The efficacy of adapalene-benzoyl peroxide combination increases with number of acne lesions

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Background: There is no direct correlation between acne severity and lesion numbers and patients with moderate acne may present with varying lesion counts. The fixed-dose adapalene 0.1%-benzoyl peroxide (BPO) 2.5% combination gel is an efficacious and safe acne treatment.

Objective: We sought to evaluate whether the benefit of adapalene-BPO relative to vehicle varies with baseline lesion counts.

Methods: Data were pooled from 3 randomized, double-blind, controlled studies, which compared efficacy in 4 treatment groups (adapalene-BPO, adapalene, BPO, and the gel vehicle). Three lesion count subgroups (Low, Mid, and High) were defined based on the number of total, inflammatory, or noninflammatory lesion at baseline. Efficacy of each treatment and benefit of each treatment relative to vehicle were evaluated on the entire population and in all lesion count subgroups. Safety was assessed by local tolerability score and adverse events.

Results: Adapalene-BPO provided significant benefit relative to vehicle and monotherapies on the entire population and in all lesion count subgroups ($P < .05$). At study end point, the benefit of adapalene-BPO relative to vehicle was greatest in the High subgroup, suggesting that patients with the highest baseline lesion counts contributed the most to the treatment benefit observed in the entire population. This effect was only observed with adapalene-BPO and not with monotherapies. Higher baseline lesion counts did not lead to more related adverse event or worse tolerability score for adapalene-BPO.

Limitation: These results were generated from clinical trials. Results in clinical practice could differ.

Conclusion: The relative benefit of adapalene-BPO increases with higher lesion counts at baseline. (J Am Acad Dermatol 2011;64:1085-91.)

Key words: acne; adapalene; benzoyl peroxide; combination therapy; lesion; severity.

Although clinicians select treatments for patients with acne based primarily on the severity of the disease presentation,[1] the clinical severity of acne can be challenging to define and does not simply correspond to the number of lesions.[2-5] For efficacy investigations of new acne therapies, both lesion counts and global assessments of primary lesions have been used as outcome standards.[6] The global assessment is a clinically relevant gestalt with categorization based on the

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experience and judgment of the dermatologist, whereas the lesion counts provide a more precise measure of specific features of disease severity.

An antibiotic-free, fixed-dose combination of adapalene 0.1% and benzoyl peroxide (BPO) 2.5% has been recently developed for once-daily treatment of acne, based on the complementary modes of action of the two agents.[7-12] Adapalene-BPO is an appropriate treatment for all but the most severe forms of acne, because the combination provided significant benefit relative to the gel vehicle, adapalene alone, and BPO alone in reduction of acne lesion counts and achieving overall global success, with an acceptable tolerability profile.[13-16] Recognizing that patients with acne may present with extremely variable lesion numbers, it was clinically relevant to determine whether the benefit of adapalene-BPO combination varied with baseline lesion counts. We pooled data from 3 double-blind, randomized, and controlled studies on adapalene-BPO[13-15] and performed a subgroup analysis, to compare the benefit of combination therapy relative to vehicle in subgroups defined by lesion counts at baseline.

CAPSULE SUMMARY

- The adapalene-benzoyl peroxide (BPO) combination was significantly more efficacious than its monotherapies and gel vehicle, regardless of the number of lesions at baseline.
- Adapalene-BPO provided greater benefit relative to vehicle as the number of lesion at baseline increased.
- This effect (increased benefit with higher lesion counts at baseline) was only observed with adapalene-BPO and not with monotherapies.
- Therefore, adapalene-BPO is particularly suitable for treatment of patients with a high number of acne lesions.

METHODS

Study design

Individual patient data were pooled and analyzed from 3 multicenter, randomized, double-blind, controlled studies of similar design.[13-15] In each of these 3 studies, the efficacy and safety of a fixed-dose combination topical gel of adapalene 0.1%-BPO 2.5% gel (Epiduo, Galderma SA, Lausanne, Switzerland) were compared with those of adapalene 0.1% gel, BPO 2.5% gel, and the gel vehicle. Three lesion count subgroups were defined based on the number of total, inflammatory, or noninflammatory lesions at baseline (defined further below in "Statistical analyses" section). Efficacy and safety analyses were performed on the entire pooled population and in each lesion count subgroup.

All studies were conducted in accordance with the ethical principles originating from the Declaration of Helsinki and Good Clinical Practices and in compliance with local regulatory requirements. The studies were reviewed and approved by institutional review boards/ethics committees. All patients provided written informed consent before entering the study.

Patients

Enrolled patients with acne vulgaris were of either sex, any race, aged 12 years or older, having 20 to 50 inflammatory lesions and 30 to 100 noninflammatory lesions on the face excluding the nose. Specified washout periods were required for patients taking certain topical and systemic treatments. Exclusion criteria prohibited enrollment of patients with severe acne requiring isotretinoin therapy or other dermatologic conditions requiring interfering treatments. Women were excluded if they were pregnant, nursing, or planning a pregnancy as were men with facial hair that would interfere with the assessments.

Efficacy and safety assessments

The efficacy variable was the percent reduction from baseline in lesion counts (total, inflammatory, and noninflammatory) at week 12/last observation carried forward. Safety variables included local tolerability scores and adverse events. At each visit of all studies, investigators evaluated adverse events and rated erythema, scaling, dryness, and stinging/burning on a scale ranging from 0 (none) to 3 (severe).

Statistical analyses

Efficacy analyses were performed on the entire population and in each lesion count subgroup.

Three subgroups were defined according to the quartiles based on counts of total, inflammatory, or noninflammatory lesion at study baseline (Table I):

- Low lesion count subgroup (Low): 25% of population with the lowest number of lesions at baseline (≤ 23 inflammatory lesions, ≤ 36 noninflammatory lesions, ≤ 63 total lesions);
- High lesion count subgroup (High): 25% of population with the highest number of lesions at baseline (≥ 34 inflammatory lesions, ≥ 62 noninflammatory lesions, ≥ 94 total lesions);
- Medium lesion count subgroup (Mid): 50% of population with the medium number of lesions