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ORIGINAL ARTICLE

Long-term safety and efficacy of a fixed-combination halobetasol propionate 0.01%/tazarotene 0.045% lotion in moderate-to-severe plaque psoriasis: phase 3 open-label study

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Abstract

Background The topical corticosteroid halobetasol propionate (HP) and the retinoid tazarotene (TAZ) are effective in psoriasis treatment. To mitigate adverse cutaneous reactions observed with monotherapy, a fixed-combination HP 0.01%/TAZ 0.045% lotion has been developed for the treatment of plaque psoriasis in adults.

Objectives To investigate the long-term safety, efficacy and maintenance of response with HP/TAZ lotion.

Methods This was a 1-year, multicentre, open-label study in 555 adults with psoriasis [Investigator's Global Assessment (IGA) score of 3 ('moderate') or 4 ('severe') and body surface area (BSA) of 3–12% at baseline]. HP/TAZ was administered once daily for 8 weeks and then intermittently as needed in 4-week intervals for up to 1 year based on achievement of treatment success [IGA score of 0 ('clear') or 1 ('almost clear')]. Maximum continuous exposure was 24 weeks.

Results Of 550 participants with postbaseline safety data, 318 (57.8%) achieved treatment success during the study. Of those, 54.4% achieved treatment success within the first 8 weeks; retreatment was not required for >4 weeks in over half (55.3%), and 6.6% did not require any retreatment. Among participants enrolled for the full 52 weeks, 77.5% maintained BSA ≤5% on treatment. There were marked improvements in severity of itching, dryness and burning/stinging over the study course. The most common treatment-related adverse events were application site reactions of dermatitis, pruritus, pain and irritation.

Conclusions Fixed-combination HP/TAZ lotion provided maintained efficacy with a favourable tolerability and safety profile, supporting its use for the long-term treatment and management of moderate-to-severe plaque psoriasis.

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Conflict of interest

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[†]Bausch Health US, LLC is an affiliate of Bausch Health Companies Inc. Ortho Dermatologics is a division of Bausch Health US, LLC. ClinicalTrials.gov registry number: NCT02462083

Incyte, Janssen Research & Development, LLC, Kyowa Hakko Kirin, LEO Pharma, Meiji Seika Pharma, Merck-Serono, Merck Sharp & Dome, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharmaceuticals and UCB and is a consultant for Almirall, Aurinia Pharmaceuticals, CanFite, Evelo, Horizon Pharma, Menlo Therapeutics, Reistone Therapeutics, Tanabe Mitsubishi. G. Han is or has been an investigator, consultant/advisor, or speaker for AbbVie, Athenex, Boehringer Ingelheim, Bond Avillion, Bristol-Myers Squibb, Celgene, Eli Lilly, Novartis, Janssen, LEO Pharma, MC2, Ortho Dermatologics, PellePharm, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharmaceuticals and UCB. D.M. Pariser has served as consultant to Atacama Therapeutics, Bickell Biotechnology, Biofrontera AG, Celgene, Dermira, LEO Pharma, Regeneron, Sanofi, TDM SurgiTech, TheraVida, and Ortho Dermatologics; investigator for Abbott Laboratories, Almirall, Amgen, AOBiome, Asana Biosciences, Bickell Biotechnology, Celgene, Dermavant, Dermira, Eli Lilly, LEO Pharma, 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. S. Harris is an employee of Bausch Health US, LLC and may hold stock and/or stock options in its parent company. A. Jacobson and T. Lin are employees of Ortho Dermatologics and may hold stock and/or stock options in its parent company.

