doi:10.36849/JDD.9018

 ORIGINAL ARTICLE Journal of Drugs in Dermatology

Clindamycin Phosphate 1.2%/Adapalene 0.15%/ Benzoyl Peroxide 3.1% for Acne: Results From a Six-Month Open-Label Study

Zoe Diana Draelos MD,[a] Mahmoud Ghannoum PhD,[b,c] Linda Stein Gold MD,[d] Julie C. Harper MD,[e] Hilary Baldwin MD,[f,g] Eric Guenin PharmD PhD MPH,[h] Emil A. Tanghetti MD[i]

[a]Dermatology Consulting Services, High Point, NC
[b]Case Western Reserve University, Cleveland, OH
[c]University Hospitals Cleveland Medical Center, Cleveland, OH
[d]Henry Ford Hospital, Detroit, MI
[e]Dermatology & Skin Care Center of Birmingham, Birmingham, AL
[f]The Acne Treatment and Research Center, Brooklyn, NY
[g]Robert Wood Johnson University Hospital, New Brunswick, NJ
[h]Ortho Dermatologics,* Bridgewater, NJ
[i]Center for Dermatology and Laser Surgery, Sacramento, CA

*Ortho Dermatologics is a division of Bausch Health US, LLC.

ABSTRACT

Background: Treatment of acne may require many months of treatment before maximal benefits are observed, and acne sequelae (eg, scarring, dyspigmentation) can persist long after lesion resolution. In 12-week clinical trials, triple-combination clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel (CAB) demonstrated efficacy and tolerability in the treatment of moderate to severe acne. This study assessed CAB long-term efficacy/tolerability and reductions in acne scarring/dyspigmentation.

Methods: This 24-week, single-center, open-label study assessed once-daily CAB in participants (N=25) aged ≥12 years with moderate acne (Investigator's Global Assessment [IGA] score=3). Endpoints included change from baseline in IGA score, inflammatory/noninflammatory lesions, skin appearance (dryness, postinflammatory hyperpigmentation [PIH], and postinflammatory erythema [PIE]), and scarring. Tolerability parameters (itching, burning, redness, swelling) and adverse events were assessed. At baseline and week 24, participants' foreheads were swabbed to assess *Cutibacterium acnes (C. acnes)*.

Results: At week 24, 68% of participants achieved treatment success (≥2-grade IGA score reduction from baseline and clear/almost clear skin), and significant inflammatory/noninflammatory lesion reductions from baseline were observed (89%; 70%; $P<0.001$, both). Decreases from baseline in investigator- and participant-assessed PIH (77%; 82%) and PIE (84%; 88%) and investigator-assessed scarring severity (33%) were statistically significant ($P\leq0.001$, all). There were no significant increases in skin dryness or any tolerability parameter, and no adverse events occurred. *C. acnes* assessment indicated no development of antibiotic resistance with long-term CAB treatment.

Conclusions: With 24 weeks of once-daily use, CAB was efficacious, well-tolerated, and significantly improved acne-related scarring and dyspigmentation. These results support the long-term use of CAB in the topical treatment of acne.

J Drugs Dermatol. 2025;24(5):516-523. doi:10.36849/JDD.9018

INTRODUCTION

The management of acne vulgaris is difficult owing to the chronic nature of the disease and frequent relapses.[1] As such, treatment duration can last for months or years.[1,2] Therapeutics that maintain efficacy, safety, and tolerability with prolonged treatment are needed for adequate disease management.[3,4] Although acne is characterized by inflammatory and noninflammatory lesions, scarring and dyspigmentation are common, with prevalence estimates of scarring ranging from 43% to 90.8%.[5-7] Acne sequelae can persist long after primary acne lesions have resolved and may be more distressing to patients than active acne lesions,[5,8,9] underscoring the need for therapies that reduce scarring and dyspigmentation in addition to treating lesions.

Combination therapy targeting multiple acne pathogenic factors is recommended for topical acne treatment.[4] Retinoids regulate epithelial proliferation, antibiotics and benzoyl peroxide (BPO) reduce viability of *Cutibacterium acnes*, and all 3 active ingredients have anti-inflammatory properties.[10-12] BPO has the additional benefit of preventing antibiotic resistance that may develop with prolonged antibiotic treatment.[13] Fixed

combinations targeting multiple drivers of acne pathogenesis in a single formulation are promising treatments, with the potential to improve efficacy and patient adherence by simplifying complex regimens.[14,15] Triple combinations containing a topical retinoid, BPO, and an antibiotic have demonstrated greater efficacy than dual combinations or topical monotherapy.[16] Clindamycin phosphate 1.2%/adapalene (ADAP) 0.15%/BPO 3.1% (CAB) gel is the only fixed-dose, triple-combination topical approved for acne vulgaris.[14] In phase 2 and phase 3 clinical trials, once-daily CAB demonstrated efficacy, safety, and tolerability in participants aged ≥9 years with moderate to severe acne over 12 weeks.[17-19]

As acne is a chronic, relapsing disease, the 12-week treatment course typically used in clinical trials may not be representative of real-world treatment. To determine the suitability of CAB for long-term treatment, a 24-week study was conducted to evaluate short- and long-term efficacy and tolerability of CAB as well as reduction of acne scarring and postinflammatory hyperpigmentation (PIH) in participants with moderate to severe acne.

