ORIGINAL ARTICLE

Safety and efficacy of a fixed combination of halobetasol and tazarotene in the treatment of moderate-to-severe plaque psoriasis: Results of 2 phase 3 randomized controlled trials

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Background: Topical corticosteroids are the mainstay of psoriasis treatment, with long-term safety considerations limiting their use. Combining them with tazarotene may optimize their efficacy and minimize safety and tolerability concerns.

Objective: To investigate the safety and efficacy of halobetasol propionate 0.01% plus tazarotene 0.045% (HP/TAZ) lotion in moderate-to-severe plaque psoriasis.

Methods: Two multicenter, randomized, double-blind, vehicle-controlled phase 3 studies (N = 418) were conducted. Subjects were randomized (2:1) to HP/TAZ lotion or vehicle once daily for 8 weeks with a 4-week follow-up. The primary efficacy assessment end point was treatment success (at least a 2-grade improvement from baseline in Investigator's Global Assessment score and a score of clear or almost clear). Safety and treatment-emergent adverse events were evaluated throughout.

Results: HP/TAZ lotion demonstrated statistically significant superiority over vehicle within as few as 2 weeks. By week 8, 35.8% (study 1) and 45.3% (study 2) of subjects were treatment successes compared with 7.0% and 12.5% of those treated with vehicle ($P < .001$). HP/TAZ lotion was also superior in reducing signs and symptoms of psoriasis and body surface area affected by psoriasis. The most frequently reported treatment-related adverse events were contact dermatitis (6.3%), application site pain (2.6%), and pruritus (2.2%).

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The trial was neither carried out at University of California, San Francisco (UCSF) nor evaluated by UCSF's Institutional Review Board.

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QST Consultations, Ltd, performed statistical analysis. The authors vouch for the accuracy of the data, analysis, and fidelity of each study to the protocols. They were involved in the writing of sections of the first draft of the manuscript, which were combined and reviewed by all, with editorial assistance provided by Konic Ltd. All the authors agreed to submit the manuscript for publication.

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Limitations: Studies did not include subjects with more than 12% of their body surface area affected by psoriasis.

Conclusions: HP/TAZ lotion was associated with significant reductions in the severity of the clinical signs of psoriasis, with no safety concerns. (J Am Acad Dermatol https://doi.org/10.1016/j.jaad.2018.03.040.)

Key words: fixed combination; halobetasol; psoriasis; tazarotene; topical.

Topical therapy is a key component of psoriasis management; it is considered first-line therapy for mild disease and is often used alone or in conjunction with systemic agents in more severe psosiasis.[1]

Use of topical corticosteroids (TCSs) is commonplace, mainly because of their immunosuppressive, anti-inflammatory, and antiproliferative properties. However, long-term safety concerns remain, particularly with more potent formulations, owing to an increased risk of local cutaneous adverse events (AEs).[1-3] Consequently, TCSs such as halobetasol propionate cream (Ultravate 0.05%, Ranbaxy Laboratories, Inc, Jacksonville, FL) are not recommended for more than 2 consecutive weeks' use.

Tazarotene has also been shown to be effective in psoriasis,[4,5] but it's use is limited by irritancy. Studies suggest that combination with TCSs may optimize the efficacy of, duration of remission resulting from, and safety of TCS treatment in addition to minimizing local irritation due to tazarotene.[6-8]

Use of fixed combination topical treatments in dermatology can provide synergistic therapeutic efficacy and tolerability benefits. Development of the formulation is key in attaining the balance between efficacy and safety; vehicles can significantly affect efficacy and adherence and increase cosmetic elegance.[9]

Recently, phase 2 clinical data on 8 weeks' treatment of moderate-to-severe psoriasis with a novel halobetasol propionate 0.01%/tazarotene 0.045% (HP/TAZ) lotion formulation were published.[10] HP/TAZ lotion was significantly more effective than the individual active ingredients or vehicle, and it was well tolerated. Here, we have further investigated the safety and efficacy of HP/TAZ lotion, reporting on 2 phase 3 clinical studies.

CAPSULE SUMMARY

- Topical corticosteroids are the mainstay of psoriasis treatment; long-term safety concerns limit their use. Combination with tazarotene may optimize efficacy, minimizing safety and tolerability concerns.
- In patients with moderate-to-severe plaque psoriasis treated with halobetasol propionate/tazarotene lotion, improvement is noted within 2 weeks, with few adverse effects observed after 8 weeks.
- Halobetasol propionate/tazarotene lotion may provide a realistic topical option for management of psoriasis.

METHODS

Study design

Two multicenter, double-blind, randomized, parallel-group phase 3 studies were conducted to assess the safety, tolerability, and efficacy of HP/TAZ lotion in subjects with moderate-to-severe psoriasis.

The studies, which were registered on ClinicalTrials.gov as NCT02462070 and NCT02462122, were conducted at 32 clinical sites in the United States from August 2015 to November 2016.

Subjects and randomization

For inclusion, subjects could be of either sex but had to be age 18 years or older and have moderate-to-severe plaque psoriasis with an Investigator Global Assessment (IGA) score of 3 or 4 and affected body surface area (BSA) of 3% to 12%.

Subjects were randomized (2:1) to HP/TAZ lotion or vehicle applied topically to the affected area once daily for 8 weeks, with initial application at the investigational center. Subjects were instructed to spread a thin layer over the affected area and avoid ultraviolet radiation (natural and artificial). The maximum allowable weekly use was 50 g.

Assessments were carried out at baseline; at weeks 2, 4, 6, and 8 of treatment; and at 4 weeks after treatment (week 12).

Study oversight

Subjects provided written informed consent; protocol and consent were approved by institutional review boards or ethics committees at all investigational sites. Investigators were trained for