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Introduction

Topical corticosteroids (TCSs) are the mainstay of treatment for psoriasis due to their anti-inflammatory properties. However, they are limited by rebound effects upon sudden cessation of treatment as well as tachyphylaxis and adverse cutaneous reactions with long-term use, including striae, telangiectasias and skin atrophy.^{1–3} The superpotent TCS halobetasol propionate (HP) has demonstrated superior efficacy over vehicle and other TCSs as monotherapy for plaque psoriasis, though labelling restrictions limit its use to 2–4 weeks of continuous treatment.⁴ Retinoids are a separate drug class that can treat psoriasis through inhibition of keratinocyte proliferation, decreasing expression of inflammatory markers, and normalizing keratinocyte differentiation. Tazarotene (TAZ) was the first topical retinoid developed for the treatment of psoriasis,⁵ but may cause cutaneous irritation when used alone.⁶

When used in combination, the anti-inflammatory properties of TCSs may reduce TAZ-induced irritation, whereas TAZ can mitigate corticosteroid safety concerns and increase the duration of treatment effects.^{3,7,8} However, there are technical challenges in creating a topical treatment that provides uniform and simultaneous disposition of multiple active ingredients onto the skin in addition to efficient delivery into the dermal layers. A fixed-combination HP 0.01%/TAZ 0.045% lotion (HP/TAZ; Duo-brii®; Ortho Dermatologics, Bridgewater, NJ, USA) was recently developed to treat psoriasis using a single formulation featuring two active ingredients with different mechanisms of action. This novel lotion formulation utilizes an innovative polymeric emulsion technology to provide uniform distribution of active ingredients and excipients onto the skin and to provide enhanced epidermal barrier for improved skin moisturization.² Application of fixed-combination 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)² and may provide synergistic efficacy beyond the additive effects of the individual active ingredients.⁹

Two phase 3 studies demonstrated the efficacy and safety of HP/TAZ lotion in the treatment of moderate-to-severe psoriasis.^{10–12} In these studies, participants received up to eight continuous weeks of treatment, with maintenance of effect observed up to 4 weeks after treatment cessation. Here, we present the results of a phase 3 open-label study assessing the long-term safety, efficacy and maintenance of response of HP/TAZ lotion in participants receiving up to 24 continuous weeks of treatment and followed for up to 1 year.

Materials and methods

Study overview

This was a 1-year, multicentre, open-label study (NCT02462083) in participants ≥ 18 years of age with plaque psoriasis. The study was conducted in 45 study centres in the United States in accordance with ethical principles from the Declaration of Helsinki, international conference on harmonization guidelines, good clinical practice, and local regulatory requirements. The study was reviewed and approved by the governing Institutional Review Board (IRB) Schulman Associates IRB, Inc (Cincinnati, OH, USA). Written informed consent was obtained prior to participation in the study.

Enrolment criteria

Participants were required to have a clinical diagnosis of moderate-to-severe plaque psoriasis, defined as an Investigator's Global Assessment (IGA) of 3 or 4, and body surface area (BSA) of 3–12%; the face, scalp, palms, soles, axillae and intertriginous areas were excluded from IGA and BSA assessments. Concurrent use

of lithium or Plaquenil during the study was prohibited and participants were excluded for the following: use of any topical antipsoriatic drug product within 14 days prior to baseline; use of phototherapy, photochemotherapy, or non-biological systemic psoriasis therapy within 4 weeks prior to baseline; use of biological therapies known to affect psoriasis within 3 months of baseline; and prolonged exposure to natural or artificial sources of ultraviolet radiation within 4 weeks prior to baseline.

Study design

All participants were treated with HP/TAZ lotion once daily for 8 weeks, with treatment used intermittently, as needed, in 4-week intervals for the remainder of the 52-week study (Fig. 1). At week 8, participants were evaluated for treatment success, defined as IGA score of 0 or 1 ('clear' or 'almost clear'). Those who achieved treatment success stopped treatment for 4 weeks and those who did not achieve treatment success continued treatment for 4 weeks. All participants were re-evaluated at week 12 for improvement, defined as ≥ 1 -grade improvement from baseline IGA; those without improvement were discontinued from the study, whereas those with improvement continued the study and were subsequently managed in 4-week cycles (e.g. treated with HP/TAZ lotion once daily for 4 weeks if they had not achieved treatment success or receiving no treatment until the next evaluation if they had achieved treatment success). Maximum continuous exposure during the study was 24 weeks; as such, if 24 weeks of continuous treatment had been received at any point in the study, the participant needed an IGA score of 0 or 1 to continue the study. CeraVe[®] hydrating cleanser and CeraVe[®] moisturizing lotion (L'Oreal, New York, NY, USA) were provided for optional use as needed for optimal moisturizing/cleaning of the skin.