MATERIALS AND METHODS

Study Design and Participants

This 6-month, open-label, postmarketing, single-center study evaluated long-term efficacy, safety, and tolerability of CAB gel in participants with moderate or severe acne (Investigator's Global Assessment [IGA] of 3 or 4). Males or females ≥12 years of age with any Fitzpatrick skin type were eligible to enroll. Participants were excluded if they had used any topical or oral prescription or over-the-counter acne product(s) for 2 or 4 weeks, respectively, prior to study entry. During the study, participants did not use other acne products. Participants were instructed to apply CAB gel to their entire face every night following washing.

Study visits occurred at baseline and every 4 weeks (weeks 4, 8, 12, 16, 20, and 24). At all study visits, participants were photographed with the Canfield VISIA CR using Standard 1 and lighting of the front, right, and left face. Study product and diaries were inspected for compliance.

The study was conducted in accordance with the International Conference on Harmonization, the Declaration of Helsinki, and Good Clinical Practice Guidelines, and was approved by the Allendale Institutional Review Board (Old Lyme, CT). All participants provided written informed consent prior to any procedures.

Efficacy Assessments

The primary efficacy endpoint was investigator-assessed improvement from baseline in global acne severity at week 24. IGA was assessed using a 6-point ordinal scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, and 5=very severe. Treatment success was defined as the percentage of participants with a ≥2-grade reduction from baseline in IGA and clear or almost clear skin. Secondary efficacy endpoints were investigator-assessed improvement from baseline in inflammatory and noninflammatory lesion counts at week 24. Participant-assessed quality of life (QoL) was evaluated via the validated Acne-specific Quality of Life questionnaire (Acne-QoL), which contains 19 questions that address the impact of facial acne on 4 domains of health-related QoL (eg, self-perception, role-social, role-emotional, and acne symptoms).[20]

Safety, Tolerability, and Skin Appearance Assessments

Safety and tolerability endpoints were the overall incidence of adverse events (AEs) and investigator-assessed skin irritation, respectively. Tolerability parameters were investigator-assessed peeling, redness, and swelling, and participant-assessed itching, burning, redness, and swelling. Skin appearance parameters assessed by the investigator and participants comprised dryness, PIH, and postinflammatory erythema (PIE). All tolerability and skin appearance assessments were made on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, 4=severe). Acne scarring was assessed by the investigator using the Goodman Qualitative Scar Scale.[21]

Statistical Analyses

Investigator and participant ordinal nonparametric data were analyzed using descriptive statistics and the Wilcoxon signed rank test. Numerical acne lesion counts (inflammatory, noninflammatory, and total lesions) were assessed using two-tailed Student's *t* test. Changes from baseline were considered significant at $P \leq 0.05$.

Cutibacterium Acnes Assessment

Skin microbiome samples were collected at baseline and week 24 for analysis of *C. acnes*. Swabs from each participant were taken from the central forehead prior to facial washing and were used to inoculate Brucella blood agar (BBA) plates with hemin and vitamin K. Plates were incubated anaerobically at 37°C, and growth was monitored daily for colony formation; after 7 days, plates with no growth were considered negative.

An Epsilometer Test (E-test) was used to determine the susceptibility of the collected *C. acnes* isolates to clindamycin. Bacterial inocula were spread onto BBA plates, followed by the addition of a clindamycin E-test strip to the surface of the plates. The minimum concentration of clindamycin needed to inhibit colony growth (MIC) was recorded after 48 hours of incubation at 37°C. The Clinical and Laboratory Standards Institute (CLSI) resistance breakpoint (MIC ≥8 µg/mL) was used to interpret the MIC obtained for each isolate (CLSI document M100-33rd Edition). *Clostridium difficile* (ATCC 700057) and *Bacteroides fragilis* (ATCC 25285) were used as quality control reference strains.

