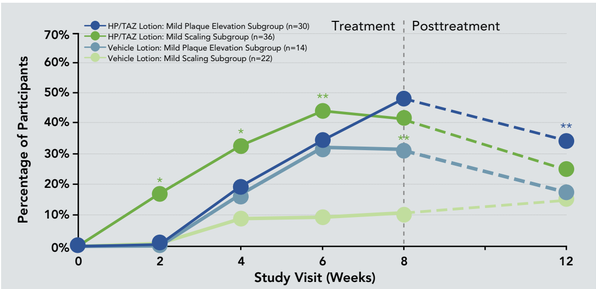
*P<0.05; **P<0.01; ***P<0.001 vs vehicle.
No imputation of missing data. N values shown for baseline only.
BSA, body surface area; HP/TAZ, halobetasol propionate 0.01% and tazarotene 0.045%; ITT, intent to treat.

TABLE 1. Participant Demographics and Baseline Characteristics

	Mild Scaling (n=58)	Mild Plaque Elevation (n=44)	Overall Population (N=418)
Age, mean, y	52.1	49.8	50.3
Males, n (%)	40 (69.0)	25 (56.8)	272 (65.1)
White race, n (%)	49 (84.5)	38 (86.4)	358 (85.6)
IGA of 3 (moderate)[a]	55 (94.8)	43 (97.7)	356 (85.2)
BSA, mean, %	5.5	4.8	5.9
Erythema			
2 – mild	0	0	36 (8.6)
3 – moderate	51 (87.9)	44 (100)	331 (79.2)
4 – severe	7 (12.1)	0	51 (12.2)
Plaque elevation			
2 – mild	0	44 (100)	44 (10.5)
3 – moderate	57 (98.3)	0	320 (76.6)
4 – severe	1 (1.7)	0	54 (12.9)
Scaling			
2 – mild	58 (100)	0	58 (13.9)
3 – moderate	0	43 (97.7)	303 (72.5)
4 – severe	0	1 (2.3)	57 (13.6)

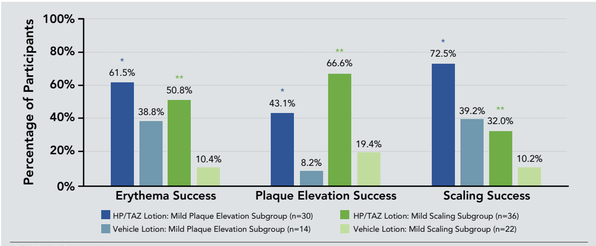
[a]All other participants had an IGA score of 4 (severe) at baseline.
BSA, body surface area; IGA, Investigator's Global Assessment.

FIGURE 2. Treatment Success[a] in Mild Plaque Elevation and Mild Scaling Subgroups (ITT Population, Pooled)



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

FIGURE 3. Erythema, Plaque Elevation, and Scaling Success[a] in Mild Plaque Elevation and Mild Scaling Subgroups at Week 8 (ITT Population, Pooled)



*P<0.05; **P<0.01 vs vehicle.
[a]For each sign of psoriasis, success defined as ≥2-grade improvement from baseline.
HP/TAZ, halobetasol propionate 0.01% and tazarotene 0.045%; ITT, intent to treat.

CLINICAL COMMENTARY

- Unlike real-world use, participants in this study were required to continue administration of HP/TAZ for 8 continuous weeks—even if they had clearance of active psoriasis—which may have contributed to increased levels of irritation in the mild subgroups versus the overall population
- Treatment-emergent irritation may potentially be addressed in the clinic by:
  - Recommending that patients temporarily interrupt drug use (eg, drug holiday) and resume application of the lotion once irritation signs/symptoms have subsided
  - Encouraging the use of moisturizers before resuming treatment

Safety

- Treatment-emergent adverse events occurred at generally similar rates in each subgroup and the overall population, and most were mild to moderate in severity (**Table 2**)
- Rates of contact dermatitis were higher in the HP/TAZ-treated mild scaling and plaque elevation subgroups versus the overall population (**Table 2**)
- Skin atrophy was reported as an adverse event in only 1 participant who received HP/TAZ lotion in the mild scaling group