Analyses

The primary objective of the study was to evaluate safety and tolerability following long-term treatment with HP 0.01%/TAZ 0.045% lotion. The sample size selected for this study (approximately 500 enrolled, with the intent that ~300 participants would be followed for 6 months and ~100 for 1 year) was expected to provide sufficient data for a long-term safety evaluation of HP/TAZ lotion when used by adult subjects with plaque psoriasis.

Adverse events (AEs) and serious AEs (SAEs) were classified using terminology from the Medical Dictionary for Regulatory Activities. Tolerability was evaluated at all study visits through assessments of selected local signs and symptoms (itching, dryness and burning/stinging) and the presence or absence of significant known drug-related reactions (skin atrophy, striae, telangiectasia and folliculitis). Any local skin reaction that required the use of a concomitant therapy or was a cause for study drug interruption or discontinuation was to be reported as an AE. Efficacy was evaluated through IGA and BSA assessments. All statistical processing was performed using SAS[®]. Descriptive statistics were used to provide an overview of safety and efficacy results; no imputations were made for missing data.

Results

Participant disposition and demographics

A total of 555 participants were treated with HP/TAZ during the study. Of these, 503 (90.6%) completed 3 months on study, 391 (70.5%) completed 6 months on study and 138 (24.9%) completed 12 months on study. At week 12, only 26 participants (4.7%) were discontinued from the study due to lack of efficacy, defined as not having ≥ 1 -grade improvement from baseline in

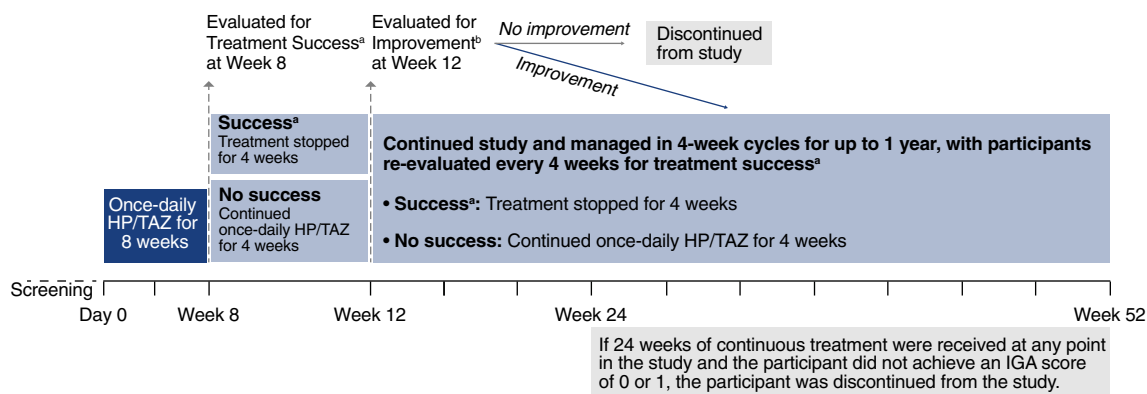


Figure 1 Open-label study design. ^aTreatment success defined as score of 0 (clear) or 1 (almost clear) on IGA. ^bImprovement defined as ≥ 1 -grade improvement from baseline IGA. Maximum continuous exposure was 24 weeks. Each tick mark on the timeline indicates 4 weeks (timeline not to scale). HP/TAZ, halobetasol propionate 0.01%/tazarotene 0.045%; IGA, Investigator's Global Assessment.

IGA score. At week 24, 116 participants (20.9%) were discontinued from the study due to lack of efficacy – defined as 24 weeks of continuous use without achieving an IGA of 0 or 1 – even though all had at least a 1-grade improvement in IGA score from baseline; through the end of the study, an additional nine participants (1.6%) were discontinued due to lack of efficacy. Subject request ($n = 87$, 15.7%) was the other most common reason for study discontinuation. A total of 33 participants (5.9%) discontinued the study due to an AE; AEs were deemed unrelated to treatment in four of these participants.

Of all study participants, 550 had postbaseline safety data and were included in the safety population. Mean age was 51.9 years and the majority of participants were male, white and not Hispanic/Latino. Baseline IGA was moderate in most of the participants, and median BSA was 5% (Table 1). Median length of study drug exposure was 172 days and the median number of applications was 164.

