

Impact of a Fixed Combination of Clindamycin Phosphate 1.2%–Benzoyl Peroxide 2.5% Aqueous Gel on Health-Related Quality of Life in Moderate to Severe Acne Vulgaris

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The acne-specific quality of life (Acne-QoL) questionnaire was developed to measure the impact of facial acne across 4 domains (acne symptoms, role-emotional, self-perception, role-social) of health-related quality of life (HRQL). This analysis assessed the impact of clindamycin phosphate 1.2%–benzoyl peroxide 2.5% (clindamycin–BPO 2.5%) gel on HRQL in a combined study population (N=2813) of participants with moderate to severe acne vulgaris. Although the results presented within do not include factors of study and study-by-treatment interaction, analyses were performed to confirm that the results were consistent across the 2 identical, double-blind, randomized studies and within each treatment group across studies to justify pooling the data from both studies.

The Acne-QoL questionnaire was administered at baseline and at the end of treatment (week 12). Treatment with clindamycin–BPO 2.5% gel significantly improved participant-reported HRQL across all 4 domains compared with individual active ingredients and vehicle (P<.001). The percentage improvement in mean Acne-QoL domain scores with clindamycin–BPO 2.5% gel ranged from 37% to 59%.

Because the negative impact of facial acne on HRQL is one of the primary motivators for patients to seek treatment, this analysis underscores the importance of physicians incorporating assessments of HRQL into their clinical decision making.

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Acne vulgaris is a common condition that affects 40 to 50 million individuals in the United States.¹ Acne is frequently localized to the face and trunk, affecting appearance² and resulting in a range of psychosocial impacts such as anxiety and depression, social withdrawal, and lack of self-confidence.³⁻⁶ These negative impacts often motivate patients to seek treatment.⁶ The effect of facial acne on health-related quality of life (HRQL) can be profound and has been found to be similar to patients with other chronic diseases such as asthma, arthritis, or diabetes mellitus.⁷ Clinical objective assessments such as lesion counts and physician grading classifications alone do not adequately capture the impact of acne severity from a patient's perspective.⁸ Assessing the impact of facial acne on HRQL is important to fully

characterize the overall burden of the disease and effectiveness of treatment.

Acne treatments can differentially impact HRQL. Consequently, HRQL is an important end point in comparative clinical trials, complementing the clinical objective assessments of efficacy and tolerability. However, prior studies of the impact of acne treatments on HRQL have had the following limitations: small number of patients,^{7,9-13} no full examination of changes in HRQL,^{3,7,13,14} patients with only mild to moderate facial acne,^{14,15} or unblinded observational studies.^{15,16}

A unique fixed combination of clindamycin phosphate 1.2%–benzoyl peroxide 2.5% (clindamycin–BPO 2.5%) in an aqueous gel formulation is approved by the US Food and Drug Administration for the treatment of acne vulgaris in patients 12 years and older. Results from 2 identical, double-blind, 12-week, pivotal studies (N=2813) indicated that clindamycin–BPO 2.5% gel was significantly superior to the individual active ingredients and vehicle in reducing the number of acne lesions (both inflammatory and noninflammatory) ($P<.001$) based on investigator assessments of overall acne severity.¹⁷ Visibly greater improvement in acne severity was observed by investigators in participants treated with clindamycin–BPO 2.5% gel at week 4 and by participants as early as week 2. The safety and tolerability of clindamycin–BPO 2.5% gel were comparable to the individual active ingredients and vehicle.¹⁷

We assessed HRQL in these pivotal studies of clindamycin–BPO 2.5% gel using the validated acne-specific quality of life (Acne-QoL) questionnaire. Because a large number of patients with facial acne were enrolled in these studies and assessed for HRQL, these data can extend the results reported from prior limited studies of the impact of acne and its treatment on HRQL.

