

## A Randomized, Parallel, Vehicle-Controlled Comparison of Two Erythromycin/Benzoyl Peroxide Preparations for Acne Vulgaris

*Diane Thiboutot, MD,<sup>1</sup> Michael Jarratt, MD,<sup>2</sup> Phoebe Rich, MD,<sup>3</sup> Toivo Rist, MD,<sup>4</sup> David Rodriguez, MD,<sup>5</sup> and Sharon Levy, MD<sup>6</sup>*

*<sup>1</sup>Pennsylvania State University College of Medicine, Hershey, Pennsylvania, <sup>2</sup>Derm Research, Inc, Austin, Texas, <sup>3</sup>NW Cutaneous Research Specialists, Portland, Oregon, <sup>4</sup>Dermatology Associates of Knoxville, PC, Knoxville, Tennessee, <sup>5</sup>International Dermatology Research, Inc, Miami, Florida, and <sup>6</sup>Dermik Laboratories, Berwyn, Pennsylvania*

### ABSTRACT

**Background:** Topical erythromycin/benzoyl peroxide (EBP), marketed for acne treatment, must be compounded by a pharmacist and requires subsequent refrigeration, warranting the development of alternate formulations.

**Objective:** This trial compared the efficacy and tolerability of a single-use EBP combination package (EBP Pak) with those of its matching vehicle control (VC Pak) and the original, reconstituted formulation packaged in a jar (EBP Jar). The matching VC for the original formulation (VC Jar) was used to achieve study blinding.

**Methods:** In this double-blind, parallel-group, multicenter study, patients were randomly assigned to the 4 treatment arms. The primary efficacy evaluations were lesion reductions from baseline and treatment success (as defined by a Physician's Global Acne Severity score of 0 [clear] or 0.5 [sparse comedones with few or no inflammatory lesions]). Secondary evaluations were Physician's Global Acne Severity scores, facial-oiliness scores, and end-point patient evaluations of global improvement and treatment acceptability. Tolerability was based on the incidence and severity of adverse events.

**Results:** Three hundred twenty-seven patients (age range, 12–46 years) were randomly assigned to the 4 treatment groups (EBP Pak, 124; VC Pak, 42; EBP Jar, 121; VC Jar, 40). Mean percent reductions in total acne lesions, inflammatory acne lesions, and comedones from baseline were significantly greater with EBP Pak than with VC Pak ( $P \leq 0.001$  for the intent-to-treat patient population after 8 weeks). Statistical significance for all lesion parameters was demonstrated at week 2 ( $P < 0.05$ ) and maintained throughout the study. At 8 weeks, a significantly greater proportion of patients demonstrated treatment success with the EBP Pak compared with VC Pak (28% vs 2%, respectively;  $P < 0.001$ ).

---

Accepted for publication March 8, 2002.

Printed in the USA. Reproduction in whole or part is not permitted.

The EBP Pak was comparable to the EBP Jar in terms of reduction in acne lesions, Physician's Global Acne Severity scores, and end-of-treatment patient evaluations of global improvement. No serious drug-related adverse events were reported.

**Conclusions:** Results of this 8-week trial demonstrate that the single-use combination package of EBP is well tolerated, effective, and comparable to the original formulation for the treatment of acne vulgaris in this selected patient population.

**Key words:** erythromycin, benzoyl peroxide, combination treatment, acne vulgaris. (*Clin Ther.* 2002;24:773-785)

## INTRODUCTION

Acne vulgaris is the most common skin disease in the United States, affecting an estimated 85% of individuals between the ages of 12 and 25 years.<sup>1,2</sup> Systemic antibiotic therapy with tetracycline, erythromycin, minocycline, and trimethoprim-sulfamethoxazole has been used successfully to treat acne due to both the antibacterial and anti-inflammatory properties of these agents.<sup>3</sup> However, interest in developing effective topical therapy continues because of the adverse effects associated with systemic therapy.<sup>4</sup>

Topical treatments for acne include benzoyl peroxide, retinoids, antibiotics, azelaic acid, sodium sulfacetamide, and salicylic acid.<sup>2,3,5</sup> Benzoyl peroxide is the most frequently used topical agent for acne and is available both in prescription (2.5% to 10%) and nonprescription formulations.<sup>3</sup> It is a powerful oxidizing agent that inhibits the growth of *Propionibacterium acnes* and may be comedolytic.<sup>5,6</sup>

