# Fixed-Dose Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel for Moderate-to-Severe Acne: Comparison of 4 Clinical Trials

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## SYNOPSIS

- Combination therapies targeting multiple processes of acne pathogenesis are recommended for most acne patients[1]
- A three-pronged treatment approach using an antibiotic, retinoid, and antibacterial may increase treatment efficacy versus monotherapy or dual-combination treatments[2]
- Simplifying the treatment regimen by delivering multiple ingredients as fixed combinations may contribute to treatment efficacy by fostering greater patient adherence[3]
- Clindamycin phosphate (CLIN) 1.2%/adapalene (ADAP) 0.15%/benzoyl peroxide (BPO) 3.1% (CAB; Cabtree®; Ortho Dermatologics) is the first fixed-dose triple-combination topical approved for the treatment of acne

## OBJECTIVE

- Evaluate efficacy and safety of once-daily CAB gel across four clinical studies of participants with moderate-to-severe acne, with a focus on treatment success and effect size

## OVERVIEW OF CLINICAL STUDIES

- Participants in two phase 2 and two phase 3, double-blind, 12-week studies were randomized to once-daily treatment with CAB gel, a dyad combination of the active ingredients, or vehicle (**Figure 1**)
  - One phase 2 study included treatment arms with BPO/ADAP, CLIN/BPO, and CLIN/ADAP dyads formulated at the same concentrations and in the same vehicle as CAB gel
  - The other phase 2 study was a head-to-head comparison of CAB and branded ADAP 0.3%/BPO 2.5% gel (Epiduo® Forte; Galderma)
- Across studies, treatment success at week 12, defined as the percentage of participants with ≥2-grade reduction from baseline in Evaluator's Global Severity Score (EGSS) and a score of 0 or 1 (clear or almost clear skin), was a co-primary endpoint
  - Additional co-primary endpoints were change from baseline to week 12 in inflammatory and noninflammatory lesions (data not presented here)
- Treatment-emergent adverse effects were also assessed

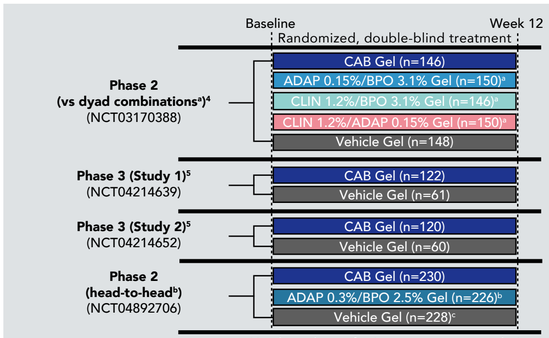
## EFFICACY AND SAFETY RESULTS

- In all studies, a significantly greater percentage of CAB-treated participants achieved treatment success at week 12 than participants treated with dyad combination or vehicle gels ($P \leq 0.001$, all; **Figure 2**)
- Inclusion of clindamycin phosphate as a third active ingredient did not negatively affect safety/tolerability of CAB gel (**Figure 3**)
  - In both phase 2 studies, rates of discontinuations and treatment-related adverse events were similar or lower with CAB gel than with ADAP/BPO dyads (not shown)
  - This may be due to the CAB vehicle formulation and/or the anti-inflammatory properties of clindamycin, which can provide a moderating effect on the cutaneous safety and tolerability of BPO and ADAP[4,5]
- Representative photographs of participants treated with CAB gel are shown in **Figure 4**

## POST HOC ANALYSIS: NUMBER NEEDED TO TREAT

- A post hoc analysis of number needed to treat (NNT) was conducted to provide a measure of treatment effect and indirectly compare data across the studies (**Figure 5**)
- NNT values for CAB gel ranged from 3-5, and were lower overall (more favorable) than for any of the dyad combination gels, including branded ADAP 0.3%/BPO 2.5% gel (**Figure 6**)

