Efficacy and Safety of Fixed-Dose Triple-Combination Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel for Moderate-to-Severe Acne Vulgaris in Children and Adolescents

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SYNOPSIS

- Acne vulgaris is one of the most common dermatologic disorders worldwide, most frequently affecting adolescents[1,2]
- Topical acne treatment in pediatric or adolescent patients may be complicated by tolerability issues and/or a perceived lack of efficacy[3,4]
- Combining topical treatments that target multiple pathogenic factors in a single, once-daily formulation may improve efficacy and adherence[3,5]
- Topical clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel (CAB; Cabtreo™, Ortho Dermatologics) is the first fixed-dose triple-combination formulation approved for acne vulgaris and is indicated for use in patients aged 12 years and older
- In two phase 3 studies of participants aged ≥9 years with moderate-to-severe acne, once-daily treatment with CAB showed superior efficacy versus vehicle gel, and was well tolerated[6]

OBJECTIVE

- To investigate the efficacy and safety of CAB in children and adolescents in two pooled phase 3 studies

METHODS

- Data were pooled from two phase 3 double-blind, randomized, 12-week studies (NCT04214639; NCT04214652)
  - Eligible participants ≥9 years of age with moderate-to-severe acne were randomized (2:1) to once-daily CAB or vehicle gel
  - CeraVe® hydrating cleanser and CeraVe® moisturizing lotion (L'Oreal, NY) were provided as needed for optimal moisturization/cleaning of the skin
- This post hoc analysis evaluated adolescents aged 12-17 years (CAB: n=123; vehicle: n=50)
  - Endpoints included ≥2-grade reduction from baseline in Evaluator's Global Severity Score and clear/almost clear skin (treatment success), least-squares mean percent change from baseline in inflammatory/noninflammatory lesion counts, and treatment-emergent adverse events (TEAEs)
- Descriptive efficacy and safety data for five children aged 10-11 years enrolled in the study (CAB: n=3; vehicle: n=2) are also summarized

RESULTS

- The majority of participants aged 12-17 years were White and Non-Hispanic, and approximately 60% were male (**Table 1**)
- Most participants had moderate acne at baseline
- At week 12, half of CAB-treated participants achieved treatment success versus one-quarter with vehicle gel (*P*<0.01; **Figure 1**)
- CAB treatment also resulted in significant reductions of >70% in inflammatory and noninflammatory lesion counts versus vehicle (50.5% and 42.9%; *P*<0.001, both; **Figures 2A** and **2B**)
- Images showing acne improvement in CAB-treated adolescents are shown in **Figure 3**
- Most TEAEs were of mild-to-moderate severity, and less than 2.5% of participants withdrew due to AEs (**Table 2**)
  - The most common (>3% in any treatment group) treatment-related TEAE was application site pain
- For the 5 children aged <12 years, all 3 treated with CAB achieved treatment success, with reductions in inflammatory and noninflammatory lesions ranging from 76% to 100% (**Table 3**)
  - Images showing acne improvement in a CAB-treated child are shown in **Figure 4**
  - Neither of the vehicle-treated participants achieved treatment success
  - Only one of the CAB-treated younger participants experienced TEAEs that were mild-moderate in severity (application site pain, application site dryness, erythema), and none discontinued the study
- While CAB gel was efficacious and well tolerated in this younger population, it is indicated for use in children aged 12 years and older due to the limited number of patients <12 years in the clinical studies

TABLE 1. Demographics and Baseline Characteristics of Adolescents Aged 12-17 Years (ITT Population)

	CAB (n=123)	Vehicle (n=50)
Female, n (%)	50 (40.7)	21 (42.0)
Ethnicity, Hispanic/Latino, n (%)	26 (21.1)	12 (24.0)
Race, n (%)		
White	93 (75.6)	43 (86.0)
Black/African American	16 (13.0)	3 (6.0)
Asian	7 (5.7)	1 (2.0)
Other[a]	7 (5.7)	3 (6.0)
Inflammatory lesion count, mean (SD)	37.2 (7.6)	38.2 (9.8)
Noninflammatory lesion count, mean (SD)	51.3 (19.9)	50.3 (18.0)
Evaluator's Global Severity Score, n (%)		
3 – Moderate	108 (87.8)	47 (94.0)
4 – Severe	15 (12.2)	3 (6.0)

