doi:10.36849/JDD.8484

 ORIGINAL ARTICLE

Clindamycin Phosphate 1.2%/Adapalene 0.15%/ Benzoyl Peroxide 3.1% Gel for Male and Female Acne: Phase 3 Analysis

Edward (Ted) Lain MD MBA,[a] Neal Bhatia MD,[b] Leon Kircik MD,[c-e] Linda Stein Gold MD,[f] Julie C. Harper MD,[g] Christopher G. Bunick MD PhD,[h] Eric Guenin PharmD PhD MPH,[i] Hilary Baldwin MD,[j,k] Steven R. Feldman MD PhD,[l] James Q. Del Rosso DO[m-o]

[a]Austin Institute for Clinical Research, Austin, TX
[b]Therapeutics Clinical Research, San Diego, CA
[c]Icahn School of Medicine at Mount Sinai, New York, NY; [d]Indiana University School of Medicine, Indianapolis, IN;
[e]Physicians Skin Care, PLLC, DermResearch, PLLC, and Skin Sciences, PLLC, Louisville, KY;
[f]Henry Ford Hospital, Detroit, MI; [g]Dermatology & Skin Care Center of Birmingham, Birmingham, AL;
[h]Yale University Department of Dermatology and Program in Translational Biomedicine, New Haven, CT;
[i]Ortho Dermatologics*, Bridgewater, NJ; [j]The Acne Treatment and Research Center, Brooklyn, NY;
[k]Robert Wood Johnson University Hospital, New Brunswick, NJ; [l]Wake Forest University School of Medicine, Winston-Salem, NC;
[m]JDR Dermatology Research/Thomas Dermatology, Las Vegas, NV; [n]Advanced Dermatology and Cosmetic Surgery, Maitland, FL;
[o]Touro University Nevada, Henderson, NV

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

ABSTRACT

Background: Clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel (CAB) is the only fixed-dose triple-combination treatment approved for acne. This post hoc analysis assessed the impact of sex on efficacy and safety/tolerability of CAB.

Methods: In two multicenter, double-blind, phase 3 studies (NCT04214639 and NCT04214652), participants aged ≥9 years with moderate-to-severe acne were randomized (2:1) to 12 weeks of once-daily treatment with CAB or vehicle gel. Pooled data were analyzed by sex. Assessments included treatment success (≥2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 [clear] or 1 [almost clear]), inflammatory/noninflammatory lesion counts, Acne-Specific Quality of Life (Acne-QoL) questionnaire, treatment-emergent adverse events (TEAEs), and cutaneous safety/tolerability.

Results: At week 12, treatment success rates were significantly greater with CAB versus vehicle irrespective of sex (females: 53.7% vs 23.0%; males: 43.1% vs 24.6%; $P<0.05$, both). CAB-treated female and male participants both experienced greater reductions from baseline versus vehicle in inflammatory (females: 77.7% vs 57.9%; males: 77.5% vs 57.1%; $P<0.001$, both) and noninflammatory lesions (females: 72.5% vs 45.6%; males: 72.3% vs 49.6%; $P<0.001$, both). Acne-QoL improvements from baseline to week 12 were significantly greater with CAB than vehicle. No significant differences in any efficacy measures between CAB-treated males and females were observed. Most TEAEs were of mild-to-moderate severity; no sex-based trends for safety/tolerability were observed.

Conclusions: CAB demonstrated comparable efficacy, quality-of-life improvements, and safety in female and male participants with moderate-to-severe acne. As the first fixed-dose, triple-combination topical formulation, CAB represents an important new treatment for acne.

J Drugs Dermatol. 2024;23(10):873-881. doi:10.36849/JDD.8484

INTRODUCTION

Acne is a chronic dermatologic condition affecting up to 50 million people in the United States annually.[1] Although acne afflicts both males and females, skin physiology and acne presentation vary by sex. Males experience higher sebum production, less transepidermal water loss, and lower skin pH compared with females.[2] Females are more likely to experience drier and more sensitive skin with age.[3] While adolescent acne is more prevalent in males, females are more likely to experience persistent adult acne[4-6] and acne flare-ups associated with monthly hormonal fluctuations.[7] Together, these sex differences may necessitate distinct acne treatment regimens.

Acne pathophysiology is multifactorial and includes follicular proliferation of *Cutibacterium acnes*, increased inflammation and sebum production, and abnormal keratinization.[8] Acne treatments can target multiple pathophysiological mechanisms, and single products containing multiple active drugs can enhance efficacy and improve adherence to the treatment regimen.[9,10] Several dual-combination topical products containing benzoyl peroxide (BPO) and an antibiotic or a retinoid are approved for acne treatment,[11] and fixed-dose combinations are recommended for the majority of patients with acne.[8] Clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide (BPO) 3.1% (CAB; Cabtreo®; Ortho Dermatologics) gel is the only triple-combination, fixed-dose topical product approved by the US Food and Drug Administration for acne treatment and is indicated for use in patients aged 12 years and older.[12] CAB gel targets 3 of 4 acne pathological mechanisms: adapalene modulates cellular keratinization, differentiation, and proliferation; BPO has antimicrobial, mild comedolytic, and keratolytic activity; and clindamycin has antibiotic and anti-inflammatory activity.[8,12]

A 3-pronged combination approach is more effective than dual combinations of its active ingredients, as supported by analyses comparing dual- and triple-combination topicals,[10,11] and a phase 2 study of CAB versus its dyad components.[13] Two identical randomized, phase 3, double-blind, vehicle-controlled trials confirmed the efficacy, safety, and tolerability of CAB.[14] For this post hoc analysis, data from the phase 3 studies were pooled to evaluate efficacy and safety of CAB in participants grouped by sex (male/female).