RESULTS

Participant Disposition and Demographics

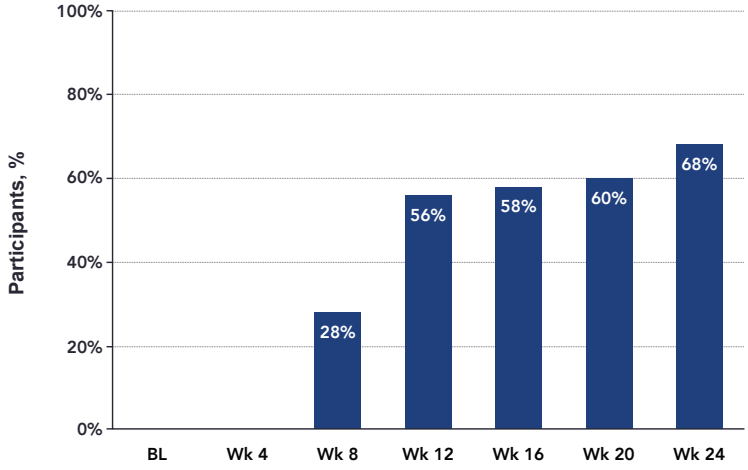
A total of 25 participants were enrolled and completed the study. One participant had missing data at week 16 (missed visit). Mean age was 23.9 years (range, 12 to 51 years) and most participants were female (n=20; 80%). A total of 18 participants were African American, 6 were White, and 1 was Asian. All Fitzpatrick skin types were represented (I–III, n=8; IV–VI, n=17). At baseline, all participants had moderate acne (IGA=3) and some degree of acne scarring (severity score mean, 1.96; range, 1 to 4), PIH (mean score, 2.76; range, 1 to 4), and PIE (mean score, 2.28; range, 1 to 3).

Efficacy

At week 24, 68% of participants achieved treatment success (Figure 1). Significant decreases from baseline in mean IGA score were noted as early as week 4 (mean, 2.12; 29% reduction from baseline), with continued improvement through week 24 (mean, 0.92; 69% reduction from baseline; $P<0.001$, all; data not shown).

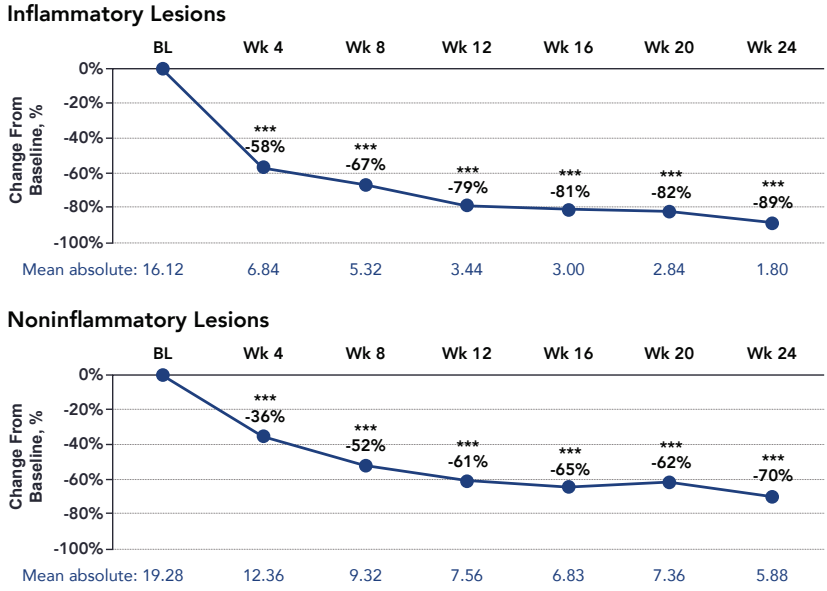
Significant reductions from baseline in lesion counts were observed as early as week 4 (inflammatory, -58%; noninflammatory, -36%; $P<0.001$, both), with cumulative improvement through week 24. At week 24, there was an 89% reduction from baseline in inflammatory lesions and a 70% reduction in noninflammatory lesions ($P<0.001$, both; Figure 2).

FIGURE 1. Treatment success[a] by week.



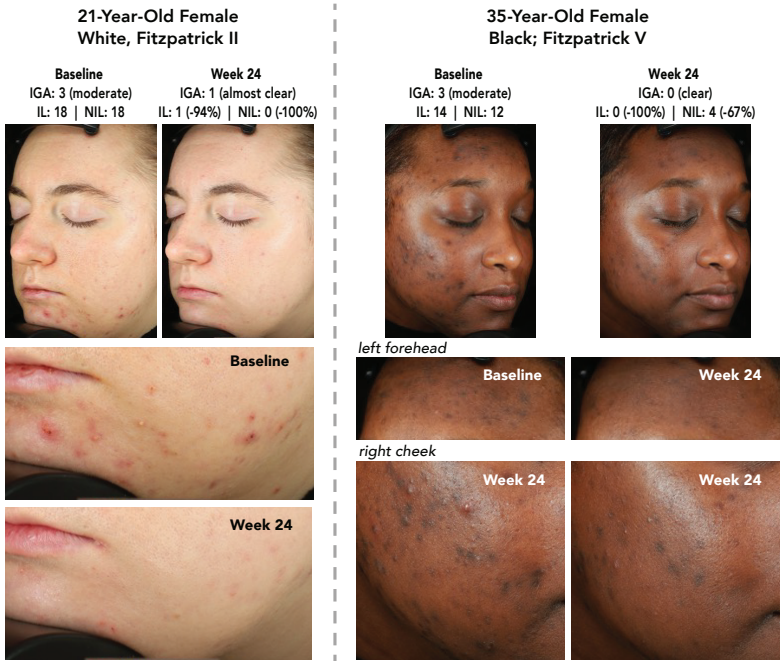
[a]Defined as ≥2-grade reduction in Investigator's Global Assessment and a score of 0 (clear) or 1 (almost clear).
BL, baseline; Wk, week.

