Early Acne Improvements With Fixed-Dose Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel: What to Expect in the First 4 Weeks of Treatment

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SYNOPSIS

- Treatments associated with fast and substantial clearance of acne lesions, as well as those that can cause fewer side effects, can increase patient adherence[1]
- While the term "acne improvement" may vary from person-to-person, a previous study has suggested that a 10-15% reduction in facial acne lesions may be relevant to patients[2]
- A three-pronged approach using once-daily application of an antibiotic, retinoid, and antibacterial may increase treatment efficacy versus monotherapy or dual-combination products,[3] though it is unknown if triple-combination would provide more rapid improvement
- The first triple-combination, fixed-dose topical approved for acne—clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide (BPO) 3.1% gel (CAB; Cabtreo™, Ortho Dermatologics)—was efficacious and well tolerated in three clinical studies, with lesion reductions of >70% after 12 weeks of treatment[4,5]

OBJECTIVE

- To evaluate the efficacy and safety of CAB gel in the first 4 weeks of treatment compared with its dyad components and vehicle gel

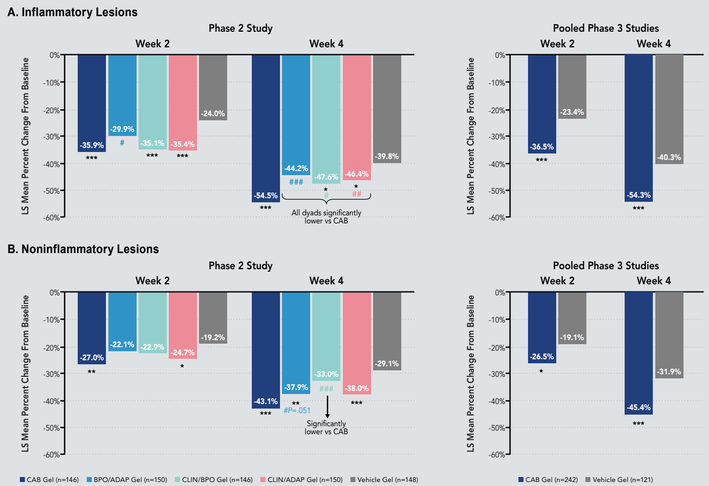
METHODS

- A phase 2 (N=741; NCT03170388) and two phase 3 (N=183; N=180; NCT04214639; NCT04214652), double-blind, 12-week studies enrolled participants aged ≥9 years with moderate-to-severe acne
- Participants were randomized to receive once-daily CAB or vehicle gel; the phase 2 study included three additional dyad gel randomization arms: BPO/adapalene; clindamycin phosphate/BPO; and clindamycin phosphate/adapalene
  - CeraVe® hydrating cleanser and CeraVe® moisturizing lotion (L'Oreal, NY) were provided as needed for optimal moisturization/cleaning of the skin
- Efficacy assessments included least-squares mean percent change from baseline in inflammatory and noninflammatory lesion counts
- Cutaneous safety and tolerability assessments were graded on a 4-point scale (0=none; 3=severe)
- Post hoc analyses included the percentage of participants achieving a one-third and one-half reduction in acne lesions