MATERIALS AND METHODS

Study Design and Participants

Data were pooled from two identical multicenter, randomized, double-blind, vehicle-controlled, parallel-group, phase 3 studies (NCT04214639 and NCT04214652), the details of which have been published previously.[14] Eligible participants were aged ≥9 years with moderate-to-severe acne (Evaluator's Global Severity Score [EGSS] of 3 or 4; Table 1), 30-100 inflammatory lesions (papules/pustules/nodules), 35-150 noninflammatory lesions (closed/open comedones), and ≤2 facial nodules. Participants were randomized (2:1) to CAB or vehicle gel, applied once daily for 12 weeks. CeraVe® hydrating cleanser and moisturizing lotion (L'Oreal) were provided as needed for optimal moisturization and cleaning of the skin; use of an investigator-approved sunscreen was recommended for skin protection. Study protocols were approved by institutional review boards or ethics committees at all investigation sites, and studies were conducted in accordance with principles of Good Clinical Practice and the Declaration of Helsinki. All participants or their legal guardians provided written informed consent.

Efficacy and Safety Assessments

Efficacy evaluations included inflammatory and noninflammatory lesion counts and treatment success, defined as the percentage of participants achieving ≥2-grade reduction from baseline in EGSS and a score of 0 (clear) or 1 (almost clear). Assessments were performed at baseline and weeks 2, 4, 8, and 12. At baseline and week 12, participants completed the Acne-Specific Quality of Life (Acne-QoL) questionnaire, which covers 4 domains: self-perception, role-emotional, role-social, and acne symptoms.[15] Questions within each domain were scored from 0 (extremely) to 6 (not at all); increases from baseline in domain scores indicated improved quality of life. Investigator assessments of cutaneous safety (scaling, erythema, hypopigmentation, hyperpigmentation) and participant assessments of tolerability (itching, burning, stinging) were scored using a 4-point scale (0=none, 1=mild, 2=moderate, 3=severe). Treatment compliance (assessed via product weight measurements and participant responses/diaries) was defined as participants missing ≤5 consecutive days of dosing and applying 80% to 120% of expected applications. Adverse events (AEs) were monitored throughout the study.

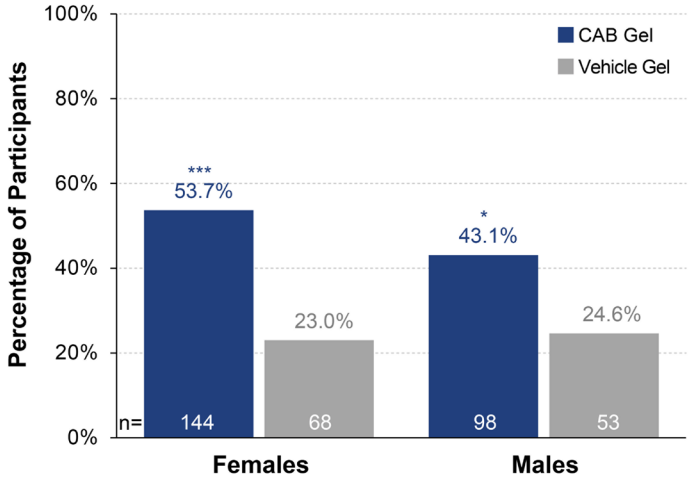
Statistical Analysis

Post hoc analysis assessed participants grouped by sex (male or female). The intent-to-treat (ITT) population included all randomized participants who were provided the study drug, and the safety population included all randomized participants who used the study drug at least once.

TABLE 1.

Evaluator's Global Severity Score		
Score	**Grade**	**Description**
0	Clear	Normal, clear skin with no evidence of acne vulgaris
1	Almost Clear	Rare noninflammatory lesions present, with rare noninflamed papules (papules must be resolving and may be hyperpigmented, though not pink-red)
2	Mild	Some noninflammatory lesions are present, with few inflammatory lesions (papules/pustules only; no nodulocystic lesions)
3	Moderate	Noninflammatory lesions predominate, with multiple inflammatory lesions evident: several to many comedones and papules/pustules, and there may be 1 nodulocystic lesion
4	Severe	Inflammatory lesions are more apparent, many comedones and papules/pustules, there may be up to 2 nodulocystic lesions

FIGURE 1. Treatment success[a] at week 12 (ITT population, pooled).



Treatment success at week 12 was significantly higher with CAB vs vehicle gel, regardless of sex.
*P<0.05; ***P<0.001 vs vehicle.
[a]Percentage of participants achieving ≥2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 (clear) or 1 (almost clear).
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat.

Percent change in inflammatory and noninflammatory lesions at weeks without significant skewness were based on non-rank-transformed data; when significant skewness was observed, a nonparametric method was used to rank transform data prior to the analysis of covariance (ANCOVA), with a factor of treatment group and covariate of the respective baseline lesion counts. For differences between CAB-treated females and males, ranked ANCOVAs with factor of sex and covariate of baseline lesion counts were used. Treatment success was analyzed using a logistic regression test (using Firth's Penalized Likelihood) with factors of treatment group or sex. For Acne-QoL questionnaire responses, domain scores were transformed from 0-6 to 1-7 prior to ANCOVA with factor of treatment group and covariate of baseline domain score. For differences between CAB-treated

TABLE 2.