### FIGURE 1. Randomized, Double-Blind, 12-Week Studies of CAB Gel




**ALL STUDIES**

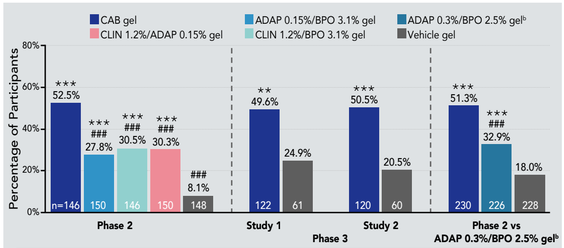
**Key Eligibility Criteria:**
- Aged ≥9 years (≥12 years in NCT04892706)
- EGSS 3 (moderate) or 4 (severe)
- Inflammatory lesions: 30–100
- Noninflammatory lesions: 35–150

**Co-Primary Endpoints:**
- Treatment success[d]
- Change from baseline in inflammatory and noninflammatory lesion counts

**Baseline Demographics/Characteristics:**
- Mean age ranged from 19.2–21.4 years across all studies
- Most participants were female, White, and non-Hispanic, with EGSS=3 (moderate)

[a]Dyad combinations were formulated at the same concentrations and in the same vehicle as CAB gel.
[b]Branded product (Epiduo® Forte; Galderma).
[c]Combined vehicle groups (gel stored at either 2-8 °C or room temp).
[d]Defined as a ≥2-grade reduction from baseline in EGSS and a score of 0 (clear) or 1 (almost clear).
ADAP, adapalene; BPO, benzoyl peroxide; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate; EGSS, Evaluator's Global Severity Score.

### FIGURE 2. Treatment Success[a] at Week 12 (ITT Populations)




In all four studies, **~50% of CAB-treated participants achieved treatment success**, significantly greater than vehicle or any dyad combination, including branded adapalene 0.3%/BPO 2.5% gel

**P<0.01; ***P≤0.001 vs vehicle. ###P≤0.001 vs CAB gel.
[a]Defined as 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).
[b]Branded product.
ADAP, adapalene; BPO, benzoyl peroxide; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate; ITT, intent to treat.

### FIGURE 3. CAB Gel Safety and Tolerability Across Studies (Safety Populations)

**Across four studies, CAB gel was well tolerated**


Most TEAEs were of mild-to-moderate severity[a,b]

Low rates of discontinuation due to AEs[a,c]

Mean cutaneous safety/tolerability scores all <1 (mild)[d]

[a]Rates for TEAE severity and discontinuations[c] were calculated using data pooled from the four studies.
[b]The most common treatment-related TEAEs (occurring in ≥2% of CAB-treated participants in any study) were: application site dermatitis, dryness, erythema, exfoliation, irritation, pain, and pruritus; erythema; and xerosis.
[c]Discontinuation of study or treatment.
[d]Investigator-assessed scaling, erythema, hyperpigmentation, and hypopigmentation and participant-assessed itching, burning, and stinging at any timepoint during the study. Assessments were made on a 4-point scale from 0 (none) to 3 (severe).
AE, adverse event; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; TEAE, treatment-emergent adverse event.

## CONCLUSIONS

- CAB gel—the first and only fixed-dose, triple-combination topical treatment approved for acne—consistently demonstrated efficacy, safety, and tolerability in participants with moderate-to-severe acne
- In 4 clinical trials, half of CAB-treated participants achieved treatment success at week 12, significantly greater than the approximately one third with dyad combinations (including branded ADAP 0.3%/BPO 2.5% gel)
- Triple-combination CAB gel had the lowest (most favorable) NNT values
- Due to the multifactorial pathogenesis of acne, a triple-combination topical treatment may result in clinical success more often than monotherapy or two-ingredient combination products

### REFERENCES

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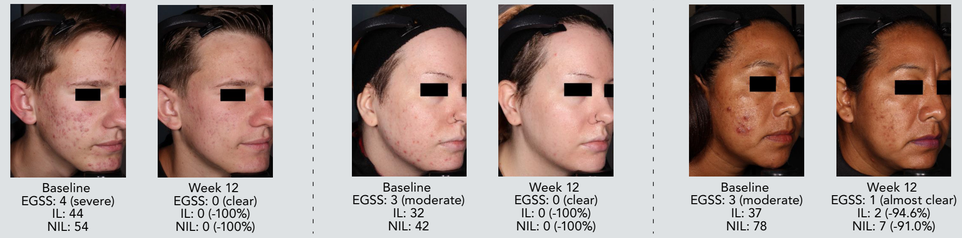
### AUTHOR DISCLOSURES