RESULTS

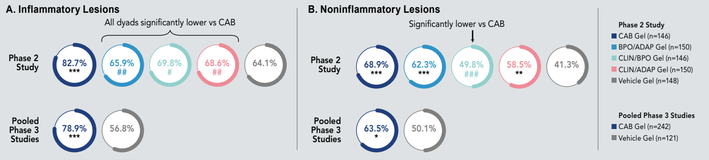
- At week 4, CAB led to ~55% reductions from baseline in inflammatory acne lesions, significantly greater than vehicle and its 3 dyads (range: 39.8%-47.6%; *P*<0.05, all; **Figure 1A**)
  - Improvements with CAB were also greater versus vehicle at week 2 (*P*<0.001), though there was no statistical separation from the dyads at this time point
- The percentage of participants with a one-third reduction of their inflammatory lesions at week 4 was substantial with CAB (~80%), and significantly greater than vehicle and dyads (range: 56.8-69.8%; *P*<0.05, all; **Figure 2A**)
- Overall, one-half reductions in inflammatory lesions were achieved by ~60% of CAB-treated participants at week 4, significantly greater than vehicle and dyads (range: 37.9-47.4%; *P*<0.05, all; **Figure 3A**)
- Generally similar trends were observed for noninflammatory lesions, though reductions were less pronounced than for inflammatory lesions (**Figures 1B, 2B, and 3B**)
- Images of representative CAB-treated participants are shown in **Figure 4**
- Transient increases from baseline to week 2 in scaling, erythema, itching, burning, and stinging were observed for CAB, BPO/adapalene, and clindamycin phosphate/adapalene, with scores beginning to normalize by week 4 (**Figure 5**); this retinization period is expected for retinoids such as adapalene
  - The greatest increases from baseline were observed for scaling, burning, and stinging, though mean scores for all active treatments remained ≤0.6 (1=mild)
  - No trends in dyspigmentation were observed
- Mean scores for all cutaneous assessments in the first 4 weeks of treatment were highest for the dyad BPO/adapalene (**Figure 5**)
- The improved cutaneous profile of CAB compared with BPO/adapalene may be due to the following[4]:
  - The polymeric technology of CAB gel, which provides more uniform distribution of active ingredients, and/or
  - The addition of clindamycin, which may be providing a moderating effect on safety/tolerability through its anti-inflammatory properties

FIGURE 1. Percent Change From Baseline in Acne Lesion Counts: First Month of Treatment



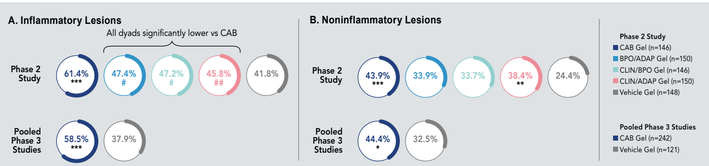
*P<0.05, **P<0.01, ***P<0.001 vs vehicle.
#P<0.05, ##P<0.01, ###P<0.001 vs CAB.
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; LS, least squares.

FIGURE 2. Percentage of Participants With One-Third Reduction in Acne Lesions at Week 4



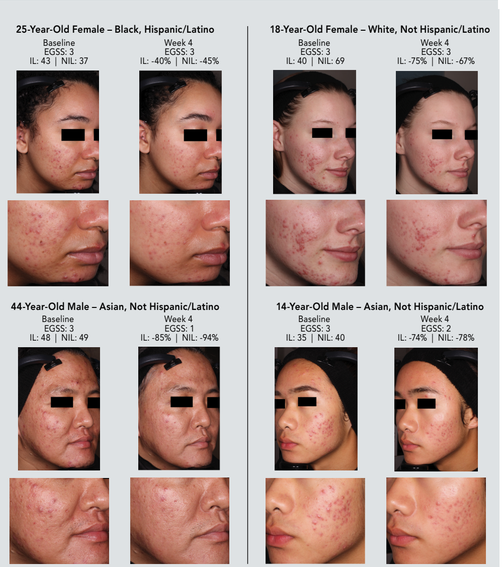
*P<0.05, **P≤0.01, ***P<0.001 vs vehicle.
#P<0.05, ##P<0.01, ###P≤0.001 vs CAB.
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%.

FIGURE 3. Percentage of Participants With One-Half Reduction in Acne Lesions at Week 4



*P<0.05, **P≤0.01, ***P≤0.001 vs vehicle.
#P<0.05, ##P<0.01 vs CAB.
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%.

