Long-Term Management of Moderate-to-Severe Plaque Psoriasis: Maintenance of Treatment Success Following Cessation of Halobetasol Propionate 0.01%/Tazarotene 0.045% Lotion

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SYNOPSIS

- Psoriasis is a chronic, inflammatory skin disorder characterized by abnormal differentiation/hyperproliferation of keratinocytes, infiltration of immune cells in the dermis and epidermis, and increased capillary density[1,2]
- A fixed combination halobetasol propionate 0.01%/tazarotene 0.045% (HP/TAZ) lotion (Duobrii,® Ortho Dermatologics) was developed to address unmet needs in the topical treatment of psoriasis (**see inset**)
  - Topical corticosteroids—such as HP—are the mainstay of treatment, though long-term safety remains a concern, limiting use[3]
  - The topical retinoid TAZ has demonstrated efficacy by modulating major causes of psoriasis and maintaining therapeutic effect, though TAZ may induce cutaneous irritation[3-6]
  - Treating psoriasis by combining HP with TAZ may enhance efficacy, reduce side effects of both HP and TAZ, and sustain treatment response posttreatment[3,6]

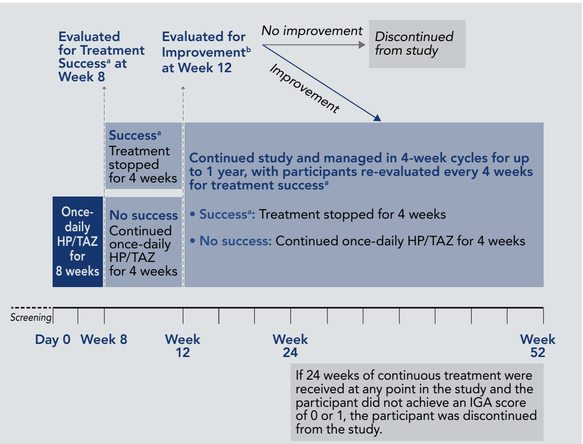
OBJECTIVE

- To investigate maintenance of effect posttreatment following once-daily application of HP/TAZ lotion in patients with moderate-to-severe psoriasis who achieved clear skin

METHODS

- This was a 1-year, multicenter, open-label study (NCT02462083) in participants ≥18 years of age with moderate-to-severe plaque psoriasis (Investigator's Global Assessment [IGA] score of 3 or 4 and affected body surface area [BSA] of 3–12%)
- 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 who achieved treatment success (IGA score of clear [0] or almost clear [1]); all other participants were treated for an additional 4 weeks
  - All participants were re-evaluated at week 12 for improvement; maximum continuous exposure was 24 weeks
- In this study, CeraVe® hydrating cleanser and CeraVe® moisturizing lotion (L'Oreal, NY) were provided as needed for optimal moisturization/cleaning of the skin
- A post hoc analysis evaluated maintenance of effect in participants who were enrolled ≥8 weeks and who achieved an IGA score of 0 (clear) during the study

FIGURE 1. Open-Label Study Design



[a]Treatment success defined as score of 0 (clear) or 1 (almost clear) on IGA.
[b]Improvement defined as ≥1-grade improvement from baseline IGA; those demonstrating improvement continued the study and were subsequently managed in 4-week cycles (eg, 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.
HP/TAZ, halobetasol propionate 0.01%/tazarotene 0.045%; IGA, Investigator's Global Assessment.

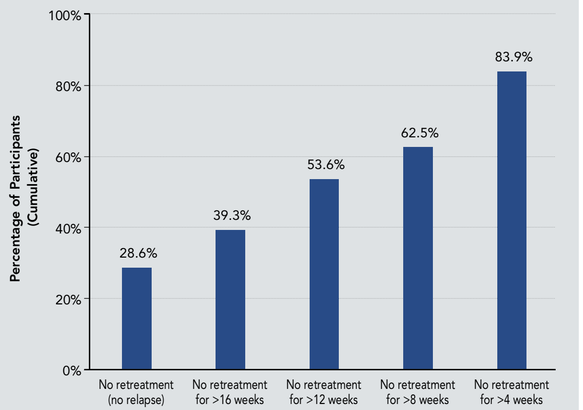
RESULTS

- A total of 555 participants in this study were treated with HP/TAZ and 550 had post-baseline safety data
  - Mean age was 51.9 years, 65.6% were male, and 86.0% were white
  - At baseline, 86.5% had an IGA score of 3 (moderate) and 13.5% had IGA of 4 (severe); mean BSA was 5.6%
- Overall, 318 participants (57.8%) achieved treatment success at some point during the study; 54.4% of those did so within the first 8 weeks

Participants Achieving Clear

- Fifty-six participants were enrolled in the study for at least 8 weeks and achieved an IGA score of 0 (clear) at ≥1 visit
- Of these participants: 28.6% did not require any HP/TAZ retreatment after first achievement of clear, 53.6% did not require retreatment for ≥85 days, 62.5% for ≥57 days, and 83.9% for ≥29 days (**Figure 2**)

FIGURE 2. Time to Retreatment with HP/TAZ After First Achievement of Clear On or After Week 8 (n=56[a])



[a]Participants still enrolled post 8 weeks in the study and who stopped therapy after achievement of clear; per the study design, all participants stopped treatment after achievement of clear or almost clear.
Cumulative data shown; participants included in the bar graphs are not mutually exclusive.
HP/TAZ, halobetasol propionate 0.01%/tazarotene 0.045%.