Participant Demographics, Baseline Characteristics, and Compliance (ITT Population, Pooled)

	Females (n=212)		Males (n=151)	
	CAB Gel (n=144)	Vehicle Gel (n=68)	CAB Gel (n=98)	Vehicle Gel (n=53)
Age, mean (SD), y	22.0 (7.9)	22.2 (7.7)	17.4 (5.3)	18.5 (5.1)
Age, median (range), y	21.0 (10–48)	21.5 (11–44)	16.0 (12–44)	17.0 (13–39)
Ethnicity, Hispanic/Latino, n (%)	38 (26.4)	11 (16.2)	19 (19.4)	12 (22.6)
Race, n (%)				
White	97 (67.4)	54 (79.4)	72 (73.5)	44 (83.0)
Black/African American	28 (19.4)	10 (14.7)	12 (12.2)	4 (7.5)
Asian	11 (7.6)	2 (2.9)	10 (10.2)	3 (5.7)
Other[a]	8 (5.5)	2 (2.9)	4 (4.1)	2 (3.8)
Inflammatory lesion count, mean (SD)	35.8 (6.7)	36.2 (8.5)	38.3 (8.8)	38.9 (10.0)
Noninflammatory lesion count, mean (SD)	49.7 (17.0)	48.2 (15.7)	48.3 (17.0)	46.8 (15.2)
Evaluator's Global Severity Score, n (%)				
3 – moderate	134 (93.1)	65 (95.6)	82 (83.7)	50 (94.3)
4 – severe	10 (6.9)	3 (4.4)	16 (16.3)	3 (5.7)
Compliance, %	88.1	93.8	94.7	98.1

[a]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Not Reported/Multiple.
CAB, clindamycin phosphate 1.2%/ adapalene 0.15%/ benzoyl peroxide 3.1%; ITT, intent to treat; SD, standard deviation.

females and males, ANCOVAs with factor of sex and covariate of baseline domain score were used. For all efficacy assessments except Acne-QoL, multiple imputation was used to impute missing values using the Markov Chain Monte Carlo method. All statistical analyses were performed using SAS® version 9.4 or later. Statistical significance was based on 2-tailed tests of the null hypothesis resulting in $P \leq 0.05$.

Treatment compliance and cutaneous safety/tolerability assessments were summarized using descriptive statistics. AEs were recorded and classified using Medical Dictionary for Regulatory Activities terminology. Imputations were not made for missing safety data.

RESULTS

Participant Demographics and Baseline Characteristics

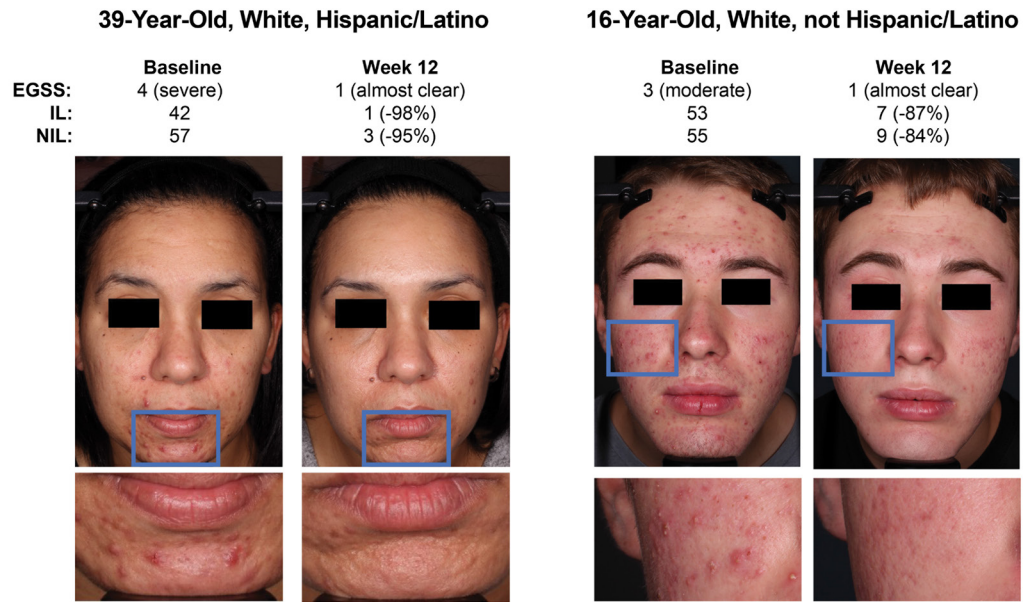
A total of 363 participants were randomized in the two phase 3 studies,[14] comprising 212 females and 151 males in the ITT and safety populations (Table 2). Female participants were 4.3 years older than males on average. More female than male participants self-reported being Black or African American (17.9% vs 10.6%). While most participants had moderate acne at baseline, a lower percentage of females had severe acne compared with males (6.1% vs 12.6%). Treatment compliance with CAB was high for both male and female participants (95.9% and 89.9%, respectively).

Efficacy

The percentage of participants with treatment success at week 12 was significantly higher with CAB compared with vehicle gel in both females (53.7% vs 23.0%; $P<0.001$) and males (43.1% vs 24.6%; $P<0.05$; Figure 1). No difference in treatment success at week 12 was observed between CAB-treated males and females ($P=0.129$). Images of CAB-treated participants are shown in Figure 2.