Efficacy

Overall, 318 participants (57.8%) achieved treatment success at some point during the study; the majority of these participants (54.4%, $n = 173$) achieved treatment success within the first 8 weeks (Fig. 2). In many participants, treatment success was rapid, being achieved within the first 2 and 4 weeks in 12.6% and 37.4% of those who achieved treatment success, respectively.

Table 1 Participant demographic and baseline characteristics (safety population)

	HP/TAZ lotion $N = 550$
Age, mean (range), year	51.9 (19–87)
Sex, n (%)	
Male	361 (65.6)
Female	189 (34.4)
Ethnicity, n (%)	
Hispanic or Latino	141 (25.6)
Not Hispanic or Latino	409 (74.4)
Race, n (%)	
White	473 (86.0)
Black or African American	46 (8.4)
Asian	15 (2.7)
Other†	16 (2.9)
IGA score, n (%)	
3 – Moderate	476 (86.5)
4 – Severe	74 (13.5)
Affected BSA, %	
Mean (SD)	5.6 (2.65)
Median (range)	5.0 (3–12)

BSA, body surface area; HP/TAZ, halobetasol propionate 0.01%/tazarotene 0.045%; IGA, Investigator's Global Assessment; SD, standard deviation.

†Includes Native Hawaiian or Other Pacific Islander ($n = 3$), American Indian or Alaska Native ($n = 1$), and Other ($n = 12$).

Of 226 participants enrolled at least 8 weeks in the study and who stopped therapy after achieving treatment success, 55.3% did not require retreatment for at least 29 days (>4 weeks), 28.3% for at least 57 days (>8 weeks), and 19.5% for at least 84 days (>12 weeks); overall, 6.6% did not relapse and therefore did not require any retreatment (Fig. 3).

Affected BSA decreased over time, from a median of 5.0% at baseline ($n = 550$) to 4.0% at week 4 ($n = 539$), 3.0% at week 8 ($n = 511$) and 2.0% at week 16 ($n = 418$); a median BSA of 2.0% was maintained for the duration of the 52-week study. For individuals participating for the full year, 77.5% maintained a BSA level of $\leq 5\%$ and 49.3% maintained a BSA level of $\leq 3\%$ during the study when on treatment (Fig. 4).

Treatment-emergent adverse events

A brief overview of safety data from this study has been previously presented.¹³ Over half of participants experienced treatment-emergent AEs (TEAEs) during the year-long study,

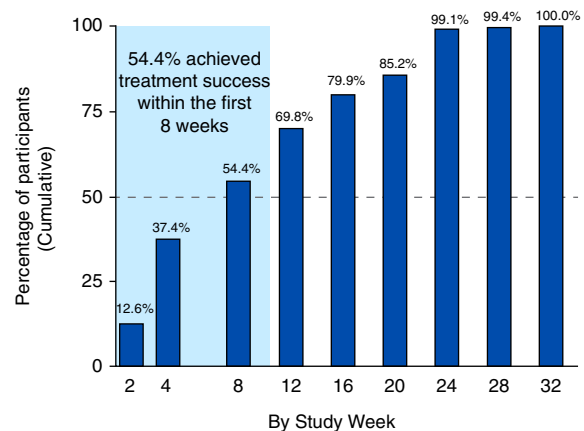


Figure 2 Time to first treatment success in participants who achieved treatment success^a with HP/TAZ ($n = 318$). ^aFigure includes only participants who achieved treatment success, defined as score of 0 (clear) or 1 (almost clear) on IGA. Cumulative data shown; as such, participants included in the bar graphs are not mutually exclusive. N values for IGA assessments were as follows: baseline $n = 550$; week 2 $n = 544$; week 4 $n = 539$; week 8 $n = 511$; week 12 $n = 478$; week 16 $n = 419$; week 20 $n = 385$; week 24 $n = 362$; week 28 $n = 261$; week 32 $n = 238$. For the three participants who achieved treatment success after week 24: one participant did not have a week 24 visit and at the early termination visit approximately 1 month later had an IGA of almost clear; one participant stopped study treatment approximately 1 month after week 24 and approximately 1 month later had an IGA of almost clear; and one participant, who temporarily interrupted study drug between weeks 20 and 24 due to a AE of contact dermatitis, had an IGA of almost clear at the week 32 visit. HP/TAZ, halobetasol propionate 0.01%/tazarotene 0.045%; IGA, Investigator's Global Assessment.