CONCLUSIONS

- In this 1-year, open-label study of HP/TAZ, 53.6% of participants who achieved clear skin (IGA score of 0) did not require retreatment for more than 12 weeks
  - Results are notable given a limitation of the study design, in which participants were required to stop using HP/TAZ lotion at the time of first treatment success (achievement of clear or almost clear)
  - This may have reduced the total number of participants who could have achieved clear skin with continued HP/TAZ treatment, potentially also reducing the duration of time to retreatment
- These data indicate a long maintenance of therapeutic effect with HP 0.01%/ TAZ 0.045% lotion in participants who achieved clear skin, likely due to the role of TAZ in sustaining efficacy posttreatment (**see inset**)

REFERENCES

1. Nestle FO, et al. *N Engl J Med*. 2009;361(5):496-509.
2. Benhadou F, et al. *Dermatology*. 2019;235(2):91-100.
3. Tanghetti E, et al. *J Dermatolog Treat*. 2019:1-8.
4. Chandrasratna RA. *J Am Acad Dermatol*. 1997;37(2 Pt 3):S12-17.
5. Duvic M, et al. *J Am Acad Dermatol*. 1997;37(2 Pt 3):S18-24.
6. Tanghetti E, et al. *J Drugs Dermatol*. 2018;17(12):1280-1287.

AUTHOR DISCLOSURES

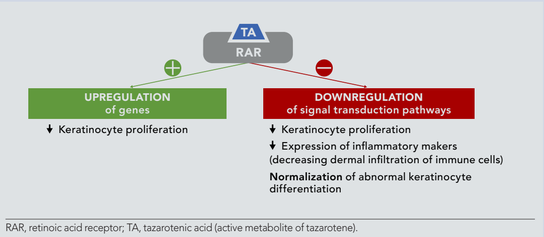
LSG has served as investigator/consultant or speaker for Ortho Dermatologics, LEO, Dermavant, Incyte, Novartis, AbbVie, and Lilly. ML is an employee of Mount Sinai and receives research funds from AbbVie, Amgen, Arcutis, AstraZeneca, Boehringer Ingelheim, Celgene, Clinuvel, Eli Lilly, Incyte, Janssen Research & Development, LLC, Kadmon Corp., LLC, Leo Pharmaceuticals, MedImmune, Novartis, Ortho Dermatologics, Pfizer, Sciderm, UCB, Inc., and ViDac, is a consultant for Allergan, Almirall, Arcutis, Inc., Avotres Therapeutics, BirchBioMed Inc., Boehringer-Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Foundation for Research and Education in Dermatology, Incyte Pharma, LEO Pharma, Meiji Seika Pharma, Menlo, Mitsubishi, Neurodrem, Pfizer, Promius/Dr. Reddy's Laboratories, Theravance, and Verrica. NB has received honoraria and investigator grants from Bausch Health. WC has nothing to disclose; AJ is an employee of Ortho Dermatologics and may hold stock and/or stock options in its parent company. RP is an employee of Bausch Health US, LLC and may hold stock and/or stock options in its parent company.

WHY TAZAROTENE + HALOBETASOL?

Combining TAZ + HP may enhance efficacy, reduce side effects, and sustain treatment response posttreatment[3,6]

Tazarotene mechanism of action in psoriasis[4,5]

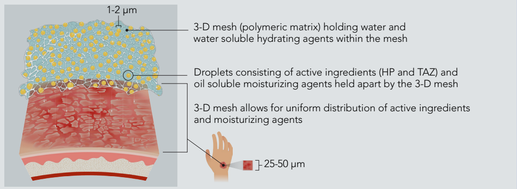
- Tazarotene is a retinoid prodrug that is rapidly metabolized to tazarotenic acid, which binds with high affinity to ligand-dependent transcription factors RARγ (enriched in the skin) and RARβ
- Tazarotene modulates pathogenic factors of psoriasis, thereby appearing to restore skin to a more quiescent, prelesional status (*figure*)
- This "normalization" of keratinocytes may be the basis of the relatively long remission after tazarotene treatment



RAR, retinoic acid receptor; TA, tazarotenic acid (active metabolite of tazarotene).

Fixed-combination HP 0.01%/TAZ 0.045% lotion formulation[3,6]

- Innovative polymeric emulsion technology formulation allows for uniform distribution of active ingredients in a lower-dose formulation (*figure*)
- Vehicle lotion formulation is non-greasy and provides enhanced barrier to the skin
- Application of HP/TAZ lotion results in higher permeation efficiency of the active ingredients compared with application of higher-dose HP or TAZ creams (alone or layered)



HP, halobetasol propionate; TAZ, tazarotene.

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