FIGURE 2. Lesion reductions by week.



***$P<0.001$ vs baseline.
BL, baseline; Wk, week.

FIGURE 3. Participant photographs.



Individual results may vary.
Photographic Images ©2025. Courtesy of Study Investigator.
IGA, Investigator's Global Assessment; IL, inflammatory lesion; NIL, noninflammatory lesion.

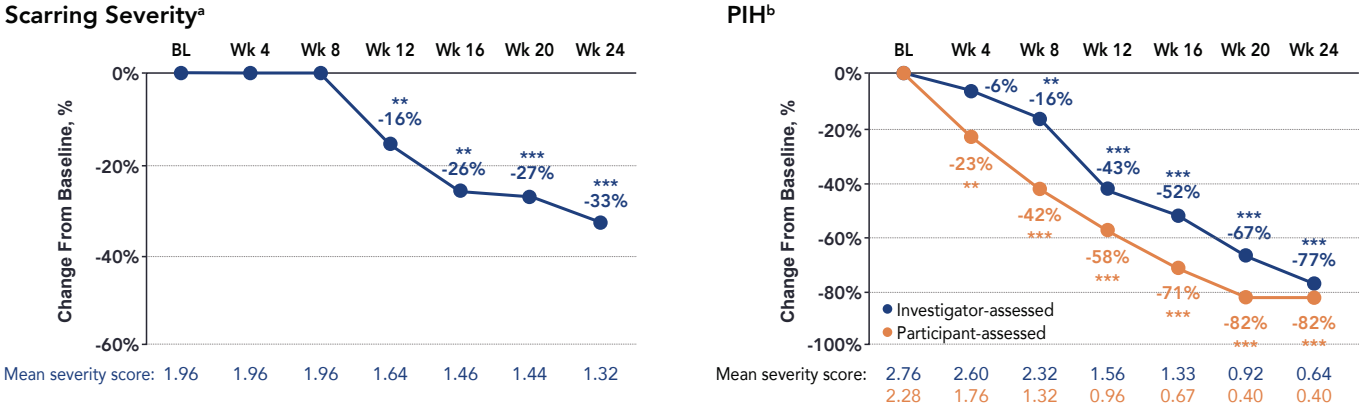
Participant photographs demonstrating improvement from baseline to week 24 are shown in Figure 3.

Quality of life was also improved for participants during the 6-month study. Significant increases (improvements) from baseline were observed for all 19 Acne-QoL items beginning at week 8 and continuing through week 24 (P<0.05, all; data not shown).

Skin Appearance, Safety, and Tolerability

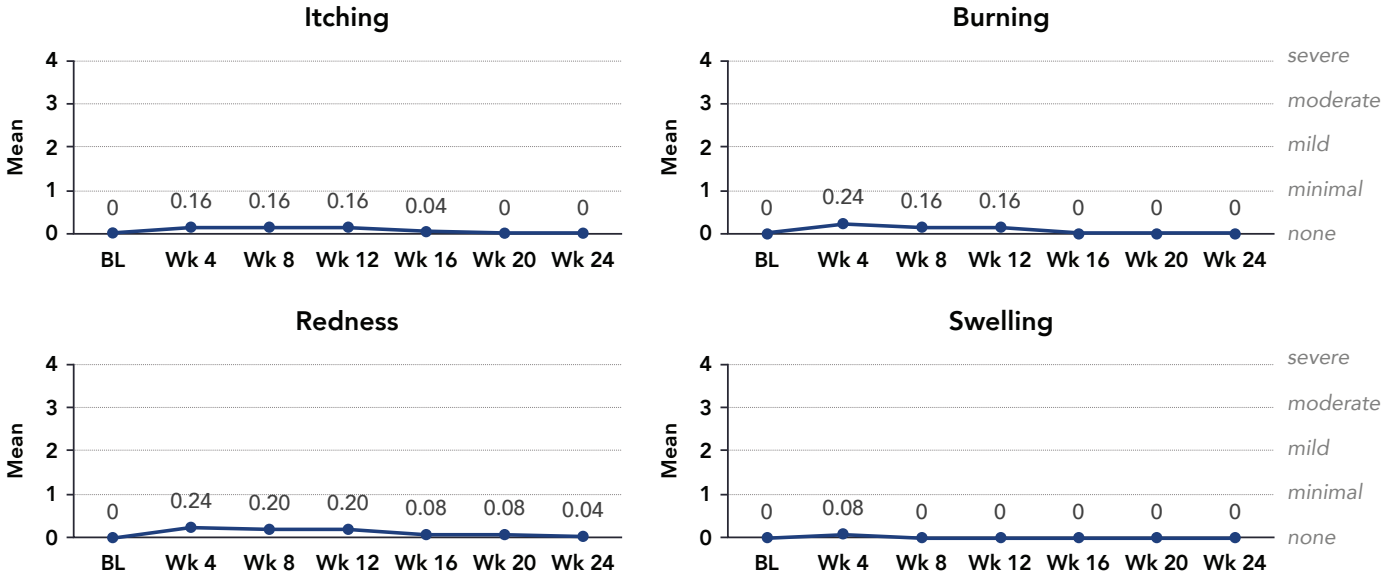
Significant improvement in facial scarring was observed by week 12, with cumulative improvement through week 24 (Figure 4). At week 24, there was a 33% reduction from baseline in facial scarring severity score (1.96 to 1.32; P<0.001). Significant improvements from baseline in PIH and PIE were noted by participants as early as week 4 and by the investigator at weeks 8 and 4, respectively. At week 24, 77% and 82% reduc-

