

Efficacy and Safety of Fixed-Dose Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Compared With Adapalene 0.3%/Benzoyl Peroxide 2.5% Gel in Participants With Moderate to Severe Acne

Zoe D. Draelos, MD¹; Hilary Baldwin, MD^{2,3}; Neal Bhatia, MD⁴; Lawrence F. Eichenfield, MD^{5,6}; Karol Wroblewski, PharmD⁷; Dawn Z. Eichenfield, MD, PhD^{5,6}; Leon H. Kirck, MD⁸⁻¹⁰

¹Dermatology Consulting Services, PLLC, High Point, North Carolina; ²The Acne Treatment and Research Center, Brooklyn, New York; ³Robert Wood Johnson University Hospital, New Brunswick, New Jersey; ⁴Therapeutics Clinical Research, San Diego, California; ⁵University of California, San Diego School of Medicine, La Jolla, California; ⁶Rady Children's Hospital, San Diego, California; ⁷Rutgers University, New Brunswick, New Jersey; ⁸Icahn School of Medicine at Mount Sinai, New York, New York; ⁹Indiana University School of Medicine, Indianapolis, Indiana; ¹⁰Physicians Skin Care, PLLC, DermResearch, PLLC, and Skin Sciences, PLLC, Louisville, Kentucky

SYNOPSIS

- The American Academy of Dermatology guidelines for treating mild to severe acne strongly recommend a combination of topical retinoids, benzoyl peroxide (BPO), and/or topical or oral antibiotics¹
- Topical clindamycin phosphate 1.2%/adapalene 0.15%/BPO 3.1% (CAB) polymeric mesh gel is the only fixed-dose, triple-combination formulation approved for acne treatment and is indicated for use in patients aged ≥ 12 years^{2,3}
- CAB showed superior efficacy to component dyads and vehicle, with good tolerability and safety in one phase 2 and two phase 3 clinical trials of participants with moderate to severe acne³⁻⁵
- Results from a second phase 2 trial of CAB gel are reported here

OBJECTIVE

- To compare efficacy and safety of CAB gel in a head-to-head trial vs commercially available adapalene 0.3%/BPO 2.5% (ADAP/BPO) gel

METHODS

- In a phase 2, double-blind, 12-week clinical trial (NCT04892706), participants with moderate to severe acne aged ≥ 12 years were randomized (2:2:1) to once-daily CAB, ADAP/BPO, or 1 of 2 vehicle gels (combined for analysis)
- Copriary endpoints included percentage of participants achieving treatment success (≥ 2 -grade reduction from baseline in Evaluator's Global Severity Score [EGSS] and clear/almost clear skin) and least squares (LS) mean absolute change from baseline in inflammatory and noninflammatory lesion counts at week 12
 - Secondary endpoints included LS mean percent change from baseline in lesion counts at weeks 2, 4, 8, and 12
- Copriary endpoints were further analyzed by subgroups defined by participant age (< 18 or ≥ 18 y) and sex
- Participants were considered treatment adherent if they did not miss > 5 consecutive treatment days and had applied 80%-120% of the study treatment
- Treatment-emergent adverse events (TEAEs) were evaluated throughout
- Investigator-assessed cutaneous safety (scaling, erythema, hypopigmentation, hyperpigmentation) and participant-assessed tolerability (itching, burning, stinging) were scored at all visits on a 4-point scale (0=none to 3=severe)

RESULTS

Participants

- A total of 686 participants were enrolled, of whom 2 did not receive study drug
 - Most participants were female and White (Table 1), with a mean age (SD) across all treatments of 20.1 (7.6) years
 - The majority of participants had an EGSS of 3 (moderate) at baseline (Table 1)

TABLE 1. Baseline Participant Demographics and Characteristics (ITT Population)

