Efficacy and Tolerability of a Fixed Combination of Clindamycin Phosphate (1.2%) and Low Concentration Benzoyl Peroxide (2.5%) Aqueous Gel in Moderate or Severe Acne Subpopulations

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ABSTRACT

Background: Oral antibiotics are commonly prescribed for moderate or severe acne, but there may be limitations due to concerns about side effects associated with systemic treatments.

Objective: To evaluate the efficacy and safety of a fixed combination clindamycin phosphate 1.2% and benzoyl peroxide 2.5% (clindamycin-BP 2.5%) aqueous gel in the treatment of moderate or severe acne subpopulations.

Methods: Two multicenter, double-blind studies randomized 2,813 subjects with moderate or severe acne to clindamycin-BP 2.5% gel, each active ingredient, or vehicle gel, once daily for 12 weeks. Efficacy evaluations included inflammatory and non-inflammatory lesion counts and evaluator’s global severity score at baseline and weeks 4, 8 and 12. Adverse events and subjects’ evaluations of product tolerability were also monitored. Subpopulation efficacy and safety analyses by baseline acne severity were performed for the combined data from the two phase 3 studies.

Results: Clindamycin-BP 2.5% gel significantly reduced inflammatory, non-inflammatory and total lesions compared with each active ingredient and vehicle in subjects with moderate acne and compared with vehicle in severe acne subjects at week 12. Significant improvements in evaluator’s global severity score were evident for subjects with moderate acne in the clindamycin-BP 2.5% group compared with each active ingredient and vehicle and compared with vehicle in subjects with severe acne at week 12. Rates of adverse events were low and similar between treatment groups and baseline acne severity.

Conclusion: Clindamycin-BP 2.5% aqueous gel is an effective and safe once-daily treatment for moderate or severe acne.

INTRODUCTION

Acne vulgaris is a common condition affecting up to 96 percent of individuals at some point in their lives and currently affects as many as 50 million adolescents and adults in the United States (U.S.). There are significant direct medical costs associated with the condition, as well as indirect costs attributed to psychological stress and impaired self-esteem. Acne most commonly affects adolescents, although eight percent of people aged 25-34 years and three percent of those in the 35-44 age category are affected. The pathophysiology of acne vulgaris is attributed to androgen-mediated stimulation of the sebaceous gland, abnormal keratinization resulting in comedo formation, proliferation of the bacterium *Propionibacterium acnes* (*P. acnes*) and inflammation. These events may be exacerbated by genetics, stress and environmental factors.

Oral antibiotics have been one of the most commonly used treatments for acne since the late 1950s, particularly for subjects with moderate-to-severe inflammatory acne, acne resistant to topical agents, acne that may cause pigmented changes and/or scarring and truncal acne. However, systemic treatments of acne vulgaris such as oral antibiotics, isotretinoin and oral contraceptives can be associated with adverse side effects (e.g., gastrointestinal upset, vulvovaginal candidiasis, photosensitivity, chilblains, teratogenicity [isotretinoin] and risk for thrombosis), and often require adherence to specific administration regimens, such as tapering the dose based on clinical response or associated side effects, and may require routine laboratory evaluations (e.g., blood counts and liver function tests). In addition, there is growing evidence of antibiotic resistance by *Propionibacteria* in response to commonly prescribed antibiotics. A case-control study in 2,266 women older than 19 years of age with primary, invasive breast cancer enrolled in a health plan for at least one year and 7,593 randomly selected female health plan members also suggests a possible link between women taking oral antibiotics and subsequent develop-
ment of breast cancer. However, among women with the highest levels of tetracycline or macrolide use, risk of breast cancer was not elevated in those using these antibiotics exclusively for acne or rosacea, compared with those using them exclusively for respiratory tract infections.13