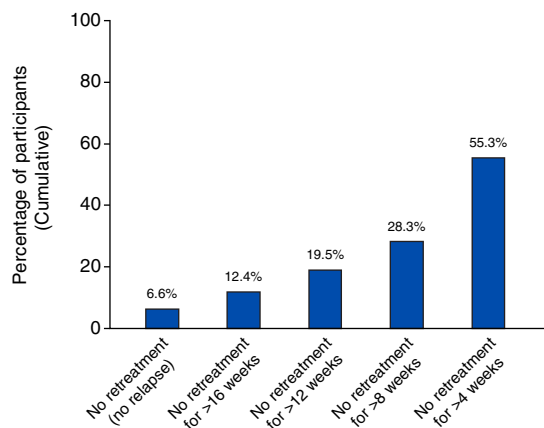


Figure 3 Time to retreatment with HP/TAZ ($n = 226^a$). ^aParticipants enrolled post 8 weeks in the study and who stopped therapy after achieving treatment success [defined as a score of 0 (clear) or 1 (almost clear) on IGA]. Cumulative data shown; as such, participants included in the bar graphs are not mutually exclusive. HP/TAZ, halobetasol propionate 0.01%/tazarotene 0.045%; IGA, Investigator's Global Assessment.

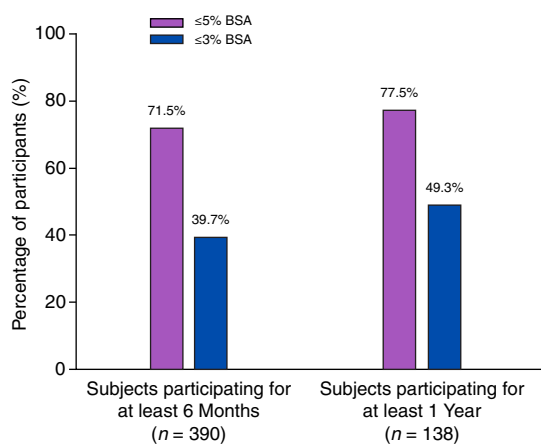


Figure 4 Maintained BSA^a from week 8 to end of study with HP/TAZ. ^aOnly BSA records considered as occurring on treatment were used in assessing if the percent BSA was maintained. BSA, body surface area; HP/TAZ, halobetasol propionate 0.01%/tazarotene 0.045%.

primarily during the first 12 weeks (Table 2). Most TEAEs were mild to moderate in severity and none of the serious AEs (SAEs) were deemed related to treatment. The most common TEAEs related to study drug were application site reactions of dermatitis, pruritus, pain and irritation (Table 2). Notably, there were

low rates of other application site disorders, including erosion (1.6%), erythema (1.5%), rash (1.3%), reaction (0.9%), atrophy (0.7%) and exfoliation (0.7%).

Overall, 7.5% of subjects discontinued due to TEAEs. Individual TEAEs that led to discontinuation in more than one participant each were application site dermatitis ($n = 7$), application site pruritus ($n = 7$), application site pain ($n = 6$), application site reaction ($n = 5$), psoriasis ($n = 4$), application site irritation ($n = 2$) and application site urticaria ($n = 2$).

Skin reactions

Select local signs and symptoms showed marked improvements in the severity of itching, dryness and burning/stinging over the course of the study. The greatest improvement was for itching, which was the most commonly reported symptom at baseline (Fig. 5). Incidence of treatment-emergent Grade 3 (severe) local skin reactions was 22.2% for itching, 6.9% for dryness and 9.8% for burning/stinging.