Methods

Data Source—The data for the present analyses were collected from 2 identical, double-blind, randomized, placebo-controlled, pivotal studies assessing the efficacy and safety of clindamycin–BPO 2.5% gel in the treatment of moderate to severe facial acne in 2813 participants aged 12 years and older.¹⁷ Participants were stratified by skin phototype and were randomized to 1 of 4 treatment groups: clindamycin–BPO 2.5%, clindamycin phosphate 1.2%, benzoyl peroxide 2.5%, or vehicle. All participants applied the study medication once daily for 12 weeks. Full details of the trial's methods and results are described elsewhere.¹⁷

The data from the 2 trials were pooled for the present analyses because the studies were conducted under identical protocols and ran concurrently, all study sites underwent the same training, the sample sizes of each treatment group were similar between studies, and the demographics and baseline characteristics of the study populations were similar in both trials.

Measures—Participants completed the 19-item Acne-QoL questionnaire prior to evaluation by the investigator, thus potentially minimizing bias in participant response by the investigator. The Acne-QoL questionnaire was developed to assess the impact of acne treatment on patients' HRQL in clinical trials. Questions were based on input from patients regarding the important determinants of HRQL as they relate to acne.¹⁰ The psychometric properties and responsiveness of the questionnaire have been established.^{16,17}

The Acne-QoL questionnaire assessed 4 HRQL domains: acne symptoms, role-emotional, self-perception, and role-social. It has a 1-week recall period and participants rated each item on a 7-point scale for all items (0=extremely; 1=very much; 2=quite a bit; 3=a good bit; 4=somewhat; 5=a little bit; 6=not at all), except for 3 questions that were rated on a 7-point scale (0=extensive; 1=a whole lot; 2=a lot; 3=a moderate amount; 4=some; 5=very few; 6=none). Four overall domain scores were calculated by summing the responses within each subscale, with higher scores indicating better HRQL. Missing item-level data were handled according to developer recommendations.¹⁹ Domain scores were computed only for participants who answered 3 or more questions within each subscale. If a participant failed to answer 1 or 2 questions within a subscale, responses for these items were imputed through mean substitution prior to computation of the domain score. Participants completed the Acne-QoL at baseline and week 12.

Statistical Analyses—All statistical analyses were completed in the intention-to-treat population, which comprised all participants randomized to treatment. For participants who discontinued treatment before week 12, the last observation was carried forward. The primary end points for the HRQL analyses were the absolute change in scores from baseline to week 12 on the 4 Acne-QoL domains. Between-group differences were evaluated using a series of analyses of covariance (ANCOVAs) with the following covariates: baseline Acne-QoL domain score, gender, and age. When comparisons involved the 3 active treatment groups, all active treatment