Topical agents such as retinoids (tretinoin, adapalene and tazarotene) are often used as treatments for acne.14-17 Fixed combination treatments with regimens including clindamycin 1% benzoyl peroxide (BP) 5% and tretinoin 0.025%-clindamycin 1%, have demonstrated greater efficacy compared with each agent alone and combination regimens are now widely accepted for the topical treatment of acne.19-23 Clindamycin phosphate and BP are topical agents commonly prescribed for the treatment of acne with favorable efficacy and safety profiles. Clindamycin phosphate reduces levels of P. acnes and decreases inflammation while BP has anti-comedogenic and antibacterial effects in addition to inhibiting the emergence of resistant bacteria.19,20,24,25 In addition, this combination is effective as a once-daily application, which is associated with treatment compliance that is considered superior to other regimens that require more frequent applications.26

A significant drawback to treatment with BP is cutaneous dryness and irritation. BP in concentrations of 5% and 10% often results in greater frequency and severity of burning, erythema and peeling than 2.5%.26 Previous studies suggest that BP concentrations of 2.5% may be equally effective as 5% and 10% concentrations for the treatment of inflammatory acne.19 This lower concentration of BP as monotherapy also significantly reduces P. acnes counts after one week of topical application to the face.17 Initiation of treatment with BP at lower concentrations is recommended to reduce risk of local side effects.26,27 A unique, fixed-dose, once-daily formulation of clindamycin phosphate 1.2% and BP 2.5% (clindamycin-BP 2.5%) has been developed for treatment of inflammatory and non-inflammatory lesions in moderate or severe acne, while minimizing the risk of skin irritation. Clindamycin-BP 2.5% is an alcohol-free aqueous gel with a humectant and solubilizing properties intended to enhance both delivery and bioavailability of micronized BP into the pilosebaceous unit.

Two 12-week, phase 3, randomized, double-blind, controlled studies were conducted to evaluate the efficacy and safety of clindamycin-BP 2.5% aqueous gel in 2,813 subjects with moderate or severe acne vulgaris. Comparator agents included each active ingredient or vehicle. All four topical treatments were applied once daily to the face. Efficacy evaluations at baseline and weeks 4, 8, and 12 included inflammatory and non-inflammatory lesion counts and evaluator’s global severity score (EGSS) ranging from clear (0) to very severe (5). Cutaneous safety evaluations were recorded by clinicians at each visit on a static scale ranging from 0 (none) to 3 (severe) for erythema and scaling. Subjects’ ratings of the tolerability of the treatment with respect to itching, burning and stinging were recorded using a similar scale at each study visit. Safety was also monitored by reports of adverse events (AEs). Separate efficacy and safety analyses were conducted in the subpopulation of subjects with moderate acne at baseline and the subpopulation of subjects with severe acne, and are reported herein.

METHODS

Study Design
A total of 2,813 subjects with moderate (n=2,282) or severe (n=531) acne were enrolled in two phase 3, multicenter, double-blind, active- and vehicle-controlled studies. Prior to randomization, subjects were stratified by Fitzpatrick skin phototype and severity of acne vulgaris based on a static EGSS ranging from 0 (clear) to 5 (severe). Moderate acne vulgaris was defined by an EGSS of 3, which was described as: predominantly non-inflammatory lesions with evidence of multiple inflammatory lesions; several to many comedones, papules and pustules; and no more than one small nodulocystic lesion. Severe acne was defined by an EGSS of 4, characterized by: inflammatory lesions; numerous comedones, papules, pustules; and possibly a few nodulocystic lesions. Subjects were stratified into four groups based on EGSS (moderate or severe) and Fitzpatrick skin phototype (phototypes 1, 2 and 3 or phototypes 4, 5 and 6).

Following stratification into one of four groups based on baseline acne severity and skin phototype, subjects were randomized using permuted blocks within strata to ensure an appropriate distribution of subjects into treatment groups and a relatively equal balance of subjects based on acne severity and skin phototype within treatment groups. Subjects who met study eligibility criteria were randomized in a 2:2:2:1 ratio into one of the four treatment groups including clindamycin-BP 2.5% gel, clindamycin phosphate 1.2% gel, BP 2.5% gel, or vehicle. Subjects applied study medication to their faces once daily for 12 weeks.

Subpopulation efficacy by baseline acne severity was performed for the combined data from the two phase 3 studies and is reported here together with summaries of the safety data.