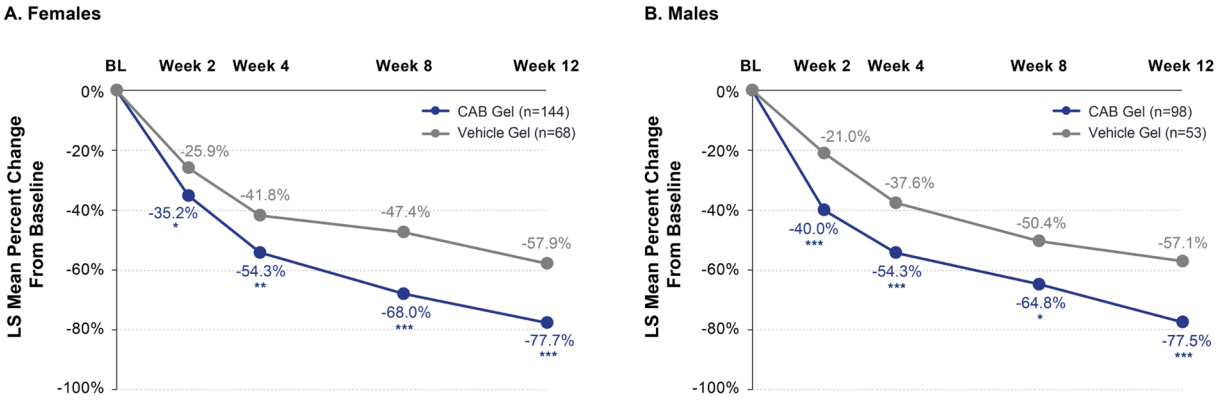
Inflammatory and noninflammatory lesions decreased over time among participants of both sexes. At week 12, least-squares mean percent reduction from baseline in inflammatory lesions was significantly greater with CAB versus vehicle gel in both females (77.7% vs 57.9%; $P<0.001$; Figure 3A) and males (77.5% vs 57.1%; $P<0.001$; Figure 3B). For both sexes, inflammatory lesion reductions were also greater for CAB than vehicle at weeks 2, 4, and 8 ($P<0.05$, all). No statistically significant difference between CAB-treated males and females was observed at any time ($P=0.125$-0.801).

FIGURE 2. Acne improvements with CAB gel.



Participant photos showing acne improvement with CAB gel; individual results may vary.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; EGSS, Evaluator's Global Severity Score; IL, inflammatory lesions; NIL, noninflammatory lesions.

FIGURE 3. Inflammatory lesion reductions (ITT population, pooled).



Inflammatory lesion reductions were greater with CAB vs vehicle gel, regardless of sex.
*P<0.05; **P<0.01; ***P<0.001 vs vehicle.
BL, baseline; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; LS, least squares.

Noninflammatory lesion reductions at week 12 were significantly greater with CAB than vehicle in females (72.5% vs 45.6%; P<0.001; Figure 4A) and males (72.3% vs 49.6%; P<0.001; Figure 4B). Noninflammatory lesion reductions were also significantly greater for CAB than vehicle at weeks 4 and 8 in females (P<0.001, each) and as early as week 2 in males (P<0.05). No difference between CAB-treated males and females was observed at any time point (P=0.295-0.902).

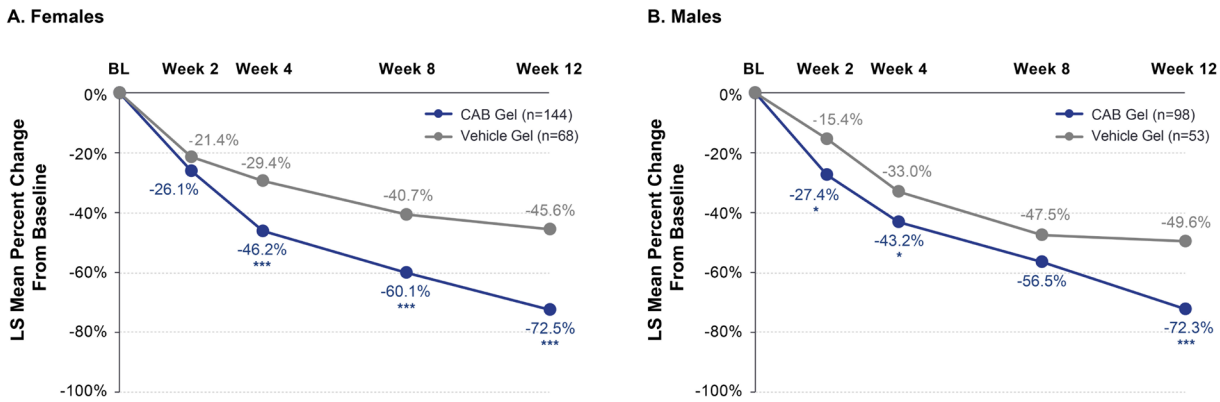
Quality of Life

At week 12, least-squares mean increases (improvements) from baseline in all 4 Acne-QoL domain scores were significantly greater with CAB versus vehicle in both female (range, CAB: 6.5-11.2; vehicle: 4.0-6.7; P≤0.001, all) and male participants (range, CAB: 3.5-6.2; vehicle: 1.9-3.6; P<0.01, all; Figure 5A-D). Increases in Acne-QoL domain scores were not different between CAB-treated males and females (P=0.44-0.81).