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

TABLE 2. Summary of Adverse Events Through Week 12 in Adolescents Aged 12-17 Years (Safety Population)

Participants, n (%)	CAB (n=123)	Vehicle (n=50)
Reporting any TEAE	31 (25.2)	3 (6.0)
Reporting any SAE	0	0
Discontinued study/drug due to AEs	3 (2.4)	0
TEAE Severity		
Mild	18 (14.6)	2 (4.0)
Moderate	12 (9.8)	1 (2.0)
Severe	1 (0.8)	0
Related TEAEs	22 (17.9)	0
Most common treatment-related TEAEs[a]		
AS pain	15 (12.2)	0

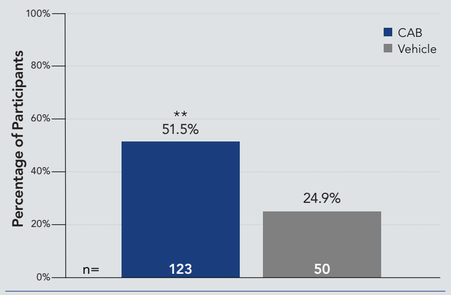
[a]Reported in >3% of participants in any treatment group.
AE, adverse event; AS, application site; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

TABLE 3. Descriptive Baseline and Week 12 Efficacy Data For Children Aged 10-11 Years (n=5)

Participant Age (Race)[a]	Treatment	Baseline			Week 12		
		EGSS	IL	NIL	EGSS	Change IL, %	Change NIL, %
10 (Black)	CAB	3	31	37	1	-83.9	-75.7
11 (White)	CAB	3	33	38	1	-90.9	-94.7
10 (White)	CAB	3	33	40	1	-100	-82.5
11 (White)	Vehicle	3	52	78	3	-30.8	11.5
11 (White)	Vehicle	4	64	89	3	-67.2	6.7

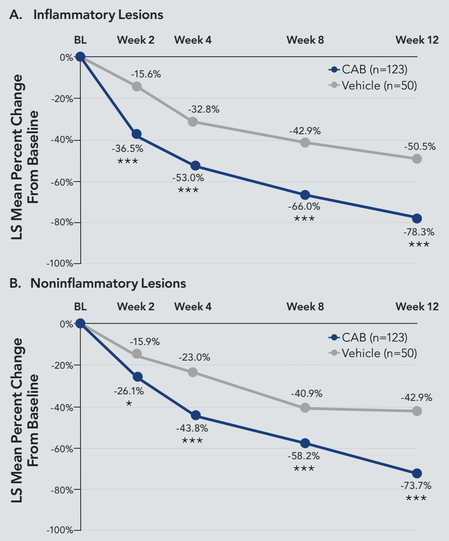
[a]All participants were female and non-Hispanic.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; EGSS, Evaluator's Global Severity Score; IL, inflammatory lesions; NIL, noninflammatory lesions.

FIGURE 1. Treatment Success[a] at Week 12 in Adolescents Aged 12-17 Years (ITT Population)