Subjects
Eligibility criteria included males and females of any race or ethnicity aged 12–70 considered to have moderate or severe acne vulgaris: 17–40 inflammatory lesions (papules, pustules, and nodules); 20 to 100 non-inflammatory lesions (open and closed comedones); no more than two nodules; and an EGSS of 3 (moderate) or 4 (severe). Women of childbearing potential were required to have a negative pregnancy test at baseline and to comply with effective contraception throughout the study period.
All subjects who had previously used prescription or over-the-counter (OTC) acne treatments were required to complete washout periods of one week for topical astringents and abrasives, two weeks for topical non-retinoid anti-acne products including antimicrobial soaps, four weeks for topical retinoids, retinol, and systemic non-retinoid acne treatments, and six months for systemic retinoids.

Efficacy Evaluations

Efficacy evaluations of the face included inflammatory and non-inflammatory lesion counts and EGSS scores at baseline and weeks 4, 8 and 12. To ensure consistency, the EGSS and lesion counts were performed by the same investigator for the same subject at each follow-up visit. All lesion counts were taken from the forehead, left and right cheeks, nose and chin. Total lesion counts were computed as the sum of inflammatory and non-inflammatory lesion counts. Subjects also completed a self-assessment of their acne severity at weeks 2, 4, 8 and 12. The Subject Self-Assessment (SSA) scores post-baseline were based on a scale that ranged from 1 (clear) to 7 (worse).

Safety and Tolerability Evaluations

Cutaneous safety and tolerability evaluations were assessed at each study visit. Cutaneous safety evaluations were recorded on a static scale ranging from 0 (none) to 3 (severe) for erythema and scaling. Subject reports of tolerability of the treatment (itching, burning, and stinging) were recorded using a similar scale at each study visit. Safety was also monitored by adverse events (AEs) and summarized by frequency, severity, and relationship to study medication for each treatment group and baseline acne severity.

Statistical Analyses

Efficacy analyses were conducted in the intent-to-treat (ITT) population. The ITT population included all subjects who were randomized to one of the four treatment groups. Safety analyses were conducted in the safety population, defined as all subjects randomized to one of the four treatment groups who were presumed to have used the study medication at least once and who provided at least one post-baseline evaluation. The last observation carried forward (LOCF) was used to impute missing data.

