

## Combination Therapies Are More Effective than Monotherapy for Mild to Moderate Acne

Thiboutot DM, Weiss J, Bucko A, et al. *Adapalene-benzoyl peroxide, a fixed-dose combination for the treatment of acne vulgaris: results of a multicenter, randomized double-blind controlled study.* *J Am Acad Dermatol* 2007;57:791–9.

### Study Overview

**Objective.** To determine the efficacy of fixed-dose adapalene 0.1% and benzoyl peroxide (BPO) 2.5% for the treatment of acne.

**Design.** Randomized, double-blind, placebo-controlled trial.

**Setting and participants.** Participants were recruited from 36 centers in the United States and were included if they were aged  $\geq 12$  years and had 30 to 100 noninflammatory facial lesions, 20 to 50 inflammatory facial lesions, and no nodules or cysts. Patients were excluded if they had severe acne requiring isotretinoin therapy, were pregnant, or had facial hair that might interfere with assessment.

**Intervention.** Patients were allocated to adapalene-BPO gel, adapalene gel monotherapy, BPO gel monotherapy, or gel vehicle.

**Main outcome measures.** Percentage of facial lesions reduced from baseline (total, inflammatory, noninflammatory) and success rate. Success rate was defined as the percentage of participants rated as “clear” or “almost clear” on the investigator’s global assessment (IGA) of acne severity. The measurement scale for the IGA ranged from 0 (clear) to 5 (very severe). Efficacy evaluations were conducted at weeks 1, 2, 4, 8, and 12.

**Main results.** Of 517 participants, 149 were allocated to the adapalene-BPO group, 148 to the adapalene-only group, 149 to the BPO-only group, and 71 to placebo. Baseline characteristics were similar between the groups. At 12 weeks, the success rate was 27.5% in the adapalene-BPO group, 15.5% in the adapalene group, 15.4% in the BPO group, and 9.9% in the placebo group. With respect to total lesion count, the median percentage change from baseline to week 12 was  $-51\%$  in the adapalene-BPO group,  $-35.4\%$  in the adapalene group,  $-35.6\%$  in the BPO group, and  $-31\%$  in the placebo group. For both endpoints, the improvements in the adapalene-BPO group were

statistically significantly greater than in any of the other 3 arms. As early as week 1, the adapalene-BPO group demonstrated a statistically significant increased success rate as compared with the other 3 groups. The safety and tolerability of the adapalene-BPO arm was similar to the adapalene group, with the majority of patients experiencing mild or no irritation.

**Conclusion.** A fixed-dose preparation of adapalene and BPO is more effective for reducing acne severity than either agent alone. This combination is well tolerated with a low incidence of side effects.

### Commentary

Acne vulgaris is the most common dermatologic condition in the United States and is associated with significant morbidity. Successful acne therapy has been shown to lessen the psychological distress associated with acne [1]. The pathophysiology of acne is complex and includes 4 hallmark factors: hyperkeratosis, increased sebum production, *Propionibacterium acnes* within the follicle, and inflammation. Despite numerous available therapies for acne, including antibiotics, retinoids, and BPO, none of these single agents address all 4 hallmark features. As such, combination therapy is an important component of acne therapy. Although data exist that support the efficacy of combination therapy with antibiotics and BPO [2], there have been no well-designed trials to assess combination therapy with a retinoid and BPO.

Adapalene is a topical retinoid with comedolytic and anti-inflammatory effects. Adapalene has been shown to reduce acne lesions as monotherapy [3] and in combination with clindamycin [4]. In this well-designed study by Thiboutot et al, the combination of adapalene and BPO was more effective than either agent alone and it had a similar side effect profile when compared with adapalene monotherapy. In addition, the beneficial effects of dual therapy were apparent after only 1 week of therapy. This study supports prior work that suggests combining agents for acne is a superior strategy to monotherapy and provides further evidence that practitioners can include retinoids and BPO within their treatment armamentarium for acne.

### Applications for Clinical Practice

For patients with mild to moderate acne, a fixed-dose combination of adapalene and BPO is more efficacious than either agent alone without added toxicities.

—Review by Harvey J. Murff, MD, MPH

### References

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