TABLE 2. Treatment-Emergent Adverse Events Through Week 8

	Mild Scaling		Mild Plaque Elevation		Overall Population	
	HP/TAZ Lotion (n=35)	Vehicle Lotion (n=22)	HP/TAZ Lotion (n=29)	Vehicle Lotion (n=14)	HP/TAZ Lotion (n=270)	Vehicle Lotion (n=140)
Any TEAE, n (%)	14 (40.0)	7 (31.8)	12 (41.4)	3 (21.4)	97 (35.9)	30 (21.4)
Treatment-related TEAEs, n (%)	9 (25.7)	3 (13.6)	10 (34.5)	2 (14.3)	55 (20.4)	11 (7.9)
Intensity of treatment-related TEAEs, n (%)						
Mild	3 (8.6)	0	3 (10.3)	2 (14.3)	20 (7.4)	3 (2.1)
Moderate	5 (14.3)	2 (9.1)	5 (17.2)	0	26 (9.6)	6 (4.3)
Severe	1 (2.9)	1 (4.5)	2 (6.9)	0	9 (3.3)	2 (1.4)
Most common TEAEs[a], n (%)						
Contact dermatitis	4 (11.4)	0	5 (17.2)	0	20 (7.4)	0
Pruritus	2 (5.7)	1 (4.5)	1 (3.4)	1 (7.1)	8 (3.0)	4 (2.9)
Pain of skin	0	0	0	1 (7.1)	0	1 (0.7)
Excoriation	3 (8.6)	0	0	0	5 (1.9)	0
Folliculitis	0	0	4 (13.8)	0	5 (1.9)	0
Burning sensation[b]	0	0	2 (6.9)	1 (7.1)	4 (1.5)	3 (2.1)

[a]At least 5% incidence in any treatment group; does not include 3 AEs in which each event was deemed unrelated to treatment (sinusitis, nasopharyngitis, and nausea).
[b]System Organ Class: nervous system disorder.
AE, adverse event; HP/TAZ, halobetasol propionate 0.01% and tazarotene 0.045%; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- In two pooled phase 3 studies, HP 0.01%/TAZ 0.045% lotion was efficacious and well tolerated following 8 weeks of treatment among participants with mild plaque elevation and mild scaling
- Results were generally similar to the overall study population, indicating that HP/TAZ lotion is a viable treatment option for patients with plaque psoriasis who have mild signs of scaling and plaque elevation, regardless of their IGA severity at baseline

REFERENCES

1. Elmets CA, et al. *J Am Acad Dermatol.* Online ahead of print, 2020 Jul 30. doi:10.1016/j.jaad.2020.07.087.
2. Tanghetti E, et al. *J Dermatolog Treat.* 2019:1-8.
3. Kircik LH, et al. *J Drugs Dermatol.* 2019;18(3):279-284.
4. Stein Gold L, et al. *J Am Acad Dermatol.* 2018;79(2):287-293.
5. Sugarman JL, et al. *J Drugs Dermatol.* 2018;17(8):855-861.
6. Leonardi C, et al. Poster Virtually Presented at Fall Clinical 2020.

AUTHOR DISCLOSURES

LSG has served as investigator/consultant or speaker for Ortho Dermatologics, LEO Pharma, Dermavant, Incyte, Novartis, AbbVie, Pfizer, Sun Pharma, UCB, Arcutis and Lilly; ET has served as speaker for Novartis, Ortho Dermatologics, Sun Pharma, Lilly, Galderma, AbbVie, and Dermira; served as a consultant/clinical studies for Hologic, Ortho Dermatologics, and Galderma; and is a stockholder for Accure; CL is a consultant for AbbVie, Amgen, Boehringer Ingelheim, Dermira, Eli Lilly, Janssen, LEO Pharma, Pfizer, Sandoz, UCB, and Vtae; an investigator for Actavis, AbbVie, Allergan, Amgen, Boehringer Ingelheim, Celgene, Coherus, Cellocutix, Corrona, Dermira, Eli Lilly, Galderma, Glenmark, Janssen, LEO Pharma, Merck, Novartis, Novella, Pfizer, Sandoz, Sienna, Stiefel, UCB, and Wyeth; and a speaker for AbbVie, Celgene, Novartis, Sun Pharma, and Eli Lilly; SK is an advisory board member/consultant for Abbvie, Galderma, Incyte Corporation, Pfizer Inc., Regeneron Pharmaceuticals, and Kiniksa Pharmaceuticals and has received grant funding from Galderma, Pfizer Inc. and Kiniksa Pharmaceuticals; AJ is an employee of Ortho Dermatologics and may hold stock and/or stock options in its parent company.

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