Incidence of other local skin reactions is shown in Fig. 6 (data shown for approximately every 12 weeks). Peak incidence occurred at week 8 for both skin atrophy (2.3%) and folliculitis (2.7%), and at week 28 for both striae and telangiectasias (1.5% each). Most local skin reactions were transient and resolved without interruption of the dosing regimen. Correlations between treatment applications (timing and/or duration), frequency of local skin reactions and duration of local skin reactions could not be drawn. A local skin reaction was deemed an AE if it required the use of a concomitant therapy or led to study drug interruption or discontinuation. Local skin reactions most frequently reported as AEs were application site folliculitis [14 participants (2.5%); one discontinued] and application site atrophy [four participants (0.7%); one discontinued]. No participant reported striae or telangiectasia AEs.

Discussion

This 1-year, long-term and open-label study evaluated the efficacy and safety of a fixed-combination HP 0.01%/TAZ 0.45% lotion as topical therapy for moderate-to-severe plaque psoriasis. HP/TAZ lotion was developed to provide uniform delivery of active ingredients at lower doses than the conventional monotherapy formulations while providing enhanced hydration and moisturization.² In this study, HP/TAZ demonstrated rapid and sustained treatment success with good tolerability and a favourable safety profile, supporting the use of this lotion formulation in patients with an affected BSA of 3 to 12%.

Patient surveys have demonstrated that rapid improvement is a primary concern among patients with psoriasis.^{14,15} The majority of participants in this study achieved treatment success over the course of this study; of those, over one-third (37.4%) did so within 4 weeks and over half (54.4%) within 8 weeks of initiating treatment. These results are consistent with findings from two previous phase 3 trials of HP/TAZ lotion, in which

Table 2 Treatment-emergent adverse event summary (safety population)

	0–12 Weeks (n = 527)	>12–24 Weeks (n = 392)	>24–36 Weeks (n = 239)	>36 Weeks (n = 219)	Total (N = 550)
Number of TEAEs	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,† 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 maximum 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,‡ 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)

SAE, serious adverse event; TEAE, treatment-emergent adverse event.

†None of the SAEs were deemed related to treatment; ‡In >2% of total participants.

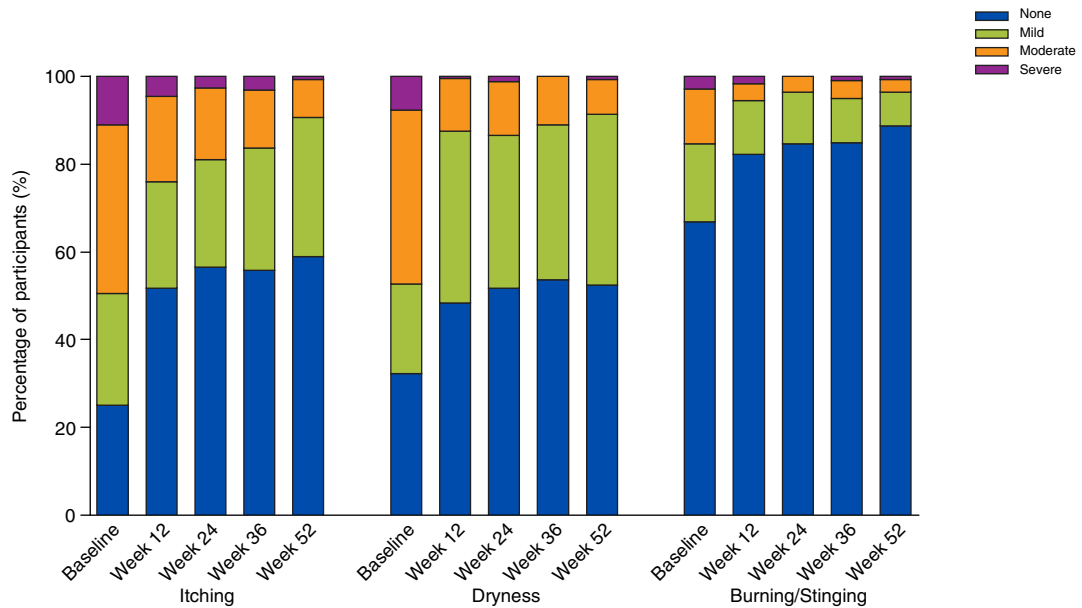


Figure 5 Local skin reactions over time, by severity (safety population). Data not shown for all timepoints assessed. *N* values were as follows: baseline *n* = 550; week 12 *n* = 480; week 24 *n* = 362; week 36 *n* = 227; week 52 *n* = 141.