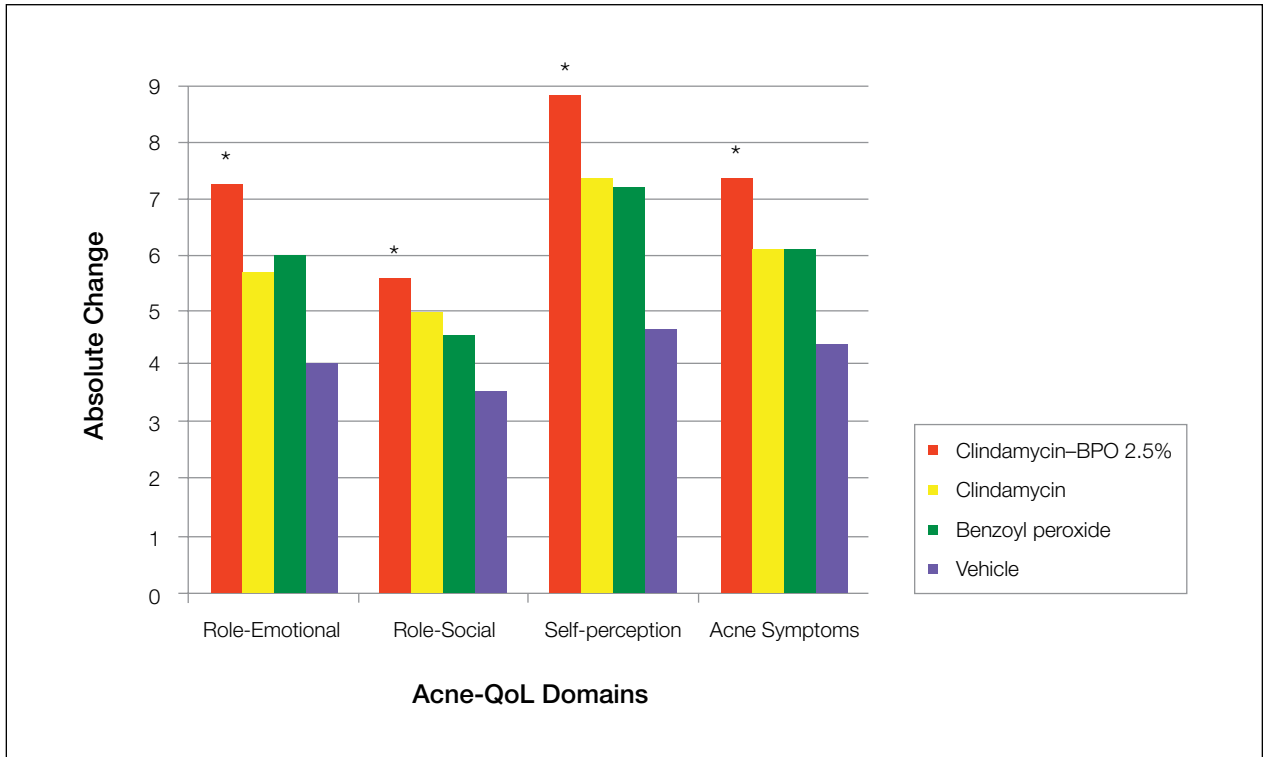


Figure 1. Absolute change of mean scores from the acne-specific quality of life (Acne-QoL) questionnaire from baseline to week 12. Improvement with clindamycin phosphate 1.2%–benzoyl peroxide 2.5% (clindamycin–BPO 2.5%) gel was significantly greater compared with active ingredients or vehicle. Asterisk indicates $P < .001$ versus active ingredients and vehicle.