Characteristic	CAB Gel (n=230)	ADAP/BPO Gel (n=226)	Vehicle Gel ^a (n=228)
Age, mean (SD), y	20.3 (7.9)	20.5 (7.6)	19.5 (7.1)
Age, median (range), y	17.5 (12-56)	18.0 (12-51)	17.0 (12-49)
Age group, n (%)			
<18 y	115 (50.0)	110 (48.7)	125 (54.8)
≥ 18 y	115 (50.0)	116 (51.3)	103 (45.2)
Sex, n (%)			
Female	140 (60.9)	135 (59.7)	131 (57.5)
Race, n (%)			
White	179 (77.8)	165 (73.0)	160 (70.2)
Black/African American	24 (10.4)	26 (11.5)	28 (12.3)
Asian	16 (7.0)	19 (8.4)	27 (11.8)
Other ^b	11 (4.8)	16 (7.1)	13 (5.7)
Ethnicity, n (%)			
Hispanic or Latino	48 (20.9)	53 (23.5)	48 (21.1)
Lesion count, mean (SD)			
Inflammatory	39.3 (11.8)	37.9 (9.1)	39.0 (10.8)
Noninflammatory ^c	54.4 (21.1)	50.1 (18.9)	51.2 (19.6)
Evaluator's Global Severity Score, n (%)			
3-Moderate	201 (87.4)	198 (87.6)	204 (89.5)
4-Severe	29 (12.6)	28 (12.4)	24 (10.5)

^aThe 2 vehicle groups were combined for analysis.
^bIncludes American Indian or Alaska Native, multiple, and unknown/not reported.
^cThere was a significant difference between the treatment groups ($P=0.014$) but it was not considered to have a meaningful effect on efficacy outcomes.
 ADAP/BPO, adapalene 0.3%/benzoyl peroxide 2.5% gel; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat.

Efficacy

- At week 12, half of participants achieved treatment success with CAB vs one-third with ADAP/BPO ($P<0.001$ vs CAB) vs less than one-fifth with vehicle ($P<0.001$ vs CAB and ADAP/BPO; Table 2 and Figure 1)
- Absolute mean reductions from baseline in lesion counts were significantly greater with CAB or ADAP/BPO vs vehicle ($P<0.001$, both; Table 2)
- Percent lesion reductions at week 12 were $> 71\%$ with CAB and $> 67\%$ with ADAP/BPO vs $\sim 50\%$ with vehicle ($P<0.001$, both; Table 2 and Figure 2)
 - Percent lesion reductions were also significantly greater vs vehicle at weeks 2, 4, and 8 for CAB ($P<0.05$, all) and weeks 4 and 8 for ADAP/BPO ($P\leq 0.01$, all; Figure 2)

TABLE 2. Efficacy Endpoints at Week 12 (ITT Population)

Endpoint	CAB Gel (n=230)	ADAP/BPO Gel (n=226)	Vehicle Gel ^a (n=228)
Copriary endpoints			
Treatment success, % ^b	51.3***, ###	32.9***	18.0
Absolute change from baseline, LS mean (SD)			
Inflammatory lesions	-29.9 (11.4)***	-27.9 (12.2)***	-19.7 (13.1)
Noninflammatory lesions	-36.8 (16.1)***	-34.4 (17.3)***	-22.7 (17.4)
Secondary endpoints^c			
Percentage change from baseline, LS mean (SD)			
Inflammatory lesions	-76.8 (28.7)***	-73.0 (31.3)***	-51.5 (32.9)
Noninflammatory lesions	-71.8 (29.4)***	-67.2 (33.1)***	-46.4 (32.1)

*** $P<0.001$ vs vehicle gel; ### $P<0.001$ vs ADAP/BPO gel.
 Values have been adjusted for multiple imputation (Markov Chain Monte Carlo).
^aThe two vehicle groups were combined for analysis.
^bDefined as ≥ 2 -grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 (clear) or 1 (almost clear).
^cSecondary endpoints not shown here comprise treatment success and absolute changes in lesion counts at weeks 2, 4, and 8; percent changes in lesion counts at weeks 2, 4, and 8; and 2-grade reduction in trunical severity score at weeks 2, 4, 8, and 12.
 ADAP/BPO, adapalene 0.3%/benzoyl peroxide 2.5%; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; LS, least squares.