Safety and Tolerability

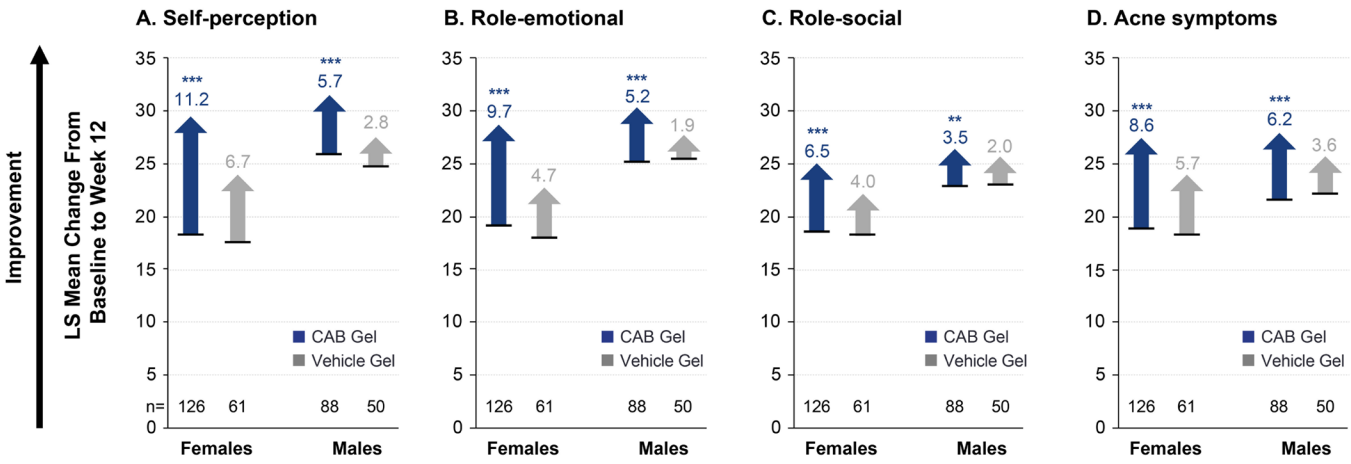
Adverse events and cutaneous safety/tolerability for the overall pooled study population have been previously reported.[14] Treatment-emergent adverse event (TEAE) rates, severity, and relationship to study drug were similar for females and males (Table 3). TEAE rates for CAB-treated females and males (27.1% and 27.6%, respectively) were greater than for vehicle-treated participants (8.8% and 7.5%). The majority of TEAEs were of mild-to-moderate severity. The most common TEAEs (occurring in ≥2% of participants in any treatment group) were pain, dryness, irritation, and exfoliation at the application site; erythema; and xerosis. Pain and dryness at the application site and erythema were reported by a greater percentage of CAB-treated males than females, whereas irritation and exfoliation at the application site and xerosis were reported by a greater percentage of CAB-treated females than males. Rates of discontinuation due to AEs were low among CAB-treated females (2.8%) and males (3.1%).

FIGURE 4. Noninflammatory lesion reductions (ITT population, pooled).



Noninflammatory lesion reductions were greater with CAB vs vehicle gel, regardless of sex.
*P<0.05; ***P<0.001 vs vehicle.
BL, baseline; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; LS, least squares.

FIGURE 5. Increases in Acne-QoL scores from baseline to week 12 (ITT population, pooled).



Acne QoL domain scores were significantly greater with CAB vs vehicle gel, regardless of sex.
** $P<0.01$; *** $P\leq0.001$ vs vehicle.
Data shown for participants with baseline and week 12 scores. Horizontal black lines indicate domain scores at baseline and arrows indicate changes from baseline.
Females CAB n=126, vehicle n=61; males CAB n=88, vehicle n=50.
Acne-QoL, Acne-Specific Quality of Life questionnaire; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; LS, least squares.

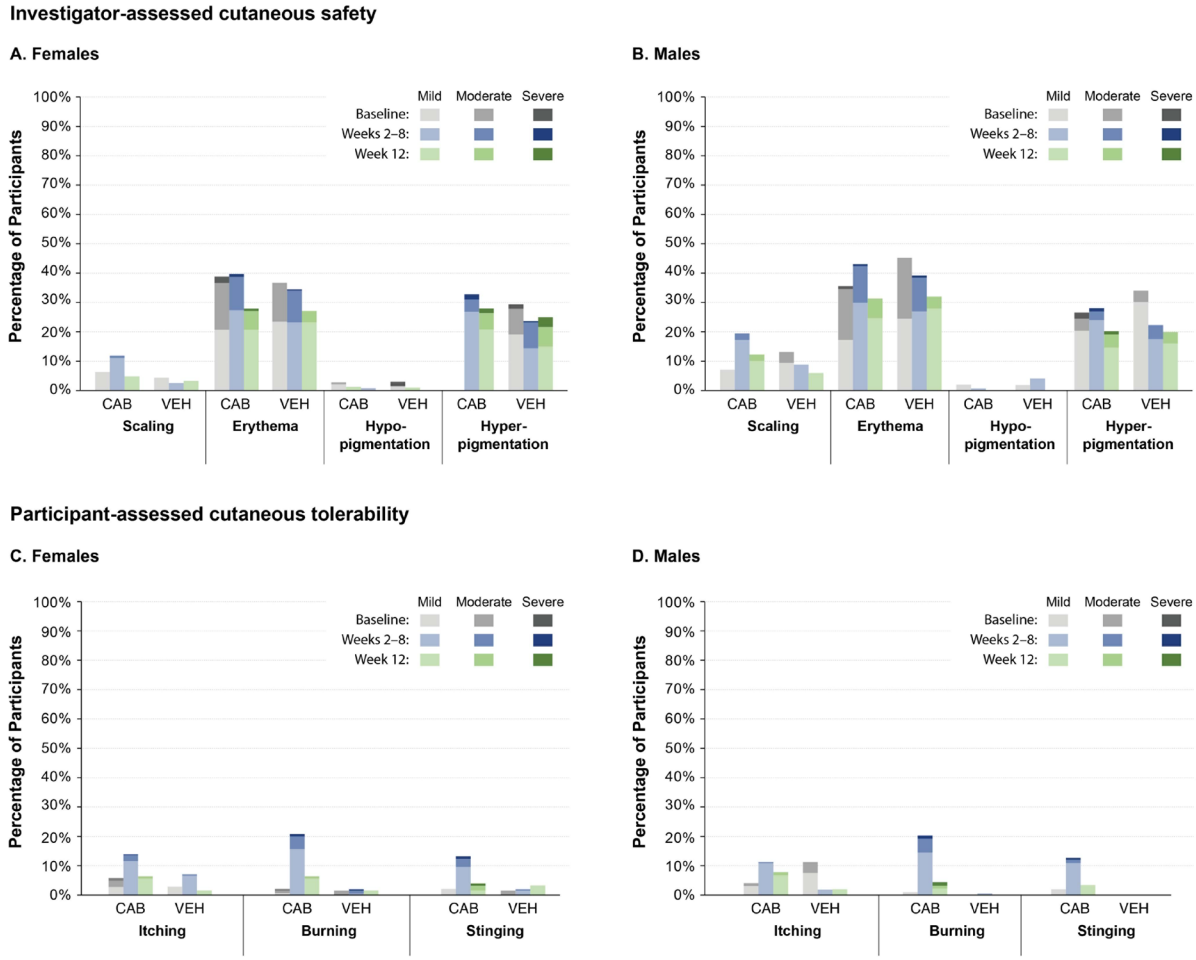
TABLE 3.