Unless acne is mild, effective treatment typically will include combinations of ther-

apies.<sup>3</sup> Topical erythromycin or clindamycin administered with benzoyl peroxide constitutes an important current strategy for the management of mild to moderate acne.<sup>2</sup> In studies to date, combination regimens consisting of benzoyl peroxide with erythromycin or clindamycin have been more effective than monotherapy with either benzoyl peroxide or antibiotics in reducing the signs of acne vulgaris.<sup>7-9</sup> The superiority of a combination of erythromycin and benzoyl peroxide (EBP) to either agent alone may result from the antibacterial effects of both agents, along with the keratolytic effect of benzoyl peroxide, or may be due to a greater degree of penetration by erythromycin after loosening of the stratum corneum by benzoyl peroxide.<sup>8</sup> Anti-inflammatory effects of erythromycin also may contribute to the mechanism of action of this combination therapy.<sup>8</sup> Furthermore, concomitant use of benzoyl peroxide and erythromycin may prevent the emergence of resistant strains of *P. acnes*.<sup>8,10</sup> Selection for highly resistant bacterial populations, which may have occurred after the introduction of topical antibiotic formulations or from decades of long-term systemic administration to patients, may be countered by the use of a broad-spectrum antibacterial agent such as benzoyl peroxide.<sup>11</sup>

The original marketed formulation of 3% erythromycin and 5% benzoyl peroxide is packaged in a jar (EBP Jar<sup>\*</sup>). This product must be compounded by a pharmacist and refrigerated by the patient. A new formulation of erythromycin/benzoyl peroxide contained in a single-dose package (EBP Pak<sup>†</sup>)

\*Trademark: Benzamycin Topical Gel® (Dermik Laboratories, Berwyn, Pennsylvania).

†Trademark: Benzamycin® Pak (Dermik Laboratories, Berwyn, Pennsylvania).

was developed to improve the convenience of using this combination product. No refrigeration is required for the new formulation, and the patient mixes 2 gels extruded from the single-use package, yielding a 3% erythromycin and 5% benzoyl peroxide gel. In the present multicenter, double-blind, parallel-group, controlled Phase III trial, the efficacy and tolerability of the EBP Pak were compared with those of its matching vehicle control (VC Pak) and the original formulation (EBP Jar) in patients with moderate to moderately severe acne vulgaris. Blinding was completed with a matching vehicle control in a jar (VC Jar).

## PATIENTS AND METHODS

### *Study Design*

Male and female patients  $\geq 12$  years of age with moderate to moderately severe acne were enrolled at 6 treatment centers. At baseline, patients were required to have 15 to 80 facial inflammatory lesions, 20 to 140 facial comedones (not including the nose or nasolabial area),  $\leq 2$  nodules or cysts  $>5$  mm, and a minimum Physician's Global Acne Severity score of 1.5. The Physician's Global Acne Severity score, determined at baseline and weeks 2, 4, 6, and 8, was the physician's comprehensive evaluation of the patient's overall acne condition at the time of evaluation. This 9-point scale (ranging from 0 to 4 with 0.5 increments) takes into account the size and intensity of lesions, the overall degree of inflammation, general erythema, and skin condition, in addition to quantifying lesions. This severity scale was designed to incorporate well-known descriptors of acne based on the Pillsbury Classification,<sup>12</sup> along with photographs

selected from the Leeds photographic acne scale,<sup>13</sup> which served as references.

The primary study objective was to test for superiority of the EBP Pak compared with the VC Pak. The secondary study objective was to test for noninferiority of EBP Pak compared with EBP Jar. Patients were randomly assigned 3:3:1:1 to twice-daily treatment with EBP Pak, EBP Jar, VC Pak, and VC Jar, respectively, for 8 weeks. Qualified participants were assigned a patient number that corresponded to a randomized treatment, and each received a box of double-blinded study medication. Visits were scheduled at baseline and at weeks 2, 4, 6, and 8. This study was approved by the institutional review board at each center, and patients  $\geq 18$  years of age gave written informed consent prior to enrollment. For patients  $< 18$  years of age, parents or guardians gave consent and children gave assent.

### *Efficacy Variables*

The primary efficacy variables included the reduction in acne lesion counts from baseline and treatment success, as defined by a Physician's Global Acne Severity score of 0 or 0.5 at week 8. Reductions in lesion counts were determined for all acne lesions (total lesions) and separately for inflammatory lesions (papules or pustules) and noninflammatory lesions (comedones). Absolute reductions were compared between study groups, and reductions as a percent of baseline count were determined as an alternate measure of treatment effect.

Secondary efficacy variables included all Physician's Global Acne Severity scores, facial-oiliness scores, and end-point evaluations of global improvement and treatment acceptability by patients.

Facial oiliness was evaluated at baseline and all follow-up visits, using a scale of 0 to 3 (0 = none, 3 = severe). The Patient's Global Improvement score was determined by patients ranking the change in their conditions using a scale of 0 to 3 (0 = no change or worse, 3 = much better) at the final study visit. Overall treatment acceptability was indicated by a patient's willingness to use the medication after conclusion of the study.

### ***Tolerability***

Assessment of treatment tolerability was based on adverse event reports. Patients were questioned by investigators in an unbiased manner (open-ended questioning) about spontaneous adverse event reports at each study visit. Information regarding the frequency and severity of these events was collected. Adverse events of all types, adverse events affecting the skin, and adverse events possibly related to treatment were summarized according to treatment group.