- Images showing acne improvements with CAB are shown in Figure 3
- Treatment success rates and absolute lesion reductions in participants stratified by age and sex were in line with the overall population (data not shown)

FIGURE 1. Treatment Success^a at Week 12 (ITT Population)

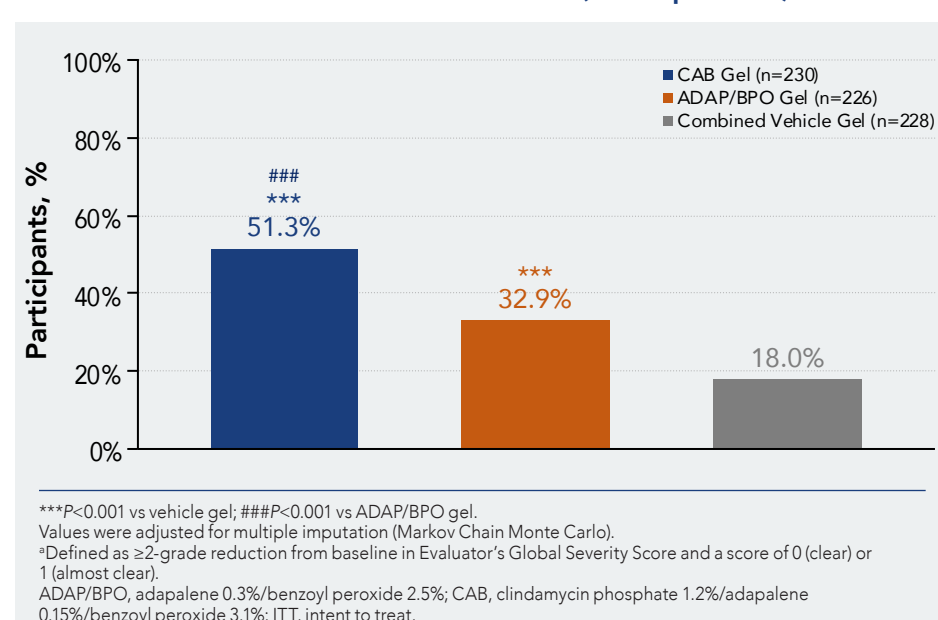


FIGURE 2. Lesion Reductions by Visit (ITT Population)

