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Efficacy of a Once-Daily Fixed Combination Halobetasol (0.01%) and Tazarotene (0.045%) Lotion in the Treatment of Localized Moderate-to-Severe Plaque Psoriasis

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Recently, clinical data on 8 weeks' once-daily treatment of localized moderate-to-severe psoriasis with a novel fixed combination halobetasol propionate 0.01%/tazarotene 0.045% (HP/TAZ) lotion were published.[1,2] HP/TAZ lotion was significantly more effective than individual active ingredients or vehicle, based on improvements in Investigator's Global Assessment (IGA), body surface area (BSA) involvement, and signs and symptoms of psoriasis (erythema, plaque elevation, and scaling) at the target lesion as well as a synergistic benefit over individual active ingredients, and good tolerability.

To address recognized limitations of Psoriasis Area and Severity Index (PASI), IGA, and BSA, alternative disease severity assessments have been developed. The product of IGA and BSA involvement (IGAxBSA) is a simple validated alternative for assessing treatment response that provides a more representative overview of psoriasis by considering both plaque qualities and disease extent. It also correlates well with PASI.[3-5]

Here, we further investigate the efficacy of HP/TAZ lotion through a post hoc analysis of two large multicenter, double-blind studies (N=418) using the IGAxBSA assessment tool to evaluate improvement in disease severity and achievement of a clinically meaningful outcome in patients with localized moderate-to-severe psoriasis.

Detailed trial methodology has been presented elsewhere,[2] and is briefly described here. Patients with a clinical diagnosis of moderate-to-severe psoriasis (IGA 3 or 4) and 3-12% BSA (N=418) were randomized (2:1) to receive HP/TAZ lotion or vehicle applied topically to affected areas once-daily for 8 weeks, with a 4-week post-treatment follow-up. IGAxBSA scores were calculated at baseline, and weeks 2, 4, 6, 8, and 12. A clinically meaningful outcome was defined as achievement of ≥75% reduction in IGAxBSA score from baseline (IGAxBSA-75).

Improvement in disease severity following treatment with HP/TAZ lotion was rapid and statistically significant compared to vehicle from week 2 (P<0.001) and at all subsequent evaluations (all P<0.001). At week 8, mean percent changes in IGAxBSA score from baseline were 51.9% and 9.21% for HP/TAZ lotion and vehicle (P<0.001) (Figure 1). Efficacy was sustained over the 4-week post-treatment period. At Week 12, mean percent changes in IGAxBSA score from baseline were 46.6% and 7.92% respectively (P<0.001).

At week 8, IGAxBSA-75 was achieved by 41.7% of patients treated with HP/TAZ lotion and 9.9% treated with vehicle (P<0.001), see Figure 2. This clinically meaningful improvement was maintained 4 weeks post-treatment (week 12) with 41.4% of HP/TAZ lotion patients achieving IGAxBSA-75 compared with 10.7% treated with vehicle (P<0.001).

In both phase 3 studies, IGAxBSA scores for patients treated with HP/TAZ lotion correlated strongly with BSA (r=0.90 and 0.95 at week 8). Improvements in baseline IGAxBSA scores were similar in patients stratified by baseline disease severity (assessed by either BSA or IGA). In patients treated with HP/TAZ lotion who had a baseline BSA >5% or ≤5%, percent changes in mean baseline IGAxBSA scores by week 8 were 49.0% and 54.3% (P=0.379 between group comparison). In patients who had severe (IGA = 4) or moderate (IGA = 3) disease at baseline, percent changes in mean baseline IGAxBSA scores at week 8 were 52.9% and 51.7% (P=0.747 between group comparison).

In this post hoc analysis of two phase 3 vehicle-controlled studies of localized moderate-to-severe plaque psoriasis treated with once-daily HP/TAZ lotion or vehicle for 8 weeks, we demonstrate a rapid reduction in IGAxBSA scores and mean change from baseline of 52% with HP/TAZ lotion, similar to results reported for apremilast by week 16 (48%).[6] Comparable

FIGURE 1. Change in IGAxBSA composite scores: Percent reductions in mean IGAxBSA from baseline at each study visit (percent change from baseline to week 12, ITT population, Phase 3 studies, pooled data).

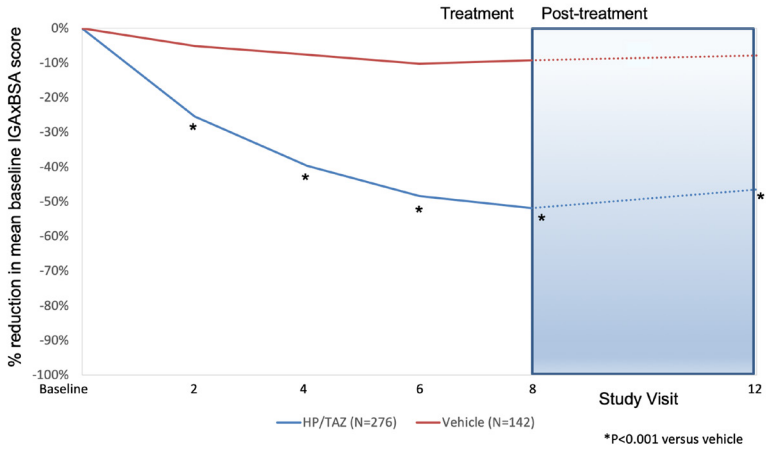


FIGURE 2. Achievement of clinically meaningful treatment success at week 8 and week 12 (four weeks post-treatment). (Percent patients achieving a 50% or 75% reduction in IGAxBSA score, ITT population, Phase 3 studies, pooled data).