Treatment-Emergent Adverse Events Through Week 12 (Safety Population, Pooled)

Participants, n (%)	Females		Males	
	CAB Gel (n=144)	Vehicle Gel (n=68)	CAB Gel (n=98)	Vehicle Gel (n=53)
Reporting any TEAE	39 (27.1)	6 (8.8)	27 (27.6)	4 (7.5)
Serious AEs	0	0	0	0
Discontinued due to a TEAE[a]	4 (2.8)	0	3 (3.1)	0
Maximum Severity of TEAEs reported				
Mild	26 (18.1)	5 (7.4)	14 (14.3)	3 (5.7)
Moderate	11 (7.6)	1 (1.5)	12 (12.2)	1 (1.9)
Severe	2 (1.4)	0	1 (1.0)	0
Relationship to study drug				
Related	28 (19.4)	2 (2.9)	20 (20.4)	0
Unrelated	11 (7.6)	4 (5.9)	7 (7.1)	4 (7.5)
Most common treatment-related TEAEs[b]				
Application site pain	16 (11.1)	1 (1.5)	15 (15.3)	0
Application site dryness	3 (2.1)	0	4 (4.1)	0
Erythema	2 (1.4)	0	4 (4.1)	0
Application site irritation	4 (2.8)	0	1 (1.0)	0
Xerosis	3 (2.1)	1 (1.5)	0	0
Application site exfoliation	3 (2.1)	0	1 (1.0)	0

[a]Includes participants who discontinued study drug or prematurely discontinued from the study.
[b]Reported in ≥2% of participants in any treatment group.
AE, adverse event; CAB, clindamycin phosphate 1.2%/ adapalene 0.15%/ benzoyl peroxide 3.1%; TEAE, treatment-emergent adverse event.

FIGURE 6. Cutaneous safety and tolerability (safety population, pooled).



Participants with mild, moderate, or severe events are shown at baseline (grey shades), pooled weeks 2-8 (blue), and week 12 (green); data for "none" are not shown.
Females BL: CAB n=144, vehicle n=68; weeks 2-8: CAB n=395[a] or 387[b], vehicle n=196[a] or 194[b]; week 12: CAB n=126[a] or 125[b], vehicle n=61[a] or 60[b].
Males BL: CAB n=98, vehicle n=53; weeks 2-8: CAB n=275[a] or 271[b], vehicle n=154[a] or 148[b]; week 12: CAB n=89, vehicle n=50.
[a]For itching, burning, and stinging; [b]For scaling, erythema, hypopigmentation, and hyperpigmentation.
BL, baseline; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; VEH, vehicle.

There were no discernible differences in rates, severity, or changes in cutaneous safety and tolerability assessments for CAB gel between the sexes (Figure 6A-D). At baseline and week 12, a majority (≥61%) of CAB-treated participants of both sexes reported ratings of 0 (none) on cutaneous safety and tolerability evaluations. Erythema and hyperpigmentation were the most reported signs at baseline in both female (38.9%, each) and male (35.7% and 26.5%, respectively) participants. By week 12, both females and males saw improvement in erythema and hyperpigmentation with CAB gel (females, 28.0%, each; males: 31.5% and 20.2%, respectively), with a larger magnitude improvement occurring in females. Transient increases in itching, burning, and stinging between weeks 2 and 8 occurred with CAB treatment in both sexes, but returned close to baseline values by week 12.

DISCUSSION

Differences in cutaneous physiology and acne presentation between the sexes may necessitate distinct approaches to acne treatment. In this pooled post hoc analysis of two phase 3 trials, fixed-dose, triple-combination CAB gel was efficacious and well tolerated in participants with moderate-to-severe acne regardless of sex. In both females and males, 12 weeks of once-daily treatment with CAB was associated with significantly greater treatment success and reductions in inflammatory and noninflammatory lesions compared with vehicle. Further, no statistically significant difference in efficacy outcomes was observed between males and females treated with CAB.

Results from this post hoc analysis are consistent with the individual phase 3[14] and phase 2 studies,[13] in which CAB was

associated with treatment success in around half of participants (range: 49.6-52.5%) and with >70% reductions in inflammatory and noninflammatory lesions (range: 71.0-80.1%). In the phase 2 study, treatment efficacy with CAB was also statistically superior to each of the component dyads.[13] In a meta-analysis, triple-combination therapies like CAB—which include an antibiotic (oral or topical), retinoid (topical), and BPO—were among the two most efficacious of all acne treatments assessed for both treatment success and total lesion count reductions.[10]

While efficacy may be improved by combining 3 active ingredients, a triple-combination product could pose worse tolerability than its individual active components; for example, the use of both retinoids and BPO can be limited by associated dryness, irritation, and erythema.[16,17] However, in this analysis, CAB gel was generally safe and well tolerated in both male and female participants, consistent with findings from the phase 2 and phase 3 studies.[13,14] Moisturizing agents within the CAB gel vehicle, such as propylene glycol, may help reduce irritation common with many acne treatments containing BPO and retinoids.[16,18,19] Additionally, BPO and adapalene in this polymeric formulation have been micronized to allow for even distribution over the skin. This improves their penetration into the pilosebaceous unit, which serves the dual function of enhancing tolerability and boosting treatment efficacy.[16,20] Finally, the anti-inflammatory properties of clindamycin may provide a moderating effect on cutaneous irritation with BPO and adapalene.[21]

In addition to efficacy and good tolerability, it is important that acne therapy improves patients' quality of life. This is particularly important for female patients, for whom the negative impact of acne on quality of life is typically greater than for males.[4,23,24] In keeping with this, Acne-QoL scores in these studies were numerically lower (worse) at baseline among CAB-treated female versus male participants across all domains (range: females, 18.4-19.2; males, 21.7-26.0). CAB-treated females experienced numerically larger QoL improvements from baseline than males (range: females, 6.5-11.2; males, 3.5-6.2) such that at week 12, Acne-QoL domain scores were comparable between groups. Notably, the largest QoL improvement in CAB-treated females was in the domain of self-perception.