### ***Statistical Analysis***

The statistical significance of treatment contrasts (EBP Pak vs VC Pak and EBP Pak vs EBP Jar) was reported with no adjustment for multiple comparisons. Patients were evaluable for efficacy if they completed the final clinical evaluations  $\geq 25$  days after starting treatment, maintained compliance, were not lost to follow-up, and completed  $\geq 70\%$  of scheduled treatment applications between the baseline and final study visit.

The intent-to-treat (ITT) population included all patients who received study medication or vehicle. Safety analyses were performed using the ITT population.

In addition, EBP Pak and VC Pak treatment groups were compared using data from the last study visit of each ITT patient. Week 8 visits for evaluable patients were used to compare the EBP Pak with the EBP Jar formulation. An analysis of covariance (ANCOVA) model was applied to assess proportional lesion reductions from baseline using log-transformed data. Percent lesion reductions are presented as geometric mean percent reductions by retransforming the least squares means of the log differences. Reductions in absolute lesion counts and Physician's Global Acne Severity scores also were analyzed by ANCOVA models, and included site and treatment group factors and a baseline covariate. A cumulative logistic model was used to compare facial-oiliness scores. Both the ANCOVA model and the logistic model were implemented using SAS version 6.12 (SAS Institute Inc, Cary, North Carolina). A *P* value of  $<0.05$  was considered statistically significant. There was  $>80\%$  power to detect superiority of EBP Pak to VC Pak and  $>80\%$  power to detect a 20% difference between EBP Pak and EBP Jar. The 20% difference in efficacy between EBP Pak and EBP Jar was considered clinically relevant. For regulatory purposes, the study was also designed for noninferiority comparisons between EBP Pak and EBP Jar. In addition, comparability of EBP Pak and EBP Jar was concluded if no significant difference was found between these products.

## **RESULTS**

### ***Patients***

Study participants ( $N = 327$ ) ranged in age from 12 to 46 years; 159 patients (48.6%) were male, and 227 patients

(69.4%) were white. No significant differences in patient demographic or baseline characteristics were noted among the 4 groups in the ITT population (Table I). These characteristics also were similar among the evaluable patient population.

Patients were randomly assigned to the 4 treatment groups (EBP Pak, 124 [37.9%]; EBP Jar, 121 [37.0%]; VC

Pak, 42 [12.8%]; VC Jar, 40 [12.2%]). The proportions of patients completing the study were similar for EBP Pak and EBP Jar (92.7% and 90.9%, respectively), as well as for the VC Pak and VC Jar (78.6% and 87.5%, respectively). Most of the patients were evaluable for efficacy: EBP Pak, 116 (93.5%); EBP Jar, 113 (93.4%); VC Pak, 36 (85.7%); VC Jar, 35 (87.5%).

Table I. Patient demographic and baseline characteristics in the intent-to-treat population.\*

Characteristic	EBP Pak (n = 124)	VC Pak (n = 42)	EBP Jar (n = 121)	VC Jar (n = 40)	All Patients (N = 327)
Mean age, y (range)	19.6 (12–43)	19.6 (13–31)	20.4 (12–46)	19.8 (14–30)	19.9 (12–46)
Sex, no. (%)					
Female	65 (52.4)	24 (57.1)	57 (47.1)	22 (55.0)	168 (51.4)
Male	59 (47.6)	18 (42.9)	64 (52.9)	18 (45.0)	159 (48.6)
Race, no. (%)					
White	86 (69.4)	30 (71.4)	82 (67.8)	29 (72.5)	227 (69.4)
Black	10 (8.1)	2 (4.8)	9 (7.4)	2 (5.0)	23 (7.0)
Asian	2 (1.6)	1 (2.4)	1 (0.8)	0 (0.0)	4 (1.2)
Hispanic	24 (19.4)	8 (19.0)	27 (22.3)	9 (22.5)	68 (20.8)
Other	2 (1.6)	1 (2.4)	2 (1.7)	0 (0.0)	5 (1.5)
Complexion, no. (%)					
Fair	56 (45.2)	22 (52.4)	58 (47.9)	20 (50.0)	156 (47.7)
Medium	53 (42.7)	16 (38.1)	50 (41.3)	17 (42.5)	136 (41.6)
Dark	15 (12.1)	4 (9.5)	13 (10.7)	3 (7.5)	35 (10.7)
Mean acne duration, y (range)	5.7 (1–28)	6.0 (0–20)	6.2 (1–32)	5.5 (1–17)	5.9 (0–32)
Previous treatment for acne, no. (%)	60 (48.4)	20 (47.6)	68 (56.2)	21 (52.5)	169 (51.7)
Comedones, mean $\pm$ SD	54.7 $\pm$ 28.5	58.2 $\pm$ 33.6	55.4 $\pm$ 29.4	53.7 $\pm$ 29.6	55.3 $\pm$ 29.5
Inflammatory lesions, mean $\pm$ SD	28.0 $\pm$ 14.6	25.8 $\pm$ 10.1	27.0 $\pm$ 12.7	28.2 $\pm$ 15.2	27.4 $\pm$ 13.5
Total lesions, mean $\pm$ SD	82.7 $\pm$ 34.3	84.0 $\pm$ 37.9	82.4 $\pm$ 35.2	81.9 $\pm$ 37.7	82.6 $\pm$ 35.4

EBP Pak = erythromycin/benzoyl peroxide single-use combination package; VC Pak = vehicle control package; EBP Jar = original erythromycin/benzoyl peroxide formulation in a jar; VC Jar = vehicle control in a jar.