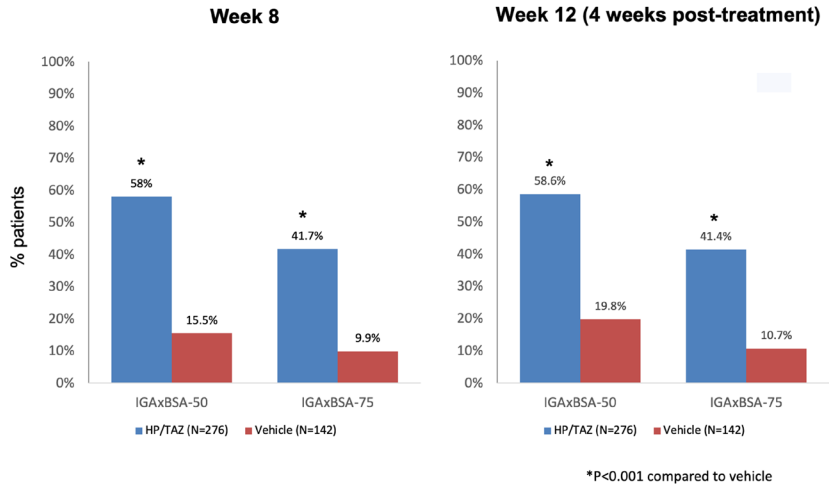
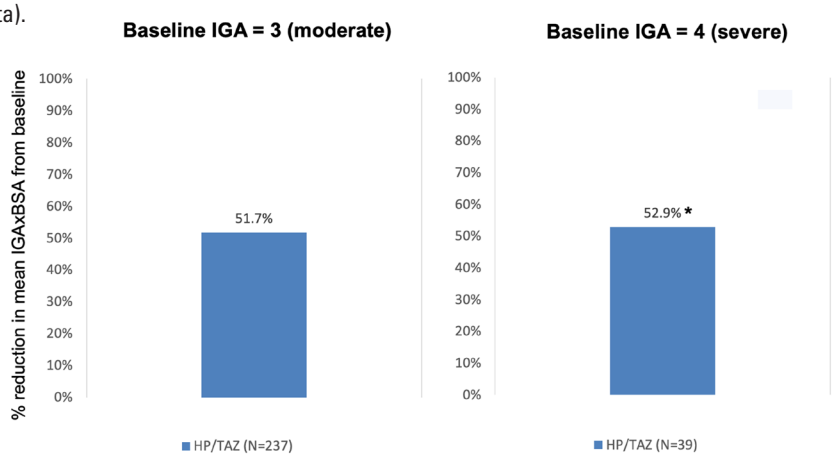


FIGURE 3. Percent change in IGAxBSA score by baseline IGA severity at week 8. (percent change from baseline to week 8 , ITT population, Phase 3 studies, pooled study data).



*P=0.747 for comparison between results for HP/TAZ lotion in patients with IGA=3 and IGA=4

improvements with HP/TAZ lotion were also noted in the post hoc analysis in patients stratified by baseline disease severity.

Achieving clinically meaningful outcomes is an important aspect of psoriasis disease management, where disease burden and quality of life impact are significant. More than 40% of patients in the two studies achieved a clinically meaningful outcome (IGAxBSA-75) by week 8, again similar to results reported for apremilast by week 16 (35%).[7] It remains to be seen whether HP/TAZ lotion treatment beyond 8 weeks would result in more patients achieving clinically meaningful outcomes.

Post-treatment return of psoriatic signs and symptoms is common with topical therapies and can be a significant concern for patients. It has been estimated that relapse can occur in 60% of patients within a month of stopping topical corticosteroid (TCS) therapy. Reductions in baseline IGAxBSA scores achieved with HP/TAZ lotion following 8 weeks' daily treatment were sustained 4 weeks post-treatment, probably due to the inclusion of tazarotene, as sustained improvements in efficacy have been reported previously when TCS and tazarotene have been used to treat psoriasis.[1,2] In conclusion, a fixed combination halobetasol propionate 0.01%/tazarotene 0.045% lotion provided rapid and sustained relief of psoriatic signs and symptoms in patients with localized moderate-to-severe disease as assessed by the IGAxBSA composite tool.

DISCLOSURE

Dr. Blauvelt has served as a scientific adviser and clinical study investigator for AbbVie, Aclaris, Akros, Allergan, Almirall, Amgen, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly and Company, Galderma, Genentech/Roche, GlaxoSmithKline, Janssen, Leo, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Revance, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB Pharma, Valeant Pharmaceuticals North America LLC, and Vidac, and as a paid speaker for Janssen, Regeneron, and Sanofi Genzyme. Dr Green is an investigator, consultant, and/or speaker for AbbVie, Amgen, Celgene, Merck, Novartis, and Valeant. Dr Lebwohl is an employee of the Mount Sinai Medical Center, which receives research funds from Amgen, Anacor, Aqua, Canfite Biopharma, Celgene, Clinuvel, Coronado Biosciences, Eli Lilly, Ferndale, Janssen, Leo, Merck, Novartis, Pfizer, Sandoz, and Valeant. Dr Yamauchi has served as an investigator for Amgen, Celgene, Dermira, Galderma, Janssen, LEO Pharma, Eli Lilly, MedImmune, Novartis, Pfizer, Regeneron, and Sandoz; he serves as an advisor and/or speaker for AbbVie, Amgen, Baxter, Celgene, Dermira, Galderma, Janssen, LEO Pharma, Eli Lilly, Novartis, Pfizer, and Regeneron.

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