<p>| TABLE 1. | Subject baseline demographics and clinical characteristics by acne severity and treatment group, ITT |</p>
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Clindamycin-BP (n=797)</th>
<th>Clindamycin Phosphate (n=832)</th>
<th>Benzoyl Peroxide (n=809)</th>
<th>Vehicle (n=395)</th>
<th>Total (n=2813)</th>
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<tbody>
<tr>
<td></td>
<td>Moderate (n=643)</td>
<td>Severe (n=154)</td>
<td>Moderate (n=863)</td>
<td>Severe (n=169)</td>
<td>Moderate (n=667)</td>
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<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Mean</td>
<td>19.5 (18.0)</td>
<td>19.9 (18.6)</td>
<td>19.2 (18.9)</td>
<td>19.6 (18.3)</td>
<td>19.5 (18.5)</td>
</tr>
<tr>
<td>• Median</td>
<td>16.8 (17.0)</td>
<td>17.1 (17.2)</td>
<td>16.6 (16.6)</td>
<td>16.7 (16.9)</td>
<td>16.8 (16.9)</td>
</tr>
<tr>
<td>• Range</td>
<td>12.1-64.7</td>
<td>12.7-43.3</td>
<td>12.1-70.2</td>
<td>12.3-48.5</td>
<td></td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Female</td>
<td>347 (64.0)</td>
<td>61 (39.6)</td>
<td>363 (55.6)</td>
<td>57 (35.8)</td>
<td>380 (57.0)</td>
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<tr>
<td>• Male</td>
<td>296 (46.0)</td>
<td>93 (60.4)</td>
<td>290 (44.4)</td>
<td>102 (64.2)</td>
<td>287 (43.0)</td>
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<td>Ethnicity, n (%)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hispanic/Latino</td>
<td>100 (15.6)</td>
<td>24 (15.6)</td>
<td>103 (15.8)</td>
<td>32 (20.1)</td>
<td>120 (18.0)</td>
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<tr>
<td>• Non-Hispanic/Latino</td>
<td>543 (84.4)</td>
<td>130 (84.4)</td>
<td>550 (84.2)</td>
<td>127 (84.2)</td>
<td>547 (82.0)</td>
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<td>Race, n (%)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>• White</td>
<td>488 (75.9)</td>
<td>130 (84.4)</td>
<td>500 (76.6)</td>
<td>128 (84.4)</td>
<td>489 (73.3)</td>
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<td>• Black/African</td>
<td>113 (17.6)</td>
<td>112 (72.2)</td>
<td>80.5 (60.5)</td>
<td>142 (21.3)</td>
<td>76.8 (50.8)</td>
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<td>• American</td>
<td>15 (9.7)</td>
<td>21 (13.2)</td>
<td>23 (16.2)</td>
<td>427 (18.7)</td>
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<td>• Native Hawaiian/Pac Islander</td>
<td>2 (0.3)</td>
<td>2 (0.3)</td>
<td>2 (0.3)</td>
<td>4 (0.6)</td>
<td>2 (0.3)</td>
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<td>• Asian</td>
<td>13 (2.0)</td>
<td>22 (3.4)</td>
<td>0 (0.0)</td>
<td>13 (1.9)</td>
<td>2 (1.4)</td>
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<td>• Amer. Indian/Alaskan</td>
<td>3 (0.5)</td>
<td>10 (1.5)</td>
<td>5 (3.1)</td>
<td>3 (0.4)</td>
<td>3 (0.4)</td>
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<tr>
<td>• Native</td>
<td>31 (4.8)</td>
<td>17 (2.6)</td>
<td>1 (0.6)</td>
<td>23 (3.4)</td>
<td>21 (3.4)</td>
</tr>
<tr>
<td>• Other</td>
<td>4 (2.6)</td>
<td>5 (2.6)</td>
<td>5 (3.1)</td>
<td>83 (3.8)</td>
<td>5 (3.5)</td>
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<td>Lesion Counts (median)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Inflammatory</td>
<td>24.0</td>
<td>34.0</td>
<td>23.0</td>
<td>33.0</td>
<td>23.0</td>
</tr>
<tr>
<td>• Non-inflammatory</td>
<td>40.0</td>
<td>49.0</td>
<td>39.0</td>
<td>46.0</td>
<td>40.0</td>
</tr>
<tr>
<td>• Total</td>
<td>66.0</td>
<td>80.5</td>
<td>63.0</td>
<td>81.0</td>
<td>65.0</td>
</tr>
</tbody>
</table>
efficacy endpoints assessed by the investigator for subjects who discontinued treatment prior to week 12 or missed follow-up visits between the baseline and final evaluations.

Statistical analyses examined changes in inflammatory, non-inflammatory, and total lesion counts, and dichotomized EGSs from baseline to week 12. Analysis of the dichotomized EGSs was undertaken using a logistic regression model controlling for treatment, analysis center, dichotomized Fitzpatrick skin phototype.

Analysis of covariance (ANCOVA) was performed to evaluate superiority for the absolute and percent changes in lesion count analyses between the clindamycin-BP 2.5% and vehicle treatment groups. The ANCOVA comparison of clindamycin-BP 2.5% with the vehicle group was restricted to just these two groups. When assumptions of normality were not met for these variables, ranked data for these variables were entered into each ANCOVA analysis.

The primary efficacy endpoints for comparison of the clindamycin-BP 2.5% and vehicle groups included absolute change from baseline to week 12 in number of inflammatory and non-inflammatory lesions and the percent of subjects who achieved treatment success defined by at least a two-grade improvement in EGSs. Supportive efficacy endpoints included absolute change in total lesion counts and percent changes in inflammatory, non-inflammatory, and total lesion counts from baseline to week 12.

AEs were recorded and classified according to the MedDRA terminology. Descriptive statistics were used to summarize the cutaneous safety and tolerability assessments at baseline and weeks 4, 8, and 12.