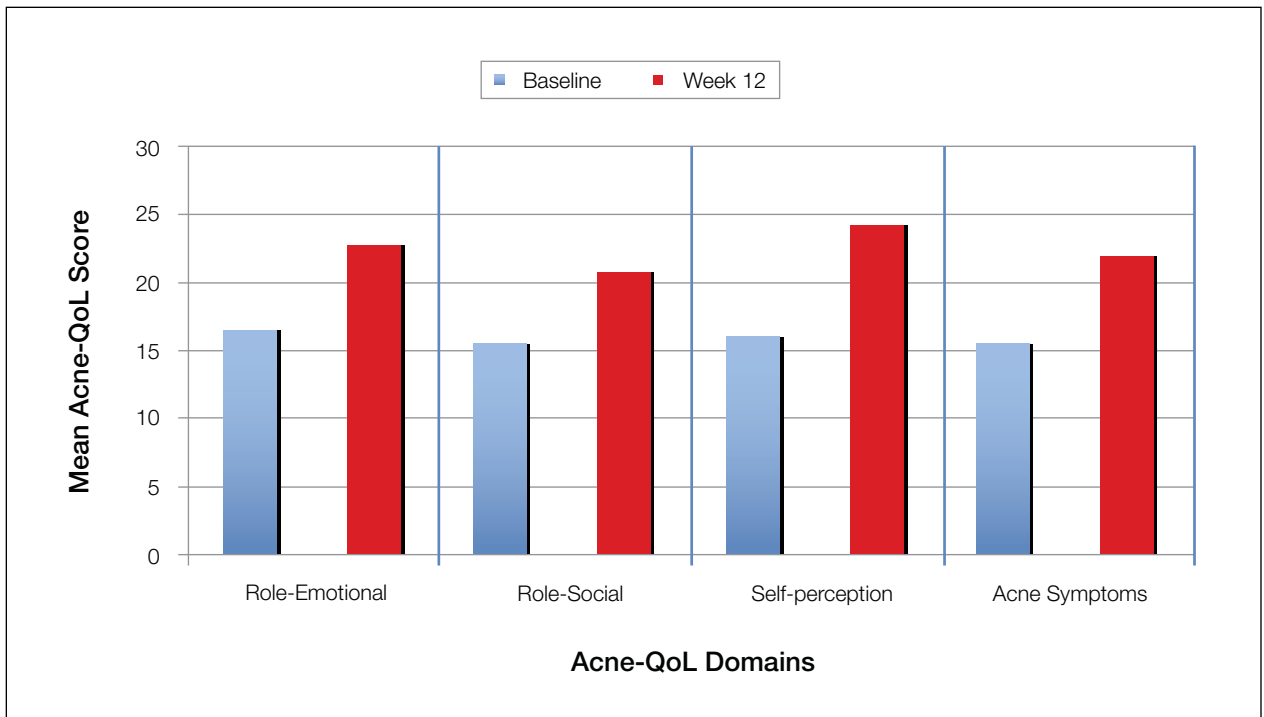


Figure 2. Treatment with clindamycin phosphate 1.2%–benzoyl peroxide 2.5% gel for 12 weeks improves health-related quality of life based on the acne-specific quality of life (Acne-QoL) questionnaire. The maximum score for each domain is 30, except role-social, which has a maximum score of 24. Higher scores indicate better health-related quality of life.

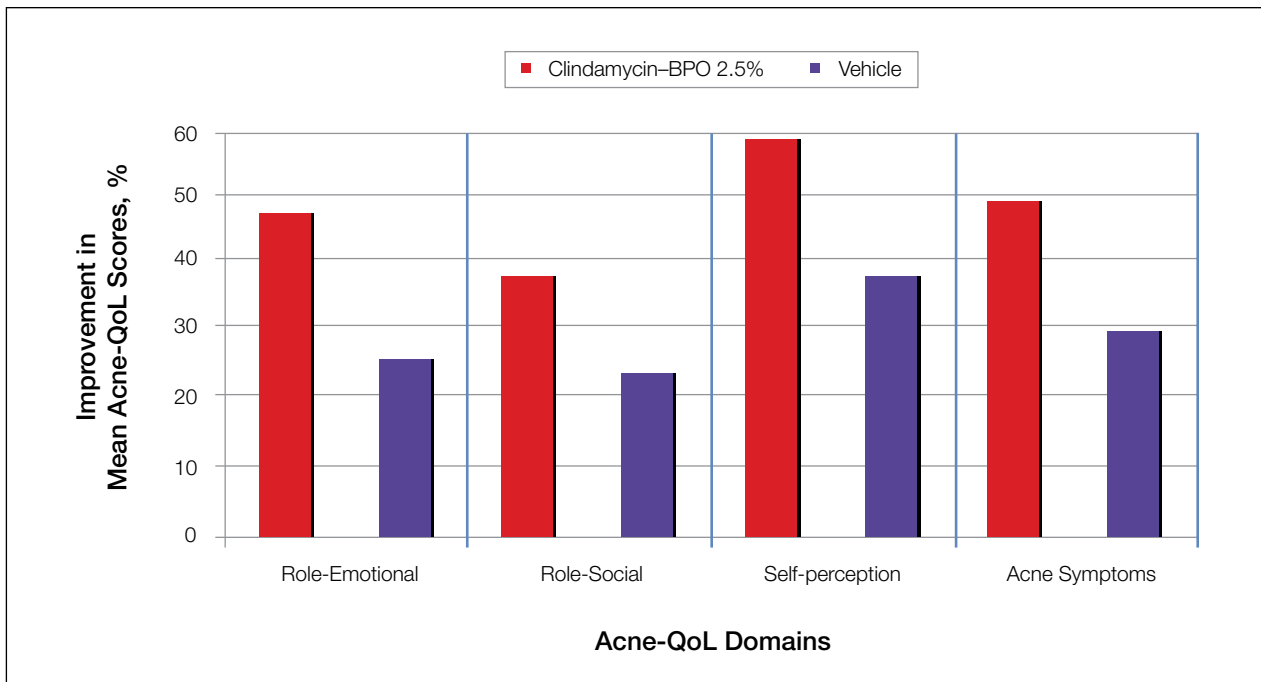


Figure 3. Treatment with clindamycin phosphate 1.2%–benzoyl peroxide 2.5% (clindamycin–BPO 2.5%) gel for 12 weeks improves health-related quality of life compared with vehicle based on the acne-specific quality of life (Acne-QoL) questionnaire.