Leon H Kircik has served as either a consultant, speaker, advisor or an investigator for Allergan, Almirall, Epi Health, Galderma, Novartis, Ortho Dermatologics, and Sun Pharma. Zoe Draelos has received funding from Ortho Dermatologics. Michael Gold has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. Neil Sadick has served on advisory boards, as a consultant, investigator, speaker, and/or other and has received honoraria and/or grants/research funding from Almirall, Actavis, Allergan, Anacor Pharmaceuticals, Auxilium Pharmaceuticals, Bausch Health, Bayer, Biorasi, BTG, Carma Laboratories, Cassiopea, Celgene Corporation, Cutera, Cynosure, DUSA Pharmaceuticals, Eclipse Medical, Eli Lilly and Company, Endo International, EndyMed Medical, Ferndale Laboratories, Galderma, Gerson Lehrman Group, Hydropeptide, Merz Aesthetics, Neostrata, Novartis, Nutraceutical Wellness, Palomar Medical Technologies, Prescriber's Choice, Regeneron, Roche Laboratories, Samumed, Solta Medical, Storz Medical AG, Suneva Medical, Vanda Pharmaceuticals, and Venus Concept. 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, SunPharma, Verrica, and Vyne.

### FIGURE 4. Acne Improvements With CAB Gel

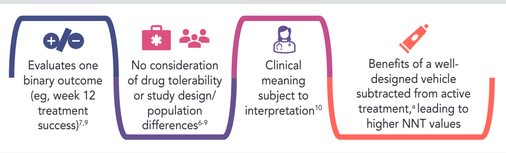



Individual results may vary.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; EGSS, Evaluator's Global Severity Score; IL, inflammatory lesions; NIL, noninflammatory lesions.

### FIGURE 5. Number Needed to Treat (NNT)

**WHAT IS NNT?**
- NNT is a metric for quantifying effect sizes of clinically relevant study endpoints[6]
- NNT represents the number of patients needed to treat to achieve an additional cure in a given timeframe[6-8]
  - For example, NNT=3 means that 3 patients would need to be treated with active drug rather than vehicle before expecting an additional responder[7]

**WHAT ARE SOME LIMITATIONS OF NNT?**



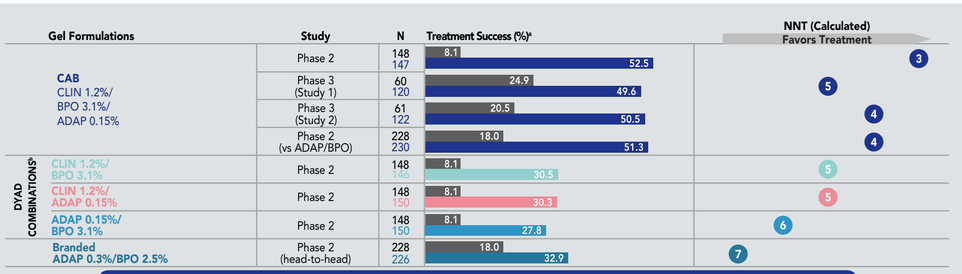

**HOW IS NNT USED?**
- In the absence of head-to-head studies, NNT may be used to indirectly assess comparative efficacy of treatments
  - Evaluation of NNT has been conducted in a variety of therapeutic areas, including psychiatry/neurology, cardiology, oncology, and dermatology
- While a clinically relevant NNT threshold has not been established for acne, lower values indicate more favorable treatment (larger effect size) versus vehicle

**HOW IS NNT CALCULATED?**
- NNT is the reciprocal of the absolute risk reduction (ARR), rounded up to the nearest whole number[6-8]

$$\frac{1}{(\%\ \text{Success With Active Treatment} - \%\ \text{Success With Vehicle})} * 100$$

[a]Due to the potential for a well-designed vehicle to result in higher efficacy rates in the control group.

### FIGURE 6. Comparison of Number Needed to Treat (ITT Populations)




**NNT values were lowest (most favorable) with CAB gel**

Grey bars indicate treatment success rates with vehicle for each study.
[a]Defined as 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).
[b]Dyad combinations were formulated in the same vehicle as CAB gel.
ADAP, adapalene; BPO, benzoyl peroxide; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate; ITT, intent to treat; NNT, number needed to treat.

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