RESULTS

Subject Demographic and Baseline Characteristics
A total of 2,813 subjects were enrolled at 68 clinical sites; 2,282 subjects (81.1%) had moderate disease at baseline and 531

![FIGURE 1A. Schematic profile of subject disposition: ITT population with moderate acne.](image1)

![FIGURE 1B. Schematic profile of subject disposition: ITT population with severe acne.](image2)
subjects (18.9%) had severe acne. The baseline demographic characteristics and disease characteristics of the moderate acne subpopulation and the severe acne subpopulation are presented in Table 1. Mean age of subjects with moderate acne was 19.5, and 18.5 years for subjects with severe acne. Slightly more than half (54.8%) of subjects with moderate acne were female while 45.2% were male. Among subjects with severe acne, 42.4% were female and 57.6% were male. The majority of subjects with moderate and severe acne were white (75.2% and 81.5%, respectively) while 18.7% of those with moderate acne and 12.6% of those with severe acne were black, respectively. In addition, 7.4% of subjects with moderate acne were Native American/Pacific Islander, Asian, American Indian/Alaskan Native or other race while 7.2% of those with severe acne were representative of these additional race groups. A similar number of subjects were of Hispanic/Latino ethnicity in both moderate (16.3%) and severe (16.2%) acne subgroups.

The median number of inflammatory lesions at baseline for all subjects with moderate acne was 23 (range, 17–41) while the median number of inflammatory lesions for subjects with severe acne was 33 (range, 16–48). Among subjects with moderate acne, the median number of non-inflammatory lesions was 40 (range, 20–100) compared with 48 (range, 20–100) for subjects with severe acne. The median number of total lesions at baseline was 65 for subjects with moderate acne (range, 37–137) while the median number of total lesions for subjects with severe acne was 80 (range, 40–141).

**Subject Disposition**

Study completion rates for subjects with moderate or severe acne who were treated with clindamycin-BP 2.5% aqueous gel were 91% and 89%, respectively compared to 88% and 91%, respectively for clindamycin phosphate 1.2%, 87% and 90%, respectively for BP 2.5%, and 86% and 78%, respectively, for vehicle. The main reasons for study discontinuation in the ITT population of both disease subgroups were lost to follow up (5.4% in subjects with moderate acne and 6.4% in subjects with severe acne) and subject request (3.8% in the moderate acne subgroup and 3.4% in the severe acne subgroup). There was a low incidence of AEs resulting in study discontinuation. Study discontinuation rates attributable to AEs among subjects with moderate acne were 0.9%, 0.5%, 1.0% and 0.3% for the clindamycin-BP 2.5%, clindamycin gel, BP gel, and vehicle groups, respectively. Among subjects with severe acne in the clindamycin-BP 2.5% group, 0.6% discontinued their study participation due to an AE compared with 0.6%, 0.7% and 1.3% of those in the clindamycin gel, BP gel, and vehicle arms, respectively. A schematic of the profile of subject disposition by baseline acne severity is presented in Figures 1A and 1B.

**Efficacy Evaluations**

**Median Percent Reductions in Lesion Counts**

The median percent changes in inflammatory, non-inflammatoty, and total lesion counts at week 12 were significantly greater in the clindamycin-BP 2.5% group compared with the individ-

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**FIGURE 2.** Median percent reduction in lesion counts from baseline to week 12: Moderate and severe acne.

**FIGURE 3.** Treatment success* by Evaluator Global Severity Score (EGSS) at weeks 4, 8 and 12.

**FIGURE 4.** Subject Self-Assessment (SSA) of clear or almost clear at weeks 2, 4, 8 and 12.

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* Treatment success was defined as at least a 2-grade improvement in EGSS from Baseline.
ual active ingredients and vehicle for subjects with moderate acne. Among subjects with moderate acne in the clindamycin-BP 2.5% arm, there was a 68.0% decrease in median number of inflammatory lesions at week 12 among subjects with moderate acne treated with clindamycin-BP 2.5% compared with 36.4% of those in the vehicle group (P<0.001, Figure 2), 55.6% in the clindamycin phosphate 1.2% group, and 57.7% in the BP 2.5% group (P<0.001) (not shown). Similarly, there were 50.0% and 54.1% median reductions in non-inflammatory and total lesions for subjects with moderate acne in the clindamycin-BP 2.5% group, 41.3% and 45.2% median reductions, respectively in the clindamycin phosphate 1.2% group (P<0.001, P<0.001), and 43.6% and 47.1% median reductions, respectively in the BP 2.5% group (P<0.001, P<0.001) while non-inflammatory lesions and total lesion counts decreased by 25.0% and 29.7%, respectively, among subjects with moderate acne treated with vehicle (P<0.001, Figure 2). At week 12, among subjects with severe acne, median reductions of 48.7%, 45.1% and 44.4% were observed for inflammatory, non-inflammatory, and total lesions, respectively, for subjects in the clindamycin-BP 2.5% group compared with 23.9%, 26.6% and 19.4%, respectively for subjects in the vehicle arm (P<0.001, Figure 2).