FIGURE 4. Improvements in acne scarring and postinflammatory hyperpigmentation.



**P<0.01; ***P≤0.001 vs baseline.
[a]Assessed by investigator using the Goodman Qualitative Scar Scale: 0=none; 1=macular disease; 2=mild disease; 3=moderate disease; 4=severe disease.
[b]Assessed by investigator and participants using a 5-point scale: 0=none; 1=minimal; 2=mild; 3=moderate; 4=severe.
Mean absolute severity scores are noted below each figure.
BL, baseline; PIH, postinflammatory hyperpigmentation; Wk, week.

FIGURE 5. Participant-assessed tolerability by visit.



Changes from baseline were not significant (P>0.10) for all time points.
Assessed using a 5-point scale: 0=none; 1=minimal; 2=mild; 3=moderate; 4=severe.
BL, baseline; Wk, week.

tions from baseline in PIH were reported by the investigator and participants, respectively (P<0.001, both; AE), with similar reductions observed for PIE (84% and 88% reductions, respectively; P<0.001, both; data not shown).There were no significant increases in investigator- or participant-assessed dryness, with maximum postbaseline mean scores of 0.08 and 1.08, respectively (1=minimal dryness; data not shown).

No AEs or adverse experiences occurred during the study. In addition, there were no significant increases from baseline in any investigator-assessed (data not shown) or participant-assessed tolerability parameters (Figure 5) at any time point (P>0.10, all), and the maximum post-baseline mean score for any assessment was 0.24 (1=minimal).

***Cutibacterium Acnes* Assessment**

At baseline, *C. acnes* was isolated from 21/25 (84%) participant samples. Following 24 weeks of CAB treatment, only 14/25 (56%) participants had cultivable isolates. Isolates from 3 participants were resistant to clindamycin at baseline and week 24; however, all 3 had improvements in acne by study end (IGA decrease, 1 to 3 points; lesion reductions, 53% to 100%) and had no dryness, peeling, redness, or swelling. For participants with cultivable *C. acnes* isolates at baseline and week 24, no decrease in susceptibility was observed (ie, no indication of antibiotic resistance development; data not shown).

DISCUSSION

This post-marketing study expands upon previously reported efficacy and safety results with 12 weeks of CAB treatment[17-19] with a long-term treatment duration of 24 weeks. Long-term CAB treatment yielded significant reductions from baseline in acne severity scores and lesion counts. Moreover, the severity of acne scarring and postinflammatory dyspigmentation were significantly reduced, with no significant safety/tolerability concerns. Long-term CAB treatment was not associated with the development of *C. acnes* resistance to clindamycin; rather, *C. acnes* was eliminated from the sampling site in one-third of participants with cultivable samples.

Acne is a chronic condition that can require months to years of treatment. Even after resolution of primary acne lesions, persistent sequelae such as post-acne scarring and dyspigmentation may be more concerning to patients than the acne itself.[5] Long-term studies of acne therapies have demonstrated cumulative improvements in efficacy over time.[22-25] However, long-term treatment outcomes are often hampered by patient perceptions of treatment ineffectiveness and treatment-related tolerability concerns, which contribute to treatment nonadherence.[26]

In the present study, significant acne improvements were observed for all efficacy assessments with as few as 4 weeks of CAB treatment; at week 12, reductions from baseline in

inflammatory lesions and global acne severity were similar to results from 12-week CAB clinical trials.[17-19] Progressively greater improvements were observed through week 24, at which point over two-thirds of participants achieved treatment success, and inflammatory lesion reductions reached nearly 90%. Although noninflammatory lesion reductions were somewhat lower at week 12 than in other CAB studies, they reached 70% by week 24.

