INTRODUCTION

Benzoyl peroxide (BPO) is poorly soluble and tends to aggregate into clusters that hinder its bioavailability and its follicular penetration. A 3-step acne system has been developed that combines a novel solubilized 5% BPO formulation together with a proprietary 2% salicylic acid cleanser and 2% salicylic acid toner. The aim of the solubilized BPO formulation is to enhance both the bioavailability and follicular penetration of BPO. Early clinical data have shown that the solubilized 5% BPO formulation can result in a greater reduction in non-inflammatory lesion count in the early weeks of treatment than a combination BPO/antibiotic product. We have now extended this research by evaluating the 3-step acne system in a larger group of patients and over a longer period of time.

METHODS

Study design

- Multicenter, investigator-blind, randomized, 10-week study

Inclusion criteria

- Mild to moderately severe facial acne vulgaris (10-100 non-inflammatory lesions, 17-66 inflammatory lesions, ≤ 2 nodulocystic lesions)
- 12-45 years of age
- Willingness to refrain from topical use of other acne medications, moisturizers, sunscreen (other than those provided in the study), fragrances, after-shave, and makeup (except oil-free non-comedogenic makeup, mascara, eyeshadow, and lipstick; eye allowed)
- Willingness to avoid excessive exposure to the sun and the use of tanning booths

Exclusion criteria

- Allergy to benzoyl peroxide, clindamycin, tetracycline, or ingredients in the study products
- Facial cosmetic procedure in the preceding 6 months
- Papulopustular rosacea and other skin diseases (apart from acne) which could interfere with study evaluation
- Facial suntan at the baseline visit
- Board or sidewalk if this could interfere with study evaluation
- Uncontrolled systemic disease, infection with human immunodeficiency virus, history of regional encephalitis, ulcetive colitis, or antibiotic-associated colitis
- Pregnancy, breastfeeding, or planning to become pregnant
- Participation in an investigational study in the preceding 30 days

Withdrawal criteria

- 1 week for any medication

- 2 weeks for topical alpha hydroxy acids and anti-acne medications other than topical retinoids and antibiotics
- 4 weeks for topical retinoids, topical and systemic antibiotics, and topical and systemic steroids
- 3 months for estrogen/progesterone control pills unless their use was stable during this period
- 6 months for systemic retinoids

Treatment regimen

- Patients randomly assigned to 10 weeks of facial treatment with one of the following:
  - The 3-step acne system (proprietary 2% salicylic acid cleanser twice daily + solubilized 5% BPO gel twice daily + proprietary 2% salicylic acid toner once daily)
  - Control cleanser twice daily + 5% BPO/1% clindamycin gel (control formulation) twice daily.

Outcome measures

- Inflammatory acne lesion count (papules, pustules, and nodules)
- Non-inflammatory acne lesion count (comedones)
- Erythema, dryness, peeling, burning/stinging, and itching (Table 1)

Statistical analysis

- Target enrollment for the study was a total of 140 patients.

- Determination of sample size was not based on a power analysis approach.
- However, the target sample size was expected to be large enough to show a clinical difference between treatments.
- Between-group differences were evaluated using a:
  - Two-sided Chi-square test or Fisher’s exact test for rate
  - Two-sided t-test or Wilcoxon rank-sum test for age and lesion counts
  - Analysis of covariance for percent change from baseline in lesion counts
- Wilcoxon rank-sum test for tolerability scores.

<table>
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<th>Score</th>
<th>Erythema</th>
<th>Dryness</th>
<th>Peeling</th>
<th>Burning/Stinging</th>
<th>Itching</th>
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<td>None</td>
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<tr>
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<td>Severe</td>
<td>Severe</td>
<td>Severe</td>
<td>Severe</td>
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</table>

RESULTS

Patients

- 105 patients have enrolled to date, with 69 (66%) having completed 6 weeks of the study at the time of baseline analysis.

- Overall, the patients were a mean of 20 years old (range, 13-44 years old) and 66% were 11-17 years old (referred to later as the pediatric subgroup).

- The majority of patients (84%) were white and had Fitzpatrick skin type II, III, or IV (26%, 34%, and 29%, respectively).