\*Percentages may not total 100% due to rounding.

### Efficacy for the ITT Population

Geometric mean percent reductions in inflammatory lesions, comedones, and total lesions from baseline were significantly greater ( $P \leq 0.001$ ) in the EBP Pak group than in the VC Pak after 8 weeks of treatment (Figure 1). The mean absolute reductions in total and inflammatory lesions from baseline were significantly greater ( $P \leq 0.013$ ) with the EBP Pak than with the VC Pak at all time points. An absolute lesion reduction of 21.7 in total lesions was observed as early as 2 weeks in patients treated with EBP Pak, compared with 12.7 for patients treated with VC Pak

( $P = 0.001$ ). In addition, a statistically significant mean reduction in inflammatory lesions from baseline was observed by week 2 in the EBP Pak group compared with the VC Pak group (9.5 and 3.4, respectively;  $P \leq 0.002$ ), and this significant effect continued throughout the study. The mean reductions in comedones from baseline were significantly greater ( $P \leq 0.035$ ) with EBP Pak than with VC Pak at weeks 6 and 8. In addition to absolute reductions, patients treated with EBP Pak experienced significantly greater ( $P < 0.05$ ) geometric mean percent reductions in all 3 lesion parameters from baseline than did patients receiving VC Pak (Figure 2).

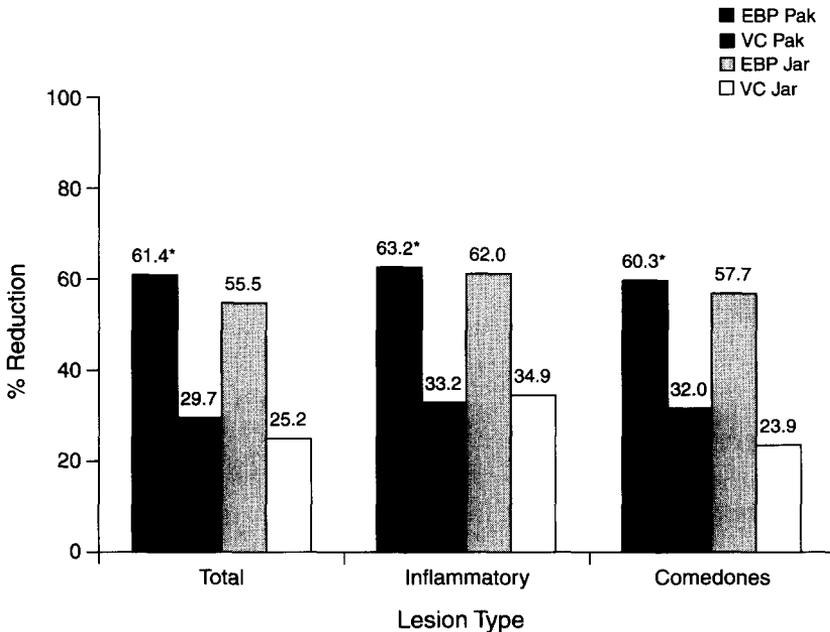
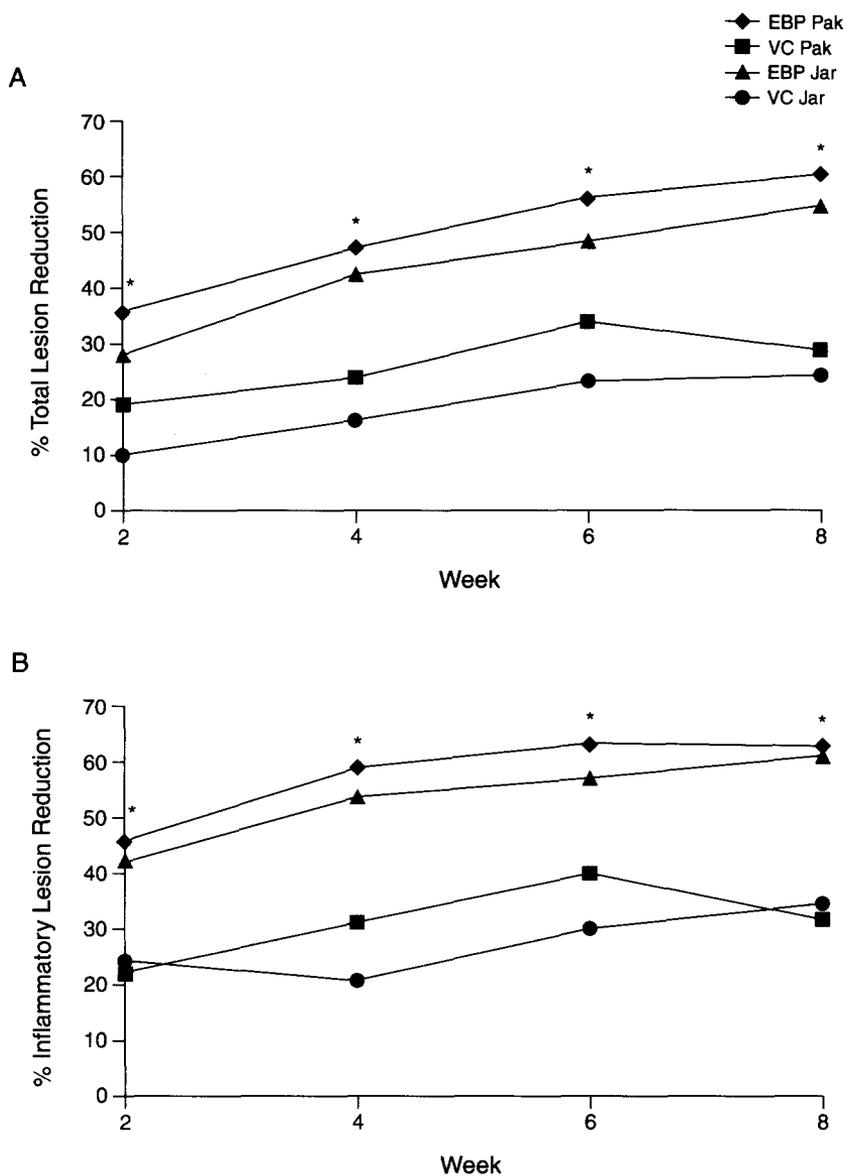