These reductions with CAB were slightly greater than those observed in two 24-week split-face studies of topical acne treatments. Participants with moderate to severe acne and atrophic acne scarring had median inflammatory and noninflammatory lesion reductions of 86.7% and 59.5%, respectively, with once-daily ADAP 0.3%/BPO 2.5% gel,[24] and mean reductions of 76.3% and 61.4%, respectively, with once-daily trifarotene 0.005% cream at week 24.[25] In an extension of the phase 3 studies of twice-daily clascoterone 1% cream, only 29.9% of participants with moderate to severe acne achieved an IGA of clear or almost clear (score=0 or 1) at 9 months of treatment, whereas 68% of participants in the present study achieved clear/almost clear skin after 6 months of once-daily CAB treatment.[23] Direct comparisons cannot be made between these studies, however, as populations and study designs differed.

For many patients, acne sequelae, such as scarring and postinflammatory dyspigmentation, are the primary motivators for seeking medical treatment.[8] These sequelae can be prevented through early and effective acne treatment, leading to significant improvements in quality of life.[5,8,27] CAB treatment yielded significant improvements in acne scarring by week 12, progressing to a 33% reduction in overall severity at week 24. Anti-scarring effects of other acne topicals have also been reported, but direct comparisons should be made with caution owing to differences in study population characteristics at baseline and assessments used. For example, after 24 weeks of treatment with trifarotene 0.005% cream, the mean global scarring severity score was ~1.3, similar to 24 weeks of CAB treatment;[25] however, severity at baseline was somewhat higher in the trifarotene study (mean score of 2.6 vs 2.0), and a different global severity scale was used (Scar Global Assessment [SGA] vs Goodman Qualitative Scar Scale). Additionally, rates of SGA success (≥2-grade reduction from baseline in severity score and a score of clear/almost clear skin) at week 24 were greater for trifarotene 0.005% cream than in the ADAP 0.3%/BPO 2.5% gel study (53.5% vs 32.9%, respectively), though mean severity scores with ADAP 0.3%/BPO 2.5% gel were not reported.[24,25]

Acne-associated inflammation can lead to excess production and abnormal deposition of melanin, leading to post-inflammatory dyspigmentation that may be more distressing to patients than acne lesions.[28] In patients with skin of color, PIH is more common, whereas PIE is more frequently observed in patients with lighter skin phototypes. Treating underlying inflammation may be key to effectively reducing acne-induced dyspigmentation.[8] Severity of both PIH and PIE was significantly reduced with CAB treatment in the present study, with the investigator reporting significant decreases at weeks 8 and 4, respectively, and ~80% reductions in severity of both by week 24. In the context of published results for other acne topicals, 24 weeks of treatment with trifarotene 0.005% cream was associated with a 19% decrease (improvement) from baseline in post-acne hyperpigmentation scores, though a different scale was used than in the present study.[8] Participant-reported severity of both PIH and PIE was significantly reduced by week 4, followed by significantly increased (improved) scores compared with baseline on all Acne-QoL questions at week 8. Although causation between improvements in acne lesions, PIH, or PIE and QoL cannot be inferred from these findings, they align with previous reports that acne psychosocial effects may not be as easy to reverse as visible symptoms[29] and underscore the importance of consistent and continued use of acne medications even after visible improvements in skin appearance.

Long-term use of acne medications has been associated with safety and tolerability concerns such as dryness and erythema.[30,31] With 24 weeks of CAB treatment, no tolerability issues, including dryness and erythema, were noted, and there were no AEs reported, suggestive of favorable safety and tolerability with long-term use. These safety/tolerability results are consistent with 12-week phase 2 and 3 studies of CAB gel,[17-19] and may be attributable to the vehicle, a proprietary polymeric mesh gel that was designed for uniform distribution of active ingredients and a moisturizing humectant with no alcohol or surfactants. Moreover, anti-inflammatory properties of clindamycin allow for the addition of a third active ingredient without worsening the safety/tolerability profile relative to ADAP/BPO fixed combinations.[32]

However, prolonged use of clindamycin and other antibiotics carries the risk of developing antibiotic resistance, which likely underlies the reduced efficacy over time that has been observed for topical erythromycin for acne.[33] In samples of *C. acnes* isolated from participants in this study, no decrease in clindamycin susceptibility was observed in any isolates, indicative of no emergent antibiotic resistance. Moreover, over one-third of participants with cultivable *C. acnes* at baseline had no cultivable *C. acnes* at week 24, indicating that CAB treatment eliminated the bacteria from the sampling site. In 3 participants, CAB delivered acne improvements in line with the overall study population despite having clindamycin-resistant *C. acnes* at baseline and week 24. Overall, microbiological results are consistent with findings that co-application of BPO with clindamycin can reduce *C. acnes* counts, prevent development of antibiotic resistance,[34,35] and align with American Academy of

Dermatology recommendations that treatment with antibiotics, even for mild acne, be accompanied by concurrent BPO use.[4] To further support long-term use of CAB for acne, an identically designed 24-week study is ongoing; additional microbiological results will be published upon completion.

