New Fixed-Dose Combination Gels for Acne Vulgaris

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Management of acne vulgaris continues to be a challenge in clinical practice. In addition to the goal of reducing acne lesions, other common hurdles include maximizing compliance and minimizing the cost of therapy. Topical combination products containing benzoyl peroxide (BPO) and a topical antibiotic, such as erythromycin and clindamycin, or a topical retinoid (tretinoin) and a topical antibiotic (clindamycin), have been highly successful in the United States, offering the benefits of efficacy and convenience. Two new combination products have been approved by the US Food and Drug Administration (FDA) and are now available. One is an aqueous gel formulation of BPO 2.5% and clindamycin phosphate (CDP) 1.2%, which is applied once daily.[1] The other formulation is a combination of adapalene 0.1% and BPO 2.5% aqueous gel and is also applied once daily.[2] An overview of the data on these formulations is presented in this article.

BPO 2.5% and CDP 1.2% Gel

Efficacy

A fixed-dosed combination aqueous gel containing BPO 2.5% and CDP 1.2% was studied in 2 randomized, multicenter, double-blind, 4-arm, 12-week trials in subjects with moderate to severe facial acne vulgaris (n=2813).[1] By study end point, the BPO 2.5% and CDP 1.2% gel (n=797) was statistically superior to BPO 2.5% (n=809), CDP 1.2% (n=812), and vehicle (n=395) in reducing inflammatory lesions ($P<.001$), noninflammatory lesions ($P<.001$), and acne severity ($P\leq.001$). Subjects included in the trial were 12 years or older, with a mean age range of 19.1 to 19.6 years. Table 1 depicts the mean percentage reductions in inflammatory, noninflammatory, and total lesions achieved in each study arm.

Tolerability

The majority of subjects in all treatment arms did not experience signs or symptoms of cutaneous application site reactions.[1] Reactions that did occur were rated as mild in severity. None of the subjects in the BPO 2.5% and CDP 1.2% study arm discontinued treatment because of adverse events, such as erythema, burning, stinging, or pruritus, and none of the subjects in this group reported application site dryness. The cutaneous tolerability profile of BPO 2.5% and CDP 1.2% proved to be very favorable.

Adapalene 0.1% and BPO 2.5% Gel

Efficacy

Phases 2 and 3 and long-term (12 mo) studies have been completed with adapalene 0.1% and BPO 2.5% gel inclusive of 2637 subjects with facial acne vulgaris of moderate severity.[2-4] In both phase 2 (n=517) and phase 3 studies (n=1668), the adapalene 0.1% and BPO 2.5% gel proved to be superior in efficacy to the individual active monads and vehicle.

The phase 2 study was a randomized, double-blind, 12-week trial of adapalene 0.1% and BPO 2.5% gel (n=149) versus adapalene 0.1% gel (n=148), BPO 2.5% gel (n=149), and vehicle gel (n=71) in subjects 12 years or older with moderate severity acne vulgaris.[2] All groups applied study medication once daily. The superiority of adapalene 0.1% and BPO 2.5% gel was demonstrated over the individual monad arms, adapalene 0.1% gel ($P=.008$), BPO 2.5%gel ($P=.003$), and vehicle gel ($P=.002$), with a statistically significant difference confirmed in all comparisons of treatment success, which was defined as subjects achieving clear or almost clear skin.[2]

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Table 1

BPO 2.5% and CDP 1.2% Gel: Mean % Lesion Count Reductions[1]

Study Arm	Inflammatory Lesions	Noninflammatory Lesions	Total Lesions
BPO 2.5% and CDP 1.2% (n=797)	54.6%	43.2%	47.9%
BPO 2.5% (n=809)	46.2%	36.2%	40.4%
CDP 1.2% (n=812)	47.5%	37.4%	41.6%
Vehicle (n=395)	29.0%	24.0%	26.2%

Abbreviations: BPO, benzoyl peroxide; CDP, clindamycin phosphate.

In the phase 3, 12-week, multicenter, randomized, double-blind study, adapalene 0.1% and BPO 2.5% gel (n=415) was compared with adapalene 0.1% gel (n=420), BPO 2.5% gel (n=415), and vehicle gel (n=418).[3] Subjects were 12 years or older, presented with moderate severity acne vulgaris, and applied study medication once daily.[3] Table 2 depicts the median percentage reductions in inflammatory, noninflammatory, and total lesions achieved in each study arm. Statistically significant superiority was also observed in the study group treated with adapalene 0.1% and BPO 2.5% gel as compared with adapalene 0.1% gel, BPO 2.5% gel, and vehicle gel for inflammatory lesions ($P<.001$, $P=0.017$, $P<.001$, respectively), noninflammatory lesions ($P=.007$, $P<.001$, $P<.001$, respectively), and total lesions ($P<.001$, $P<.001$, $P<.001$, respectively).[3]

In a multicenter, 12-month, open-label study, subjects (n=452) with acne vulgaris were treated with adapalene 0.1% and BPO 2.5% gel once daily.[4] All subjects presented with facial acne vulgaris of moderate severity and were 12 years or older. In this trial, adapalene 0.1% and BPO 2.5% gel once daily was used as monotherapy in all subjects. Inflammatory, noninflammatory, and total lesion reductions at study end point were 76%, 70%, and 70.8%, respectively.[4] The discontinuation rate due to adverse events was 2%, and none of the subjects stopped treatment due to lack of efficacy.

Tolerability

In phases 2 and 3 and long-term studies, skin tolerability parameters, including erythema, scaling, stinging/burning, and dryness were assessed. In all 3 studies, the mean tolerability scores were rated as below mild in the subjects treated with adapalene 0.1% and BPO 2.5% gel, which included 1016 subjects in total.[2-4]

Table 2

Adapalene 0.1% and BPO 2.5% Gel: Median % Lesion Count Reductions[3]

Study Arm	Inflammatory Lesions	Noninflammatory Lesions	Total Lesions
Adapalene 0.1% and BPO 2.5% (n=415)	62.1%	53.8%	56.3%
Adapalene 0.1% (n=420)	50.0%	49.1%	46.9%
BPO 2.5% (n=415)	55.6%	44.1%	48.1%
Vehicle (n=418)	34.3%	29.5%	28.1%

Abbreviations: BPO, benzoyl peroxide.

As expected, the highest mean cutaneous tolerability scores were recorded at the first follow-up study visit, followed by a marked accommodation trend as mean scores progressively approached their baseline level. The overall tolerability profile was similar and favorable in subjects actively treated with adapalene 0.1% and BPO 2.5% gel, adapalene 0.1% gel, or BPO 2.5% gel.

Summary

This article provides an overview of efficacy and tolerability data from studies evaluating 2 new, fixed-dose, topical combination formulations, BPO 2.5% and CDP 1.2% gel, and adapalene 0.1% and BPO 2.5% gel. Both agents offer the potential for use in acne vulgaris based on results from studies that have been completed. Ultimately, their success will depend on whether or not real world use matches what was shown in the pivotal trials that brought these products successfully through the FDA-approval process and into a very competitive acne marketplace.

References

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