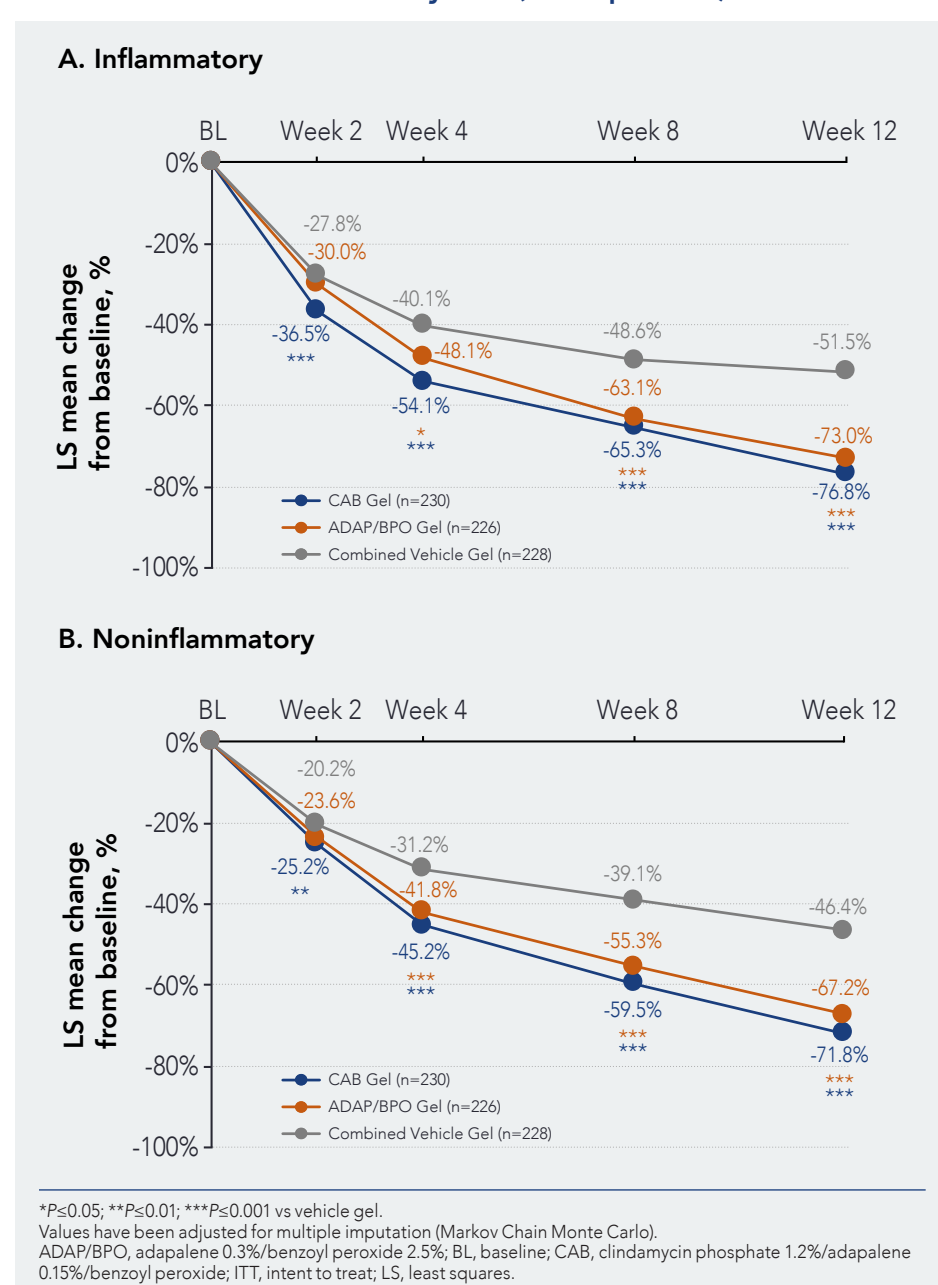
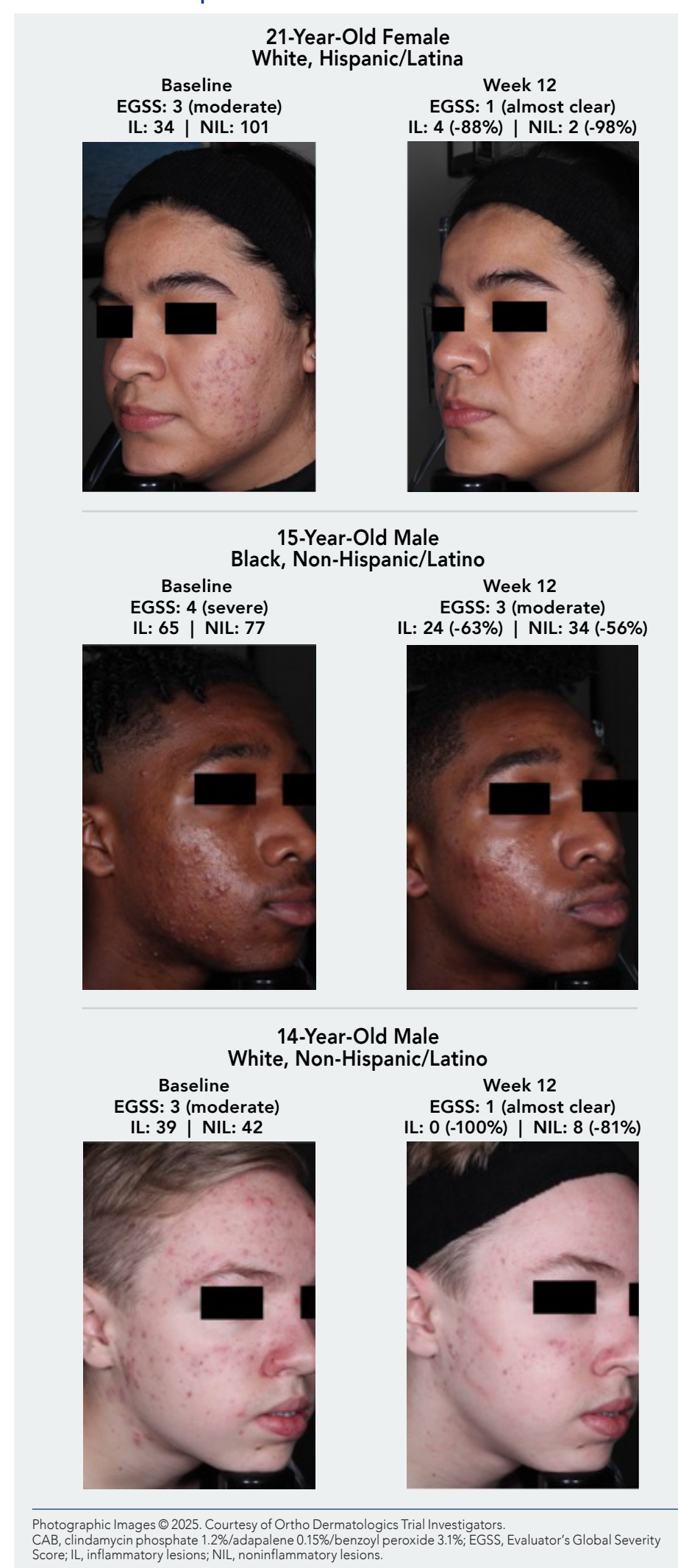