Interpretation of these results is limited by factors such as the open-label study design that did not include a vehicle comparator. In addition, the study population was small, the majority comprised females and individuals with skin of color (>75% each), and all participants presented with moderate acne. Therefore, results may not be generalizable to the overall population of patients with acne, particularly for those with severe acne.

Overall, this study confirms and expands on findings from 12-week clinical studies of CAB gel,[17-19] with significant and continuing improvements in acne lesions, scarring, PIH, and PIE through 24 weeks of treatment with no new safety/tolerability signals or emergence of antibiotic resistance. CAB gel is an appropriate and effective option for the long-term topical treatment of acne vulgaris.

DISCLOSURES

Zoe Diana Draelos received funding from Ortho Dermatologics. Mahmoud Ghannoum has acted as a consultant or received contracts from Scynexis, Inc, Bausch & Lomb, Pfizer, and Mycovia. Linda Stein Gold has served as investigator/consultant or speaker for Ortho Dermatologics, LEO Pharma, Dermavant, Incyte, Novartis, AbbVie, Pfizer, Sun Pharma, UCB, Arcutis, and Lilly. Julie Harper has received honoraria from Almirall, Cutera, Galderma, LaRoche-Posay, Ortho Dermatologics, and Sun Pharma. Hilary Baldwin has served as advisor, investigator, and on speaker's bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. Emil Tanghetti has served as speaker for Novartis, Ortho Dermatologics, Sun Pharma, Lilly, Galderma, AbbVie, and Dermira; and served as a consultant/clinical studies for Hologic, Ortho Dermatologics, and Galderma; and is a stockholder for Accure. Eric Guenin is an employee of Ortho Dermatologics and may hold stock and/or stock options in its parent company.

ACKNOWLEDGMENT

This study was funded by Ortho Dermatologics. Medical writing support was provided by Amel Alqadah PhD and Kevin Corcoran PhD, from Citrus Health Group, Inc. (Chicago, Illinois), with financial support from Ortho Dermatologics. Ortho Dermatologics is a division of Bausch Health US, LLC.

REFERENCES

1. Chilicka K, Gold MH, Nowicka D. Acne vulgaris and the most popular and new cosmetological treatments. *J Cosmet Dermatol.* 2023;22:1946-1950.
2. Eichenfield DZ, Sprague J, Eichenfield LF. Management of acne vulgaris: a review. *JAMA.* 2021;326:2055-2067.
3. Sevimli Dikicier B. Topical treatment of acne vulgaris: efficiency, side effects, and adherence rate. *J Int Med Res.* 2019;47:2987-2992.
4. Reynolds RV, Yeung H, Cheng CE, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol.* 2024;90:1006.e1001-1006.e1030.
5. Layton A, Alexis A, Baldwin H, et al. Identifying gaps and providing recommendations to address shortcomings in the investigation of acne sequelae by the Personalising Acne: Consensus of Experts panel. *JAAD Int.* 2021;5:41-48.
6. Tan J, Kang S, Leyden J. Prevalence and risk factors of acne scarring among patients consulting dermatologists in the USA. *J Drugs Dermatol.* 2017;16:97-102.
7. Hayashi N, Miyachi Y, Kawashima M. Prevalence of scars and "mini-scars", and their impact on quality of life in Japanese patients with acne. *J Dermatol.* 2015;42:690-696.
8. Conte S, Li MK. A multimodal approach to acne-induced post-inflammatory hyperpigmentation: trifarotene as a long-term intervention. *Skin Therapy Lett.* 2024;29:1-5.
9. Abad-Casintahan F, Chow SK, Goh CL, et al. Frequency and characteristics of acne-related post-inflammatory hyperpigmentation. *J Dermatol.* 2016;43:826-828.
10. Del Rosso JQ, Schmidt NF. A review of the anti-inflammatory properties of clindamycin in the treatment of acne vulgaris. *Cutis.* 2010;85:15-24.
11. Blaskovich MAT, Elliott AG, Kavanagh AM, et al. In vitro antimicrobial activity of acne drugs against skin-associated bacteria. *Sci Rep.* 2019;9:14658.
12. Fuchs E, Green H. Regulation of terminal differentiation of cultured human keratinocytes by vitamin A. *Cell.* 1981;25:617-625.
13. Leyden JJ, Wortzman M, Baldwin EK. Antibiotic-resistant Propionibacterium acnes suppressed by a benzoyl peroxide cleanser 6%. *Cutis.* 2008;82:417-421.
14. Podwojniak A, Tan IJ, Sauer J, et al. Updates on topical dyad and triple combination therapies approved for acne vulgaris. *Cureus.* 2024;16:e61413.
15. Yentzer BA, Ade RA, Fountain JM, et al. Simplifying regimens promotes greater adherence and outcomes with topical acne medications: a randomized controlled trial. *Cutis.* 2010;86:103-108.
16. Huang CY, Chang IJ, Bolick N, et al. Comparative efficacy of pharmacological treatments for acne vulgaris: a network meta-analysis of 221 randomized controlled trials. *Ann Fam Med.* 2023;21:358-369.
17. Stein Gold L, Lain E, Del Rosso JQ, et al. Clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel for moderate-to-severe acne: efficacy and safety results from two randomized phase 3 trials. *J Am Acad Dermatol.* 2023;89:927-935.
18. Kircik LH, Stein Gold L, Gold M, et al. Triple combination clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% for acne: efficacy and safety from a pooled phase 3 analysis. *Dermatol Ther (Heidelb).* 2024;14:1211-1227.
19. Stein Gold L, Baldwin H, Kircik LH, et al. Efficacy and safety of a fixed-dose clindamycin phosphate 1.2%, benzoyl peroxide 3.1%, and adapalene 0.15% gel for moderate-to-severe acne: a randomized phase II study of the first triple-combination drug. *Am J Clin Dermatol.* 2022;23:93-104.
20. Merck & Co, Inc. Acne-Specific Quality of Life Questionnaire (Acne-QoL) Manual & Interpretation Guide. Available at: https://www.anzctr.org.au/Steps11and12/376709-(Uploaded-11-01-2019-20-05-40)-Study-related%20document.pdf. Accessed January 17, 2025.
21. Goodman GJ, Baron JA. Postacne scarring: a qualitative global scarring grading system. *Dermatol Surg.* 2006;32:1458-1466.
22. Santer M, Lawrence M, Renz S, et al. Effectiveness of spironolactone for women with acne vulgaris (SAFA) in England and Wales: pragmatic, multicentre, phase 3, double blind, randomised controlled trial. *BMJ.* 2023;381:e074349.
23. Eichenfield LF, Gold LS, Han J, et al. Integrated short-term and long-term efficacy of topical clascoterone cream 1% in patients aged 12 years or older with acne vulgaris. *J Drugs Dermatol.* 2024;23:1278-1283.
24. Dreno B, Bissonnette R, Gagne-Henley A, et al. Prevention and reduction of atrophic acne scars with adapalene 0.3%/benzoyl peroxide 2.5% gel in subjects with moderate or severe facial acne: results of a 6-month randomized, vehicle-controlled trial using intra-individual comparison. *Am J Clin Dermatol.* 2018;19:275-286.
25. Schleicher S, Moore A, Rafal E, et al. Trifarotene reduces risk for atrophic acne scars: results from a phase 4 controlled study. *Dermatol Ther (Heidelb).* 2023;13:3085-3096.
26. Moradi Tuchayi S, Alexander TM, Nadkarni A, Feldman SR. Interventions to increase adherence to acne treatment. *Patient Prefer Adherence.* 2016;10:2091-2096.
27. Tan JK. Psychosocial impact of acne vulgaris: evaluating the evidence. *Skin Therapy Lett.* 2004;9:1-3, 9.
28. Elbuluk N, Grimes P, Chien A, et al. The pathogenesis and management of acne-induced post-inflammatory hyperpigmentation. *Am J Clin Dermatol.* 2021;22:829-836.