Figure 1. Geometric mean percent reductions from baseline in acne lesions at week 8. EBP Pak = erythromycin/benzoyl peroxide single-use combination package; VC Pak = vehicle control package; EBP Jar = original erythromycin/benzoyl peroxide formulation in a jar; VC Jar = vehicle control in a jar. \* $P \leq 0.001$  versus VC Pak.



(continued)

Figure 2. Geometric mean percent reductions in (A) total lesions and (B) inflammatory lesions at weeks 2, 4, 6, and 8; intent-to-treat population. EBP Pak = erythromycin/benzoyl peroxide single-use combination package; VC Pak = vehicle control package; EBP Jar = original erythromycin/benzoyl peroxide formulation in a jar; VC Jar = vehicle control in a jar. \* $P \leq 0.001$  versus VC Pak.

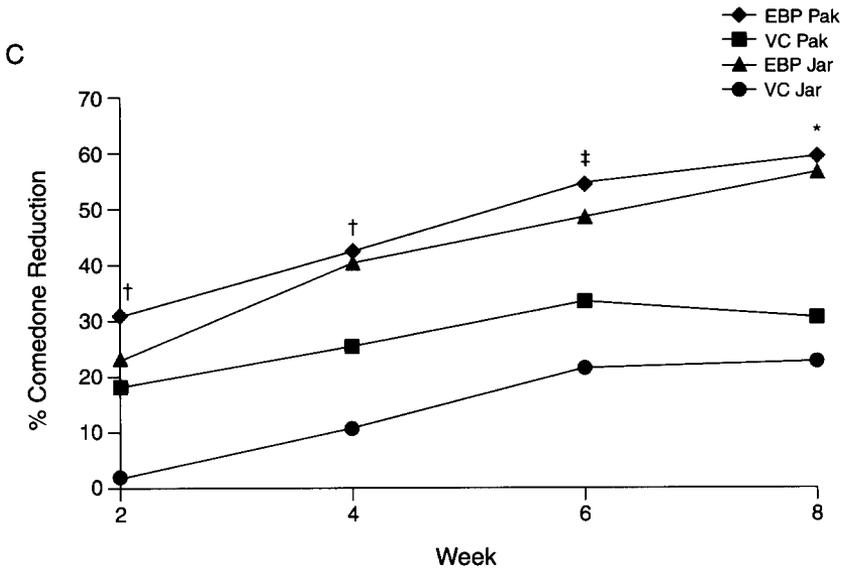


Figure 2. (continued). Geometric mean percent reductions in (C) comedones at weeks 2, 4, 6, and 8; intent-to-treat population. EBP Pak = erythromycin/benzoyl peroxide single-use combination package; VC Pak = vehicle control package; EBP Jar = original erythromycin/benzoyl peroxide formulation in a jar; VC Jar = vehicle control in a jar. \* $P \leq 0.001$ ,  $^{\dagger}P < 0.05$ , and  $^{\ddagger}P < 0.01$ , all versus VC Pak.

These differences were noted at all time points. Significantly greater proportions of patients in the EBP Pak group achieved treatment success compared with patients in the VC Pak group at weeks 4, 6, and 8 ( $P \leq 0.004$ ) (Figure 3).