CAB gel's fixed-dose formulation combined with its once-daily application confers additional advantages to its optimized efficacy and good tolerability. Delivering 3 ingredients in a simple, fixed-dose treatment regimen may benefit treatment adherence, which is improved when patients are prescribed only one product versus 2 or 3 acne treatments.[9,22] Moreover, including 3 active ingredients in a fixed-dose formulation precludes the development of substance incompatibilities due to application errors that may arise from combining monotherapies (eg, oxidation by using incompatible single agents).[22]

This post hoc analysis is subject to some limitations. First, there might be inter-observer bias and variation associated with global acne severity assessments such as the EGSS.[26] Second, the treatment duration (12 weeks) may not reflect real-world patient experiences, in which acne resolution may take longer than 3 months[27]; however, the rapid and sustained effects of CAB on moderate-to-severe acne within the 12-week timeframe suggests further improvements could occur with continued treatment.[28] Third, patients may be less adherent to treatment in the real world than in a clinical trial.[29] Finally, these studies were not powered for post hoc analyses or to detect treatment-related differences between sexes. Therefore, *P* values from the post hoc analyses in this manuscript are for informative purposes only.

CONCLUSION

In two identical phase 3 studies, treatment with CAB gel (clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%)—the only fixed-dose triple-combination treatment approved for acne—was associated with >70% reductions in inflammatory and noninflammatory lesions and with treatment success in nearly half of both male and female participants. Overall TEAE rates were low, with favorable tolerability. CAB gel is an efficacious and a well-tolerated treatment for acne in both females and males, making CAB an important new treatment option for patients with acne.

DISCLOSURES

Edward (Ted) Lain has served as investigator, consultant and/or speaker for Ortho Dermatologics, AbbVie, Almirall, Amgen, Arcutis, Dermavant, EPI Health, Galderma, Incyte, LEO Pharma, Novartis, Eli Lilly, Pfizer, Sun Pharma, UCB, Endo International, ChemoCentryx, Biorasi, Sirnaomics, Evelo Biosciences, Concert Pharmaceuticals, Cara Therapeutics, Castle Biosciences, Mindera, Biofrontera, Alfasigma, AiViva Biopharma, Anaptys Bio, Bausch Health, Dr Reddy's, and Trevi Therapeutics. Neal Bhatia has served as advisor, consultant, and investigator for AbbVie, Almirall, Biofrontera, BI, Brickell, BMS, EPI Health, Ferndale, Galderma, InCyte, ISDIN, J&J, LaRoche-Posay, LEO Pharma, Ortho Dermatologics, Regeneron, Sanofi, Sun Pharma, Verrica, and Vyne. Leon H. Kircik has served as either a consultant, speaker, advisor, or investigator for Allergan, Almirall, EPI Health, Galderma, Novartis, Ortho Dermatologics, and Sun Pharma. 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 C. Harper has received honoraria from Almirall, Cutera, Galderma, LaRoche-Posay, Ortho Dermatologics, and Sun Pharma. Christopher G. Bunick has served as an investigator for AbbVie, Almirall, Timber, and Palvella; a consultant for AbbVie, Almirall, Apogee, Arcutis, Eli Lilly, EPI Health/Novan, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Sanofi-Regeneron, and UCB; and a speaker for and received honoraria from Allergan, Almirall, LEO Pharma, and UCB. Eric Guenin is an employee of Ortho Dermatologics and may hold stock

and/or stock options in its parent company. Hilary Baldwin has served as an advisor, investigator, and on speakers' bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. Steven R. Feldman has received research, speaking and/or consulting support from BMS, Eli Lilly and Company, GlaxoSmithKline/Stiefel, AbbVie, Janssen, Alovtech, vTv Therapeutics, Bristol-Myers Squibb, Samsung, Pfizer, Boehringer Ingelheim, Amgen, Dermavant, Arcutis, Novartis, Novan, UCB, Helsinn, Sun Pharma, Almirall, Galderma, Leo Pharma, Mylan, Celgene, Ortho Dermatologics, Menlo, Merck & Co, Qurient, Forte, Arena, Biocon, Accordant, Argenx, Sanofi, Regeneron, the National Biological Corporation, Caremark, Teladoc, Eurofins, Informa, UpToDate, and the National Psoriasis Foundation. He is the founder and part owner of Causa Research and holds stock in Sensal Health. James Q. Del Rosso has served as a consultant, investigator, and/or speaker for Ortho Dermatologics, AbbVie, Almirall, Amgen, Arcutis, Biofrontera, Cassiopea, Cutera, Dermavant, EPI Health, Evommune, Galderma, Incyte, JEM Health, Journey, La Roche-Posay, LEO Pharma, Lilly, L'Oreal, MC2 Therapeutics, Novan, Nutrafol, Pfizer, Sente, Strata, Sun Pharma, UCB, and Vyne.

ACKNOWLEDGMENT

This study was funded by Ortho Dermatologics. Medical writing and editorial support were provided by Kavitha Abiraman PhD and Kevin Corcoran PhD from Prescott Medical Communications Group, a Citrus Health Group, Inc., company (Chicago, Illinois), with support from Ortho Dermatologics. Ortho Dermatologics is a division of Bausch Health US, LLC.