over 40% of participants achieved treatment success by week 8.^{10,11} The rapid response to treatment with fixed-combination HP/TAZ lotion may be due to the unique properties of its formulation. With polymeric emulsion technology, HP and TAZ are encapsulated within oil droplets along with moisturizing and hydrating ingredients, which are uniformly dispersed in an oil-

in-water emulsion separated by a 3D mesh matrix. Upon skin contact, the mesh immediately breaks apart, providing rapid and uniform distribution of the active ingredients across the skin, which allows for more efficient absorption than with the individual ingredients applied either alone or in layers.² In *in vitro* studies, fixed-combination HP/TAZ lotion demonstrated >2-fold

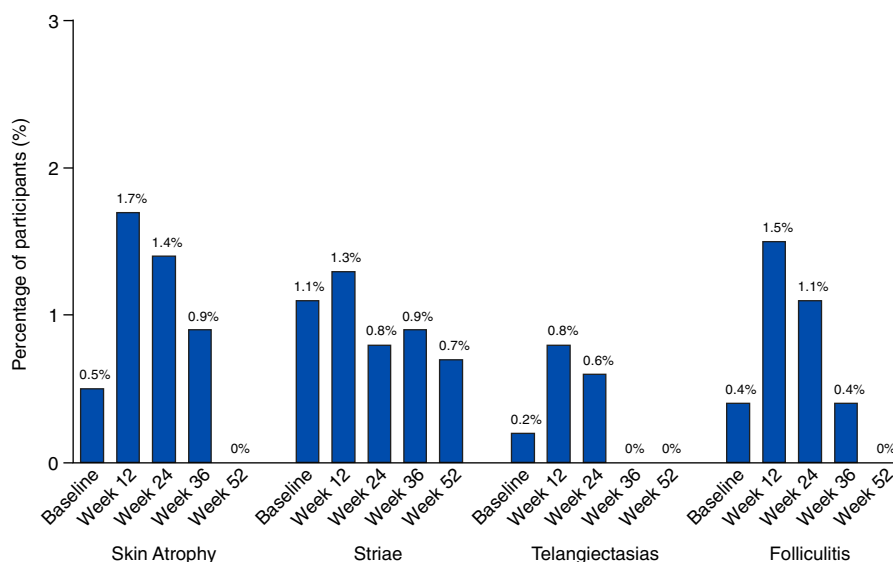


Figure 6 Incidence of local skin reactions over time (safety population). Data not shown for all timepoints assessed; incidence peaked at week 8 for skin atrophy (2.3%) and folliculitis (2.7%), and at week 28 for both striae and telangiectasias (1.5% each). *N* values were as follows: baseline *n* = 550; week 12 *n* = 480; week 24 *n* = 362; week 36 *n* = 227; week 52 *n* = 141.

and >1.5-fold increases in dermal tissue permeation of HP and TAZ, respectively, over HP cream or TAZ cream individually. In contrast, layering TAZ on top of HP decreased the permeation of TAZ.² Additionally, HP/TAZ lotion may provide synergistic efficacy; depending on the measure used, HP/TAZ lotion was 27–44% more efficacious than what might have been expected based on the individual efficacies of HP and TAZ. The mechanism for this improvement is not known, but may reflect the combined anti-inflammatory properties of HP and TAZ.⁹

Maintenance of therapeutic effect is also important in psoriasis treatment. The efficacy of HP/TAZ lotion in this study was maintained for over 1 month after treatment cessation in 55.3% of participants who achieved treatment success. Further, almost 20% of treatment successes did not require retreatment for over 3 months and 6.6% required no retreatment at all. Decreases in median BSA from 5.0% at baseline to 2.0% at week 16 were maintained through week 52. Further, 40% of individuals participating at least 6 months in the study maintained $\leq 3\%$ BSA from week 8 to the end of the study when on treatment. These maintenance results are consistent with an earlier study demonstrating that adding TAZ to once-daily TCS treatment resulted in sustained improvements up to 12-weeks post-treatment compared with <4 weeks with twice-daily TCS treatment alone.⁸ TAZ may support the maintenance of corticosteroid treatment efficacy by modulating abnormal differentiation and hyperproliferation of keratinocytes,¹⁶ which has been hypothesized to restore skin to a quiescent, prelesional status.⁵