Evaluation of secondary efficacy variables demonstrated significant differences between the EBP Pak and VC Pak groups. At weeks 2, 4, 6, and 8, Physician's Global Acne Severity scores were significantly improved ( $P \leq 0.002$ ) in the ITT population receiving EBP Pak compared with VC Pak (Figure 4). Significant improvements ( $P \leq 0.035$ ) also were observed in facial oiliness in patients receiving EBP Pak compared with VC Pak for weeks 4

and 8 (Figure 5). Patients treated with EBP Pak had significantly greater ( $P < 0.001$ ) Patient's Global Improvement scores at the end of the treatment phase than did patients receiving VC Pak (means of 2.2 and 1.4, respectively). In addition, the proportion of patients who considered treatment to be acceptable was significantly higher in the EBP Pak group than in the VC Pak group (87% vs 67%;  $P = 0.007$ ).

#### Comparability to EBP Jar

In this study, comparison of absolute reductions in total lesions demonstrated that EBP Pak was comparable to EBP Jar at all time points. EBP Pak also was comparable

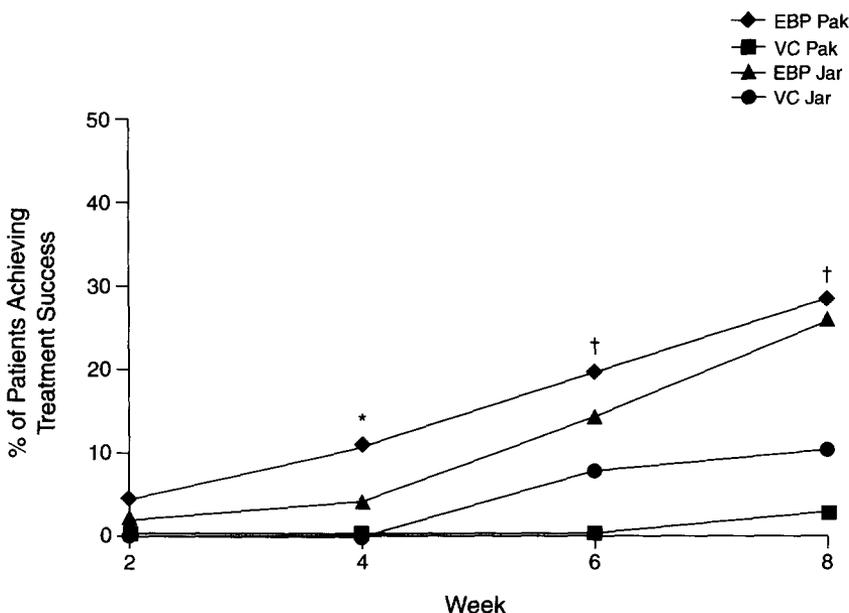


Figure 3. Proportion of patients who achieved treatment success, defined as a score of 0 (clear) or 0.5 (sparse comedones, none or very few inflammatory lesions) on the Physician’s Global Acne Severity scale; intent-to-treat population. EBP Pak = erythromycin/benzoyl peroxide single-use combination package; EBP Jar = original erythromycin/benzoyl peroxide formulation in a jar; VC Jar = vehicle control in a jar. \* $P = 0.004$  and † $P < 0.001$ , both versus VC Pak.

to EBP Jar in terms of proportional reductions in total lesions at all time points. In addition, absolute and proportional reductions in inflammatory lesions from baseline demonstrated that EBP Pak treatment was similar to EBP Jar. Absolute reductions in comedones at weeks 2, 4, and 6 and proportional reductions in comedones from baseline at weeks 2, 4, 6, and 8 also demonstrated that EBP Pak was similar to EBP Jar.

The proportions of patients in the evaluable population who achieved treatment success at week 8 were similar for the

EBP Pak and EBP Jar groups (31.1% and 27.9%, respectively). The underlying global severity scores demonstrated that EBP Pak was <20% different from EBP Jar at each evaluation interval.

EBP Pak also was similar to EBP Jar with respect to secondary efficacy variables. Criteria for similar efficacy were met at all evaluation intervals for Physician’s Global Acne Severity scores. Facial-oiliness scores were similar in the 2 active treatment groups; contrasts for weeks 2 and 8 in ratings of facial oiliness were consistent, with similar efficacy found be-