FIGURE 3. Acne Improvements With CAB Gel



Safety

- TEAE rates with CAB and ADAP/BPO were similar, and most TEAEs were of mild or moderate severity (Table 3)
- For CAB-treated participants, TEAE rates were similar to the other phase 2 and the two phase 3 trial populations (24.6%-36.2%)³⁻⁵
- Mean cutaneous and tolerability scores remained low (< 0.8) in both active treatment groups during the trial (where 1=mild)

TABLE 3. TEAEs Through Week 12 (Safety Population)

Participants, n (%)	CAB Gel (n=230)	ADAP/BPO Gel (n=226)	Vehicle Gel ^a (n=228)
TEAEs	83 (36.1)	79 (35.0)	39 (17.1)
Related to treatment	39 (17.0)	44 (19.5)	5 (2.2)
Serious AEs related to treatment	0	0	0
Discontinued drug or study due to AE	6 (2.6)	8 (3.5)	0
TEAE severity			
Mild	43 (18.7)	49 (21.7)	22 (9.6)
Moderate	38 (16.5)	28 (12.4)	16 (7.0)
Severe	2 (0.9)	2 (0.9)	1 (0.4)
Most common treatment-related TEAEs ($\geq 2\%$ participants in any treatment)			
AS pain	22 (9.6)	16 (7.1)	0
AS dryness	9 (3.9)	11 (4.9)	2 (0.9)
AS dermatitis	3 (1.3)	7 (3.1)	0
AS irritation	2 (0.9)	6 (2.7)	2 (0.9)

^aThe two vehicle gel groups were combined for analysis.
 ADAP/BPO, adapalene 0.3%/benzoyl peroxide 2.5%; AE, adverse event; AS, application site; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- Fixed-dose, triple-combination polymeric mesh CAB gel was efficacious and well tolerated in participants with moderate to severe acne over 12 weeks, consistent with results from other CAB phase 2 and 3 clinical trials³⁻⁵
- In this head-to-head trial, CAB was statistically superior to commercially available ADAP/BPO gel with regard to treatment success at week 12, provided $> 70\%$ lesion reductions, showed efficacy as early as week 2, and was efficacious regardless of participant age or sex
- CAB also demonstrated a good safety and tolerability profile

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AUTHOR DISCLOSURES

Zoe D. Draelos received funding from Ortho Dermatologics. Hilary Baldwin has served as advisor, investigator, and on speakers bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. Neal Bhatia has served as advisor, consultant, and investigator for AbbVie, Almirall, Biofrontera, BI, Brickell, BMS, EPI Health, Ferridale, Galderma, Incyte, ISDIN, Johnson & Johnson, LaRoche-Posay, LEO Pharma, Ortho Dermatologics, Regeneron, Sanofi, Sun Pharma, Verrica, and Vyne. Lawrence F. Eichenfield has received honoraria for consulting services from AbbVie, BMS, Amgen, Arcutis, Dermata, Dermira, Dermavant, Eli Lilly, Forte Pharma, Galderma, Incyte, Johnson & Johnson, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi Genzyme, and Ortho Dermatologics and study support (to institution) from AbbVie, Amgen, Bausch Health, Dermata, Dermira, Eli Lilly, Galderma, Incyte, Pfizer, Regeneron Pharmaceuticals, Inc., and Sanofi Genzyme. Karol Wroblewski has nothing to disclose. Dawn Z. Eichenfield has served as a consultant, speaker, or investigator for Arcutis, Chiesi, Apogee, Beiersdorf, Eli Lilly and Company, Galderma, Incyte, Johnson & Johnson, Nobelpharma, Ortho Dermatologics, Pelthos, Regeneron Pharmaceuticals, Sanofi Genzyme, Solis, Sun Pharmaceutical, and Verrica. Leon H. Kirck has served as a consultant, speaker, advisor, or an investigator for Allergan, Almirall, EPI Health, Galderma, Novartis, Ortho Dermatologics, and Sun Pharma.