FIGURE 4. Acne Improvements with CAB Gel From Baseline to Week 4

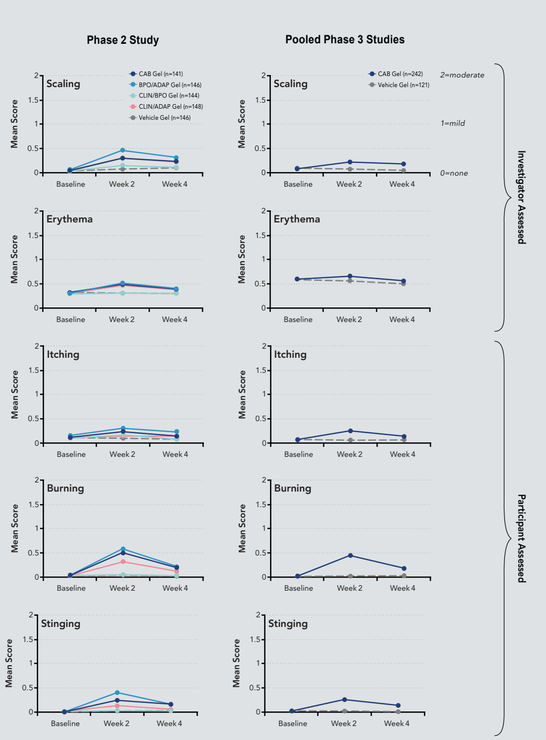


Individual results may vary.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; EGSS, Evaluator's Global Severity Score (0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe); IL, inflammatory lesions; NIL, noninflammatory lesions.

CONCLUSIONS

- Fixed-dose, triple-combination clindamycin phosphate 1.2%/adapalene 0.15%/BPO 3.1% (CAB) gel was well tolerated, with rapid therapeutic effects
  - Acne lesion reductions were significantly greater with triple-combination gel versus its dyads and vehicle gel as early as week 4
  - Cutaneous safety and tolerability assessments with CAB were better than BPO/adapalene, indicating that the additional product in the triple combination did not worsen tolerability
- While extended acne treatment is recommended to achieve clear skin, the faster-acting efficacy of the first triple-combination acne product—coupled with its optimized formulation, once-daily dosing, and tolerability—may positively impact patient satisfaction and treatment adherence

FIGURE 5. Cutaneous Safety and Tolerability Assessments: First Month of Treatment



Cutaneous safety and tolerability assessments were graded on a 4-point scale (0=none; 1=mild; 2=moderate; 3=severe). Investigator-assessed hyperpigmentation and hypopigmentation are not shown, as no trends in dyspigmentation were observed.
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%.

REFERENCES

1. Sevimli Dikicier B. *J Int Med Res*. 2019;47(7):2987-2992.
2. Gerlinger, et al. *Ther Innov Regul Sci*. 2008;42:607–615.
3. Huang CY, et al. *Ann Fam Med*. 2023;21(4):358-369.
4. Stein Gold L, et al. *Am J Clin Dermatol*. 2022;23(1):93-104.
5. Stein Gold L, et al. *J Am Acad Dermatol*. 2023;89(5): 927-935.

AUTHOR DISCLOSURES

Julie Harper has received honoraria from Aclaris, Almirall, BioPharmX, Cassiopea, Cutanea, Dermira, Foamix, Galderma, LaRoche-Posay, Ortho Dermatologics, and Sun. Leon Kircik has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. Michael Gold has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. Adelaide A. Hebert has received honoraria from Galderma, LEO Pharma, Amirall, Cassiopea, Ortho Dermatologics, Cutanea, Ferrer, Pfizer, Demira; the UTHealth McGovern Medical School had received research grants from Cassiopea, Demira, Ortho Dermatologics. Jeffrey L Sugarman is a consultant for Ortho Dermatologics, Bausch Health, Regeneron, Sanofi, Verrica, and Pfizer. Lawrence Green has served as investigator, consultant, or speaker for Almirall, Cassiopea, Galderma, Ortho Dermatologics, Sol Gel, Sun Pharma, and Vyne. 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. Hilary Baldwin has served as advisor, investigator, and on speakers' bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. James Q. Del Rosso has served as a consultant, investigator, and/or speaker for Ortho Dermatologics, AbbVie, Amgen, Arcutis, Dermavant, EPI Health, Galderma, Incyte, LEO Pharma, Lilly, MC2 Therapeutics, Pfizer, Sun Pharma, and UCB. Eric Guenin is an employee of Ortho Dermatologics and may hold stock and/or stock options in its parent company.

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