29. Zhou C, Vempati A, Tam C, et al. Beyond the surface: a deeper look at the psychosocial impacts of acne scarring. *Clin Cosmet Investig Dermatol.* 2023;16:731-738.
30. Chovatiya R. Acne treatment. *JAMA*. 2021;326:2087.
31. Eichenfield L, Hebert A, Gold LS, et al. Open-label, long-term extension study to evaluate the safety of clascoterone (CB-03-01) cream, 1% twice daily, in patients with acne vulgaris. *J Am Acad Dermatol.* 2020;83:477-485.
32. Del Rosso JQ, Bunick CG, Kircik L, Bhatia N. Topical clindamycin in the management of acne vulgaris: current perspectives and recent therapeutic advances. *J Drugs Dermatol.* 2024;23:438-445.
33. Del Rosso JQ, Webster GF, Rosen T, et al. Status report from the Scientific Panel on Antibiotic Use in Dermatology of the American Acne and Rosacea Society: Part 1: antibiotic prescribing patterns, sources of antibiotic exposure, antibiotic consumption and emergence of antibiotic resistance, impact of alterations in antibiotic prescribing, and clinical sequelae of antibiotic use. *J Clin Aesthet Dermatol.* 2016;9:18-24.
34. Ghannoum M, Gamal A, Kadry A, et al. Avoiding the danger of rising resistance in cutibacterium acnes: criticality of benzoyl peroxide and antibiotic fixed combinations. *SKIN J Cutan Med.* 2024;8:s354.
35. Cunliffe WJ, Holland KT, Bojar R, Levy SF. A randomized, double-blind comparison of a clindamycin phosphate/benzoyl peroxide gel formulation and a matching clindamycin gel with respect to microbiologic activity and clinical efficacy in the topical treatment of acne vulgaris. *Clin Ther.* 2002;24:1117-1133.

AUTHOR CORRESPONDENCE

Zoe Diana Draelos MD
E-mail:..... zdraelos@northstate.net