**Evaluator Global Severity Score (EGSS)**

Treatment success was defined as at least a two-grade improvement in EGSS from baseline. At the week 12 assessment, 32.3% of subjects with moderate acne and 45.5% of those with severe acne treated with clindamycin-BP 2.5% met the criterion for treatment success. These improvements in moderate acne subjects were statistically significant compared with the clindamycin phosphate 1.2% gel (24.3%, P = 0.001), BP 2.5% (23.5%, P = 0.001), and vehicle groups (14.7% P = 0.001) and statistically significant in severe acne subjects treated with clindamycin-BP 2.5% compared with the clindamycin phosphate 1.2% group (34.6%, P = 0.040) and vehicle group (23.7%, P = 0.001). The percent of subjects with treatment success was significantly different for both acne severity groups as early as week 4 (P = 0.001 vs vehicle and P = 0.011 versus vehicle for moderate and severe acne, respectively) and continued to increase through the end of treatment (Figure 3). In addition, 13.0% of subjects with severe acne at baseline treated with clindamycin-BP 2.5% were judged by the investigator to have a three- or four-grade improvement in EGSS (“clear” or “almost clear”) at week 12 compared with only 3.9% of those in the vehicle group (P = 0.005).

**Subject Self-Assessment (SSA)**

Beginning as early as week 2, 71.1% of subjects with moderate acne in the clindamycin-BP 2.5% group evaluated their skin as “clear” or “almost clear” by SSA compared with only 2.2% of subjects in the vehicle arm (P = 0.005). These differences were sustained through completion of treatment when 43.1% of those with moderate acne in the clindamycin-BP 2.5% group indicated their acne was “clear” or “almost clear” compared with 17.3% of those in the vehicle group (P < 0.001, Figure 4). An improvement in SSA was evident for subjects with severe acne at week 12 with 22.9% in the clindamycin-BP 2.5% group reporting their skin as “clear” or “almost clear” compared with 13.6% of those treated with the vehicle, although this did not achieve statistical significance (P = 0.082, Figure 4).

**Safety Evaluations**

**Adverse Events**

The incidence of AEs in the safety population considered “possibly,” “probably” or “related” to treatment as determined by the investigator was low and similar between the clindamycin-BP 2.5% and vehicle arms for subjects with moderate or severe acne. Only 1.4% of subjects with moderate acne experienced treatment-related AEs compared with 1.6% of those with moderate acne treated with vehicle. Among subjects with severe acne, 0.7% of the clindamycin-BP 2.5% group and 2.9% of the vehicle group reported a treatment-related AE. Study discontinuation rates attributable to AEs in the ITT population of subjects with moderate acne were 0.9% and 0.3% for the clindamycin-BP 2.5% and vehicle groups, respectively. Among subjects with severe acne in the clindamycin-BP 2.5% group, 0.6% discontinued their study participation due to an AE compared with 1.3% of those in the vehicle arm.

**Cutaneous Safety and Tolerability Evaluations**

Mean cutaneous tolerability scores at weeks 4, 8 and 12 were less than 1 (1 = mild) for each of burning, stinging, scaling, erythema, and itching (possible range was 0 = none to 3 = severe), regardless of baseline acne severity. No subjects in either the clindamycin-BP or vehicle groups discontinued study participation due to burning, stinging, scaling, erythema or itching.