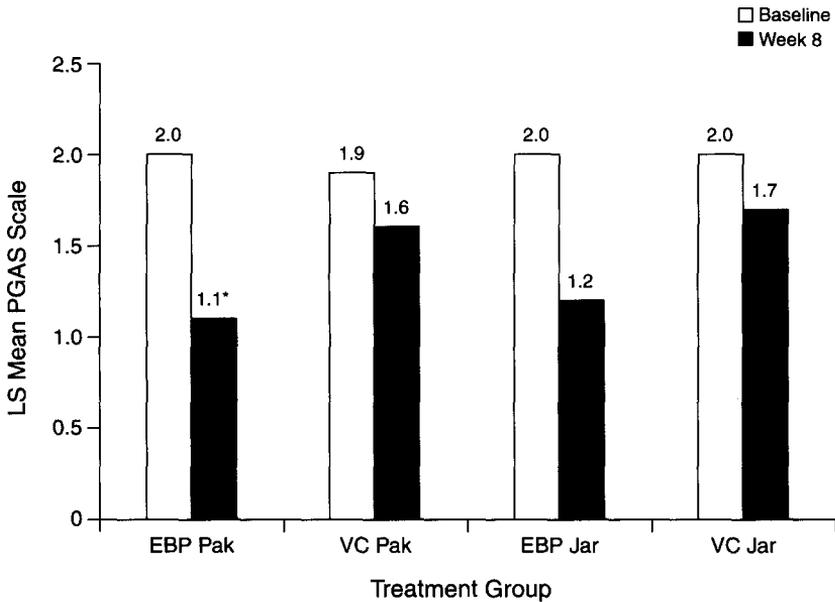


Figure 4. Least squares (LS) mean scores on the Physician's Global Acne Severity (PGAS) scale (0 = clear, no inflammatory lesions, to 4 = severe or cystic, nodular acne, resulting in exclusion from the study) for patients in the intent-to-treat population at baseline and week 8. EBP Pak = erythromycin/benzoyl peroxide single-use combination package; VC Pak = vehicle control package; EBP Jar = original erythromycin/benzoyl peroxide formulation in a jar; VC Jar = vehicle control in a jar. \* $P < 0.001$  versus VC Pak.

tween EBP Pak and EBP Jar. Moreover, global ratings of improvement obtained from patients at the end of the treatment period demonstrated that EBP Pak was comparable to EBP Jar.

### Tolerability

Adverse events were reported at similar overall incidence rates in all study groups. Dry skin was the most frequently reported skin-related adverse event, occurring in 3.2% of patients in the EBP Pak study group and 5.0% of patients in the EBP Jar study group (Table II). Most

of the skin-related adverse events were mild to moderate in severity; only 1 patient reported a severe event (photosensitivity) in the EBP Pak group. This event was considered by the investigator to be unrelated to study treatment because the patient was also sunburned on untreated areas of the body. In addition, no patients discontinued treatment prematurely due to a drug-related adverse event.

### DISCUSSION

This 8-week study demonstrates the superior efficacy of EBP Pak compared with

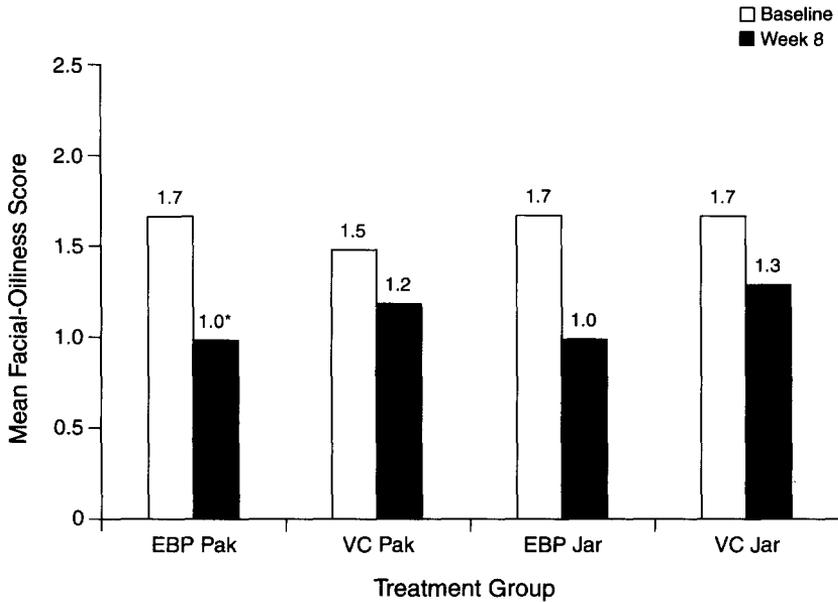


Figure 5. Mean facial-oiliness scores (0 = none to 3 = much better) for patients in the intent-to-treat population at baseline and week 8. EBP Pak = erythromycin/benzoyl peroxide single-use combination package; VC Pak = vehicle control package; EBP Jar = original erythromycin/benzoyl peroxide formulation in a jar; VC Jar = vehicle control in a jar. \**P* = 0.031 versus VC Pak.

Table II. Number (%) of skin-related adverse events occurring in >1% of patients.