REFERENCES

1. Bickers DR, Lim HW, Margolis D, et al. The burden of skin diseases: 2004. A joint project of the American Academy of Dermatology Association and the Society for Investigative Dermatology. *J Am Acad Dermatol.* 2006;55(3):490-500.
2. Luebberding S, Krueger N, Kerscher M. Skin physiology in men and women: In vivo evaluation of 300 people including TEWL, SC hydration, sebum content, and skin surface pH. *Int J Cosmet Sci.* 2013;35(5):477-483.
3. Thiboutot DM, Dreno B, Abanmi A, et al. Practical management of acne for clinicians: An international consensus from the Global Alliance to Improve Outcomes in Acne. *J Am Acad Dermatol.* 2018;78(2 Suppl 1):S1-S23 e21.
4. Skroza N, Tolino E, Mambrin A, et al. Adult acne versus adolescent acne: A retrospective study of 1,167 patients. *J Clin Aesthet Dermatol.* 2018;11(1):21-25.
5. Zeichner JA, Baldwin HE, Cook-Bolden FE, et al. Emerging issues in adult female acne. *J Clin Aesthet Dermatol.* 2017;10(1):37-46.
6. Chang J, Nock MR, Cohen JM, et al. Acne accounts for an almost 2.5-fold higher proportion of dermatology visits among adult females compared to adult males in the United States: A study of the national ambulatory medical care survey from 2002-2016. *PLoS One.* 2023;18(9):e0290763.
7. Stoll S, Shalita AR, Webster GF, et al. The effect of the menstrual cycle on acne. *J Am Acad Dermatol. 2*001;45(6):957-960.
8. Reynolds RV, Yeung H, Cheng CE, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol.* 2024;90(5):1006.e1-1006.e30
9. Moradi Tuchayi S, Alexander TM, Nadkarni A, et al. Interventions to increase adherence to acne treatment. *Patient Prefer Adherence.* 2016;10:2091-2096.
10. 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(4):358-369.
11. Feldman SR, Han G, Callender VD, et al. Benefit of topical combination therapy for acne: Analyzing effect size using number needed to treat. *J Drugs Dermatol.* 2024;23(2):42-49.
12. Cabtreo® [package insert]. Bausch Health US, LLC, Bridgewater, NJ; October 2023.
13. 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(1):93-104.
14. Stein Gold L, Lain E, Del Rosso JQ, et al. Clindamycin phosphate 1.2%, benzoyl peroxide 3.1%, and adapalene 0.15% gel for moderate-to-severe acne: Efficacy and safety results from two randomized phase 3 trials. *J Am Acad Dermatol.* 2023;89(5):927-935.
15. Martin AR, Lookingbill DP, Botek A, et al. Health-related quality of life among patients with facial acne -- assessment of a new acne-specific questionnaire. *Clin Exp Dermatol.* 2001;26(5):380-385.
16. Baldwin H, Webster G, Stein Gold L, et al. 50 years of topical retinoids for acne: Evolution of treatment. *Am J Clin Dermatol.* 2021;22(3):315-327.
17. Foti C, Romita P, Borghi A, et al. Contact dermatitis to topical acne drugs: A review of the literature. *Dermatol Ther.* 2015;28(5):323-329.
18. Hoffman LK, Bhatia N, Zeichner J, et al. Topical vehicle formulations in the treatment of acne. *J Drugs Dermatol.* 2018;17(6):s6-s10.
19. Tanghetti EA, Draelos ZD, Grimes P. Moisturizer use enhances facial tolerability of tazarotene 0.1% cream without compromising efficacy in patients with acne vulgaris. Poster presented at: Fall Clinical Dermatology, Las Vegas, NV, October 2008.
20. Kircik LH, Draelos ZD, Berson DS. Polymeric emulsion technology applied to tretinoin. *J Drugs Dermatol.* 2019;18(4):s148-154.
21. Del Rosso JQ, Schmidt NF. A review of the anti-inflammatory properties of clindamycin in the treatment of acne vulgaris. *Cutis.* 2010;85(1):15-24.
22. Thielitz A, Gollnick H. Recent therapeutic developments for acne. *Exp Rev Dermatol.* 2013;8(1):37-50.
23. Tan JK, Li Y, Fung K, et al. Divergence of demographic factors associated with clinical severity compared with quality of life impact in acne. *J Cutan Med Surg.* 2008;12(5):235-242.
24. Berg M, Lindberg M. Possible gender differences in the quality of life and choice of therapy in acne. *J Eur Acad Dermatol Venereol.* 2011;25(8):969-972.
25. Tanghetti EA, Stein Gold L, Del Rosso JQ, et al. Optimized formulation for topical application of a fixed combination halobetasol/tazarotene lotion using polymeric emulsion technology. *J Dermatolog Treat.* 2021;32(4):391-398.
26. Tan JK, Fung K, Bulger L. Reliability of dermatologists in acne lesion counts and global assessments. *J Cutan Med Surg.* 2006;10(4):160-165.
27. Eichenfield DZ, Sprague J, Eichenfield LF. Management of acne vulgaris: A review. *JAMA.* 2021;326(20):2055-2067.
28. Harper JC, Kircik LH, Gold M, et al. Early and sustained acne lesion reductions with fixed-dose clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel. *J Drugs Dermatol.* 2024;23(3):125-131.
29. Carls GS, Tuttle E, Tan RD, et al. Understanding the gap between efficacy in randomized controlled trials and effectiveness in real-world use of GLP-1 RA and DPP-4 therapies in patients with type 2 diabetes. *Diabetes Care.* 2017;40(11):1469-1478.

AUTHOR CORRESPONDENCE

Edward (Ted) Lain MD MBA
E-mail:.....drlain@atxresearch.com