- Baseline demographics were comparable in both treatment groups.

- At baseline, patients had a mean of:
  - 22 non-inflammatory lesions (range, 18 to 22)
  - 29 inflammatory lesions (range, 17 to 50).

Efficacy in overall population

- The 3-step acne system was associated with a numerically greater percent reduction in non-inflammatory lesion count than BPO/clindamycin in the first 4 weeks of treatment (Figure 1), a mean of:
  - 27% vs. 15% at week 2 (NS)
  - 40% vs. 30% at week 4 (NS)
  - 35% vs. 30% at week 6 (NS)

- The 3-step acne system was also associated with a numerically greater percent reduction in inflammatory lesion count from week 4 onward (Figure 2), a mean of:
  - 37% vs. 41% at week 2 (NS)
  - 35% vs. 38% at week 6 (NS)

- The 3-step acne system was also associated with a numerically greater percent reduction in inflammatory lesion count from week 4 onward (Figure 2), a mean of:
  - 32% vs. 25% at week 2 (NS)
  - 35% vs. 30% at week 6 (NS)

- The 3-step acne system was also associated with a numerically greater percent reduction in inflammatory lesion count from week 4 onward (Figure 2), a mean of:
  - 32% vs. 25% at week 2 (NS)
  - 35% vs. 30% at week 6 (NS)
NING SOLUBILIZED BPO/CLINDAMYCIN: A MULTICENTER, WEEK ANALYSIS OF INTERIM DATA

Figure 1. Reduction in non-inflammatory lesion count (overall population).

Figure 2. Reduction in inflammatory lesion count (overall population).
- 42% vs. 41% at week 4 (NS)
- 49% vs. 41% at week 6 (NS)

Efficacy in pediatric subgroup
- Efficacy in the subgroup of pediatric patients (n = 66, with at least 6 weeks of the study) was similar to that in the overall population with the added advantage of statistical significance in favor of the BPO system for the reduction in non-inflammatory lesion count at week 4 (Figure 3).

Thus, compared with BPO/clindamycin, the 3-step acne system reduced the non-inflammatory lesion count (Figure 3) by a mean of:
- 24% vs. 13% at week 2 (NS)
- 33% vs. 25% at week 4 (P<0.05)
- 29% vs. 29% at week 6 (NS)

The acne system was also associated with a numerically greater percent reduction in inflammatory lesion count than BPO/clindamycin at all timepoints (Figure 4), a mean of:
- 31% vs. 34% at week 2 (NS)
- 41% vs. 41% at week 4 (NS)
- 47% vs. 36% at week 6 (NS)

Tolerability
- Both treatments were generally well tolerated with mean levels of erythema, dryness, peeling, burning, stinging, and itching less than mild in both groups at all timepoints (Figures 5-9). Nevertheless, at week 6, mean levels of dryness, peeling, and burning/stinging were significantly higher in the acne system group than BPO/clindamycin.

Tolerability scores in the pediatric subgroup were similar to those in the overall population.

Figure 3. Reduction in non-inflammatory lesion count (pediatric population).

Figure 4. Reduction in inflammatory lesion count (pediatric population).

Figure 5. Mean erythema score (overall population).
CONCLUSIONS

Compared with BFG/clohexacin, the 3-step acne system appears to offer the potential for greater improvements in acne in the early weeks of treatment in this interim analysis. It is likely that this improvement in efficacy is a result of the stabilizing BFG formulation enhancing the bioavailability and follicular penetration of BFG. The unique solven technology employed in the BFG formulation may aid in dissolving lipids in the comedones, which may play a role in enhancing efficacy in the early weeks of treatment.

The 3-step acne system offers an effective approach to treating acne with the added advantage of avoiding antibiotic exposure.

ACKNOWLEDGMENT

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REFERENCES


3. Del Rosso JU. Evaluation of a novel stabilized BFG gel—a pivotal analysis from three randomized investigator-blind trials. Poster presented at the Fall Clinical Dermatology Conference, October 18-21, 2007, Las Vegas, NV.

DISCLOSURE

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