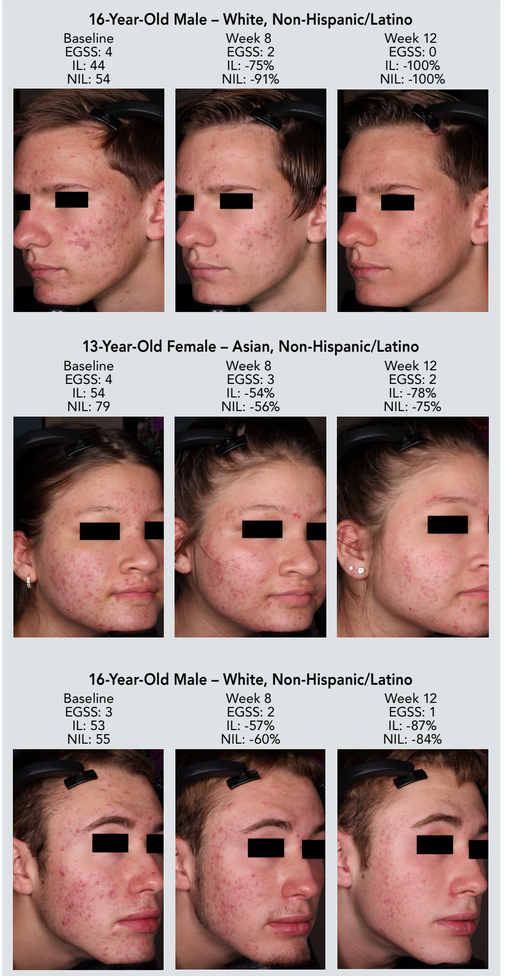
**P<0.01 vs vehicle.
[a]At least 2-grade reduction from baseline in Evaluator's Global Severity Score and clear/almost clear skin.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat.

FIGURE 2. Mean Percent Change from Baseline in Lesion Counts by Visit Adolescents Aged 12-17 Years (ITT Population)



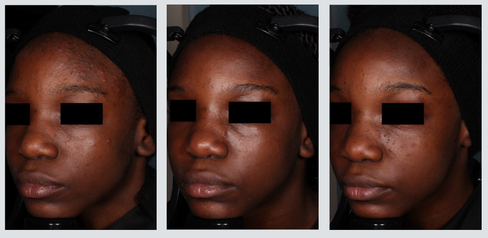
*P<0.05; ***P≤0.001 vs vehicle.
BL, baseline; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat; LS, least squares.

FIGURE 3. Acne Improvements with CAB in Adolescents Aged 12-17 Years



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

FIGURE 4. Acne Improvements with CAB in a Child Aged <12 Years



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

CONCLUSIONS

- Once-daily clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel (CAB)—the first approved fixed-dose, triple-combination topical for acne vulgaris—was well tolerated and efficacious in pediatric participants with moderate-to-severe acne, with >50% achieving treatment success at week 12
- The >70% acne reductions at week 12 with CAB treatment are greater than those observed in other studies of pediatric participants treated for 10-12 weeks with fixed-combination gels (clindamycin/benzoyl peroxide or adapalene/benzoyl peroxide)[7-11]; however, differences in populations and trial designs are important considerations
- These results support a recent meta-analysis showing that triple-combinations are among the top two most effective acne treatments[5]
- Additionally, the simple once-daily dosing of CAB may improve adherence[3]

REFERENCES

1. Vos T, et al. *Lancet*. 2012;380(9859):2163-2196.
2. Skroza N, et al. *J Clin Aesthet Dermatol*. 2018;11(1):21-25.
3. Moradi Tuchayi S, et al. *Patient Prefer Adherence*. 2016;10:2091-2096.
4. Hester C, et al. *Pediatr Dermatol*. 2016;33(1):49-55.
5. Huang C-Y, et al. *Ann Fam Med*. 2023;21:358-369.
6. Stein Gold L, et al. *J Am Acad Dermatol*. 2023;89(5):927-935.
7. Cook-Bolden FE. *J Clin Aesthet Dermatol*. 2015;8(5):28-32.
8. Stein Gold L. *Cutis*. 2013;91:152-159.
9. Eichenfield LF, et al. *J Clin Aesthet Dermatol*. 2009;2(11):21-26.
10. Stein Gold L, et al. *J Drugs Dermatol*. 2017;16(6):582-589.
11. Keating GM. *Am J Clin Dermatol*. 2011;12(6):407-420.

AUTHOR DISCLOSURES

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