Adverse Event	EBP Pak (n = 124)	VC Pak (n = 42)	EBP Jar (n = 121)	VC Jar (n = 40)
Dry skin	4 (3.2)	0	6 (5.0)	0
Application site reaction	2 (1.6)	0	1 (0.8)	0
Pruritus	1 (0.8)	0	3 (2.5)	0
Rash	0	2 (4.8)	1 (0.8)	1 (2.5)
Eczema	0	1 (2.4)	0	0
Nail disorder	0	0	0	1 (2.5)

EBP Pak = erythromycin/benzoyl peroxide single-use combination package; VC Pak = vehicle control package; EBP Jar = original erythromycin/benzoyl peroxide formulation in a jar; VC Jar = vehicle control in a jar.

its vehicle for the treatment of moderate to moderately severe acne in the selected patient population. In addition, this formulation was comparable to the currently marketed EBP Jar formulation. Twice-daily application of the EBP Pak over an 8-week period resulted in reductions in inflammatory lesions, comedones, and total acne lesions that were significantly greater than those achieved with the VC Pak. These reductions in lesion counts were demonstrated after only 2 weeks of treatment with EBP Pak, and results were maintained throughout the 8-week study. At week 8, the curves for percent reduction in comedones and total lesions from baseline had not reached a plateau, suggesting that added benefits may be achieved over longer periods of time.

Treatment was successful in a significantly greater proportion of patients who were treated with EBP Pak than in those receiving VC Pak. Significantly greater reductions in the Physician's Global Acne Severity score were demonstrated for EBP Pak than for VC Pak. Facial oiliness also was significantly reduced at study end point in the EBP Pak group compared with the VC Pak group. EBP Pak was comparable to EBP Jar in terms of all lesion count parameters, Physician's Global Acne Severity scores, and end-of-treatment patient evaluations of global improvement. These findings suggest that patients may be switched from their current EBP Jar formulas to the more convenient EBP Pak formulations without a loss of efficacy.

The overall incidence of adverse events in this study was similar in all treatment groups. Dry skin occurred in comparable proportions of patients in active and VC groups.

## CONCLUSIONS

In the present trial, EBP Pak was well tolerated in the population studied. In addition, patients rated the EBP Pak formulation comparable to the original EBP Jar formulation in terms of overall acne improvement and willingness to continue using the product. Future studies comparing EBP Pak and EBP Jar with other acne products are warranted. EBP Pak is provided in a single-use package; it is fast acting, does not require refrigeration, and can be mixed in the palm of the patient's hand. This packaging design may lead to improved patient compliance with the added benefit of dual antimicrobial therapy. The results of this study suggest that EBP Pak is an effective alternative to EBP Jar for the treatment of acne vulgaris, with potentially improved patient acceptability, onset of action, and ease of use.

## ACKNOWLEDGMENT

This work was supported by a research grant from Dermik Laboratories, Berwyn, Pennsylvania.

## REFERENCES

1. Leyden JJ, Shalita AR. Rational therapy for acne vulgaris: An update on topical treatment. *J Am Acad Dermatol*. 1986;15:907-915.
2. Weiss JS. Current options for the topical treatment of acne vulgaris. *Pediatr Dermatol*. 1997;14:480-488.
3. Yonkosky DM, Pochi PE. Acne vulgaris in childhood: Pathogenesis and management. *Dermatol Clin*. 1986;4:127-136.
4. Chalker DK, Smith JG Jr. Systemic antibiotics and acne [editorial]. *JAMA*. 1975;234:1058.

5. Hurwitz S. Acne vulgaris: Pathogenesis and management. *Pediatr Rev.* 1994;15: 47–52.
6. Cotterill JA. Benzoyl peroxide. *Acta Derm-Venereol Suppl (Stockh).* 1980;89: 57–63.
7. Lookingbill DP, Chalker DK, Lindholm JS, et al. Treatment of acne with a combination clindamycin/benzoyl peroxide gel compared with clindamycin gel, benzoyl peroxide gel and vehicle gel: Combined results of two double-blind investigations. *J Am Acad Dermatol.* 1997;37:590–595.
8. Chalker DK, Shalita A, Smith JG Jr, Swann RW. A double-blind study of the effectiveness of a 3% erythromycin and 5% benzoyl peroxide combination in the treatment of acne vulgaris. *J Am Acad Dermatol.* 1983;9:933–936.
9. Packman AM, Brown RH, Dunlap FE, et al. Treatment of acne vulgaris: Combination of 3% erythromycin and 5% benzoyl peroxide in a gel compared to clindamycin phosphate lotion. *Int J Dermatol.* 1996;35: 209–211.
10. Harkaway KS, McGinley KJ, Foglia AN, et al. Antibiotic resistance patterns in coagulase-negative staphylococci after treatment with topical erythromycin, benzoyl peroxide, and combination therapy. *Br J Dermatol.* 1992;126:586–590.
11. Eady EA, Farmery MR, Ross JI, et al. Effects of benzoyl peroxide and erythromycin alone and in combination against antibiotic-sensitive and -resistant skin bacteria from acne patients. *Br J Dermatol.* 1994;131:331–336.
12. Pillsbury DM. *A Manual of Dermatology.* Philadelphia, Pa: WB Saunders; 1971:173.
13. Cunliffe WJ. *Assessment of Acne in the Clinic: Acne Grading.* London, England: Mediscript Medical Publishers; 1989.

---

**Address correspondence to:** Sharon Levy, MD, Dermik Laboratories, 1050 Westlakes Drive, Berwyn, PA 19312. E-mail: sharon.levy@aventis.com