**DISCUSSION**

These two large, randomized, double-blind, controlled 12-week trials demonstrated the superior efficacy, and the safety and tolerability of once-daily treatment with clindamycin-BP 2.5% aqueous gel versus each active ingredient versus vehicle in subjects with moderate and severe acne and has been reported previously. Additional subpopulation analyses of efficacy and safety according to baseline disease severity further confirms that the once-daily treatment with clindamycin-BP 2.5% aqueous gel is effective and has a favorable safety profile in patients with severe acne, in addition to moderate acne. Statistically significant improvements were noted for median percent reductions in inflammatory, non-inflammatory, and total lesion counts at week 12 in subjects with moderate acne treated with clindamycin-BP 2.5% aqueous gel compared to the individual active ingredients and vehicle, and in severe acne subjects who were treated with clindamycin-BP 2.5% aqueous gel compared to vehicle. The percent of subjects receiving clindamycin-BP 2.5% gel who had treatment success was statistically significant versus vehicle for both acne severity groups at week 4 and
continued to increase through week 12: 45.5% of subjects with severe acne and 32.3% of those with moderate acne demonstrated at least a two-grade improvement in their acne at week 12 versus 23.7% and 14.7% in the vehicle arms, respectively. Treatment success was higher (45.5%) for subjects with severe acne as compared to those with moderate acne; however, it should be noted that the numbers of severe subjects was considerably less than the number of moderate subjects enrolled in the study and the study was not powered to demonstrate a difference in efficacy based on acne severity. In addition, three times as many subjects with severe acne treated with clindamycin-BP 2.5% gel achieved a 3 or 4 grade improvement in EGSS (“clear” or “almost clear”) compared with subjects in the vehicle group, suggesting that the clindamycin-BP 2.5% aqueous gel combination product may be effective in appropriate patients with severe acne as defined in these studies.

There was a very low rate of treatment-related AEs in both the clindamycin-BP 2.5% aqueous gel and vehicle groups for both acne severity subgroups. Most AEs were mild to moderate in severity and in the clindamycin-BP 2.5% aqueous gel arm less than 1% of AEs resulted in study discontinuation in both acne severity groups compared to less than 1% in the respective vehicle arms. Furthermore, study completion rates for subjects with moderate or severe acne who were treated with clindamycin-BP 2.5% aqueous gel were high, suggesting that the product may be well-accepted and used by subjects, perhaps due to favorable efficacy results and tolerability.

It is perhaps counter-intuitive that patients with more severe disease would show clinically significant improvement to topical monotherapy, but this is not the first such report. In a comparison study of the various topical retinoids it was found that more severely inflamed patients had a greater percentage improvement than patients with more mild disease. This report taken together with the findings presented in this paper suggest that topical therapy may be more valuable than often assumed in patients with severe acne.

**CONCLUSION**

These results confirm the efficacy and tolerability of clindamycin-BP 2.5% gel for the treatment of both moderate and severe acne when applied once daily. The convenience of once daily application may increase patient adherence to treatment. Furthermore, these results suggest that clindamycin-BP 2.5% aqueous gel may offer a treatment option for individuals with severe acne with a favorable safety profile.

**DISCLOSURES**

Dr. Webster has served as an investigator and consultant for Arcutis, a consultant for Allergan Inc., Stiebel Inc, Galderma Inc., Coris Inc., Cutanea Inc. and has received honoraria or grant support.


Dr. Gold has served as a consultant and investigator for Arcutis, Aesthera Inc., Alima Lasers Inc., Dusa Inc., Hoya ConBio Inc., Lumenis Inc., Neocutis Inc, Sciton Inc, Stiefel Inc., a consultant for Aerolase Inc., and an investigator for Cynosure Inc. and has received honoraria or grant support.

Dr. Mraz has served as an investigator and/or consultant for Abbott, Allergan, Amgen, Arcutis, Basilea, Bavarian Nordic, Centocor, Collagenex, Galderma, Graceway Pharmaceuticals, Hana BioSciences, Incyte, Inhibitex, Intercell, LEO Pharmaceuticals, Merck & Co, Neurocrine, Biosciences, Peplin, Perrigo, Pfizer, Photocure, Sanofi Pasteur, Tarol Pharmaceuticals, and is an employee of Dow Pharmaceutical Sciences Inc.

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