groups were included in one ANCOVA and pairwise comparisons were conducted when the overall treatment effect was significant. The vehicle treatment was not included in the between-group analysis of the active treatments because of the possibility that the variance of the vehicle group was different than the active treatment groups, which would interfere with the sensitivity of the ANCOVA to discriminate among the active treatment groups. A separate series of ANCOVAs with the same covariates were used to compare clindamycin–BPO 2.5% gel to vehicle.¹⁷ A hierarchical, closed-test procedure was used to handle the multiplicity of the Acne-QoL end points. The Acne-QoL domains were prioritized as follows: acne symptoms, role-emotional, self-perception, and role-social. All statistical tests were 2-sided at $\alpha=.05$. All analyses were carried out using SAS (version 9.1.3).

Results

Baseline Demographics and Clinical Characteristics—The baseline demographics and clinical characteristics were similar across the 4 treatment groups (N=2813). The mean age was 19.3 years and the majority of participants were not of Hispanic or Latino ethnicity (83.7%).¹⁷ The mean lesion counts and Acne-QoL domain scores were similar across the treatment groups. The internal consistency

reliability of the Acne-QoL domain scores was acceptable (>0.70) and ranged from 0.82 for acne symptoms to 0.95 for self-perception.

Impact on HRQL—The absolute change of mean Acne-QoL scores from baseline to week 12 for participants treated with clindamycin–BPO 2.5% was 7.4 for acne symptoms, 7.3 for role-emotional, 8.9 for self-perception, and 5.6 for role-social. Participants treated with clindamycin–BPO 2.5% had significantly greater improvements in all 4 Acne-QoL domains compared with participants treated with each individual active ingredient and vehicle ($P<.001$), which is consistent with lesion count reduction results¹⁷ (Figure 1).

At baseline the mean Acne-QoL scores in the clindamycin–BPO 2.5% group ranged from 15.1 to 15.6. After 12 weeks of treatment with clindamycin–BPO 2.5%, mean scores increased to 22.9, 24.1, and 22.5 for role-emotional, self-perception, and acne symptoms, respectively (out of a total score of 30), and increased to 20.7 for role-social (out of a total score of 24)(Figure 2).

At week 12 the percentage improvement in mean Acne-QoL scores with clindamycin–BPO 2.5% was 47%, 37%, 59%, and 49% for role-emotional, role-social, self-perception, and acne symptoms, respectively, compared with 25%, 23%, 37%, and 29%, respectively, with vehicle (Figure 3).

Comment

These Acne-QoL findings demonstrate that treatment with clindamycin-BPO 2.5% gel significantly improved participant perceptions of moderate to severe acne across all 4 domains of the Acne-QoL questionnaire (acne symptoms, role-emotional, self-perception, role-social) ($P < .001$) compared with participants who received the individual active ingredients and vehicle. When used to assess mild to moderate facial acne, the Acne-QoL questionnaire revealed changes in all 4 domains of the Acne-QoL in studies involving standard therapy¹⁶ and placebo-controlled clinical trials.^{18,19} The results from the present study confirm the utility of the Acne-QoL questionnaire in assessing changes in patients' HRQL in a clinical trial setting and extend the data to include patients with moderate to severe facial acne. Similar to prior studies,^{18,19} the present study found significant changes in all 4 domains of the Acne-QoL questionnaire over the treatment period with greater improvements in those treated with clindamycin-BPO 2.5% gel compared with individual active ingredients or vehicle ($P < .001$).

Conclusion

The 2 pivotal studies of clindamycin-BPO 2.5% gel represent a large number of patients with acne in whom the impact on HRQL was evaluated. The Acne-QoL analyses demonstrate that treatment with clindamycin-BPO 2.5% significantly improved participants' perceptions of moderate to severe facial acne compared with individual active ingredients and vehicle ($P < .001$). The efficacy of clindamycin-BPO 2.5% gel reported by others¹⁷ has been extended to include benefits in participant-reported HRQL.

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