A strength of the current study was the ability to evaluate extended treatment with a superpotent TCS (up to 24 weeks of continuous use) and long-term follow-up (up to 44-week post-treatment) in patients with psoriasis; this is notable given the paucity of clinical trials investigating long-term (>6 months) efficacy of TCSs.¹⁷ Further, to our knowledge, this is the first study to assess a superpotent TCS for more than eight continuous weeks. As part of the study design, participants were discontinued due to protocol-defined lack of efficacy. Less than 5% of participants were discontinued at week 12 (defined as no improvement in baseline IGA) and 22.5% were discontinued at or after week 24 (defined as 24 weeks of continuous treatment and IGA score >1), even though all participants in the study beyond 12 weeks experienced improvement in their psoriasis of ≥ 1 grade in IGA score. This unique study design feature may have contributed to the 24.9% of participants that completed all 52 weeks on study; though the target completion rate was met, it was lower than the approximately 50% rate observed in a 52-week randomized study of calcipotriol/betamethasone dipropionate.¹⁸ However, the completion rate in our study was comparable to the 27% rate observed in a real-life, 52-week observational effectiveness study of calcipotriol/betamethasone dipropionate.¹⁹ An additional study design limitation is that after 8 weeks of once-daily use of HP/TAZ lotion, participants were required to halt treatment for at least 4 weeks upon treatment success, defined as achievement of ‘almost clear’ or ‘clear’ skin. If participants had been able to continue treatment until

achieving clear skin, it is possible that time to retreatment would have increased and that a greater proportion would not have required any retreatment at all. Treatment to clear skin would also better reflect the goals of both patients and clinicians in a real-world setting, particularly given the low incidence of AEs with up to 24 weeks of continuous use. Further analyses comparing participants who achieved clear vs. almost clear skin would be beneficial to determine if treatment to clear confers prolonged maintenance of effect.

Adverse events reported in this long-term study were consistent with the known safety profile of fixed-combination HP/TAZ lotion. There were no new or late-onset safety concerns emerging with prolonged treatment and none of the serious AEs were considered related to treatment. The most common treatment-related AEs were application site reactions, similar to those observed in the HP/TAZ pivotal phase 3 studies.^{10,11} Rates of AEs and discontinuations due to TEAEs in this study were greatest in the first 12 weeks of HP/TAZ treatment and decreased over time; AE rates were lowest after 36 weeks of treatment, with individual TEAEs reported in two or fewer participants. Survey data indicate that concerns about AEs from TCS use are common among both patients and clinicians,^{20,21} and contribute to non-adherence in up to 28% of patients.²⁰ As the study population after week 12 was enriched for participants that had achieved IGA score improvement, these decreasing AE rates over time suggest that treatment with HP/TAZ lotion may minimize safety concerns for patients, potentially contributing to improved long-term adherence.

No clinically meaningful trends in local skin reactions were observed. For patients with psoriasis, skin atrophy is the AE of greatest concern.²⁰ Although atrophy is among the most common adverse reactions associated with TCS therapy,²² the atrophogenic potential of TCSs is reduced by combination with TAZ.²³ In this study, instances of atrophy with fixed-combination HP/TAZ lotion were low, peaking at week 8 (2.3%) and declining through study end; atrophy was reported as an AE in only four participants (0.7%) and led to only one discontinuation.

Conclusion

Fixed-combination HP/TAZ lotion has consistently demonstrated greater efficacy over placebo and may potentially provide a synergistic benefit in the treatment of moderate-to-severe plaque psoriasis.^{9–11} The rapid and beneficial effects of HP/TAZ lotion in this study were maintained in patients who achieved clear or almost clear skin over 1 year of treatment and follow-up, with minimal safety concerns. These results support the use of fixed-combination HP/TAZ lotion for the long-term treatment and management of moderate-to-severe plaque psoriasis.

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