Efficacy and Safety of Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel in Females with Moderate-to-Severe Acne: Post Hoc Analysis by Age

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SYNOPSIS

- While acne is common in adolescents, the overall prevalence in adults may be increasing, especially among females[1,2]
  - Acne in adult females is associated with greater negative impacts on quality of life, which along with increased acne severity in this population, may lead to greater healthcare utilization versus adult males[2-4]
  - Additionally, adult females are more likely to have dry skin,[5] which can increase the risk of cutaneous irritation associated with topical treatments
- Combination therapies are recommended in the US for most patients with acne,[6] and a recent meta-analysis showed that triple-combinations are among the top two most effective treatments[7]
- With topical treatments, however, vehicle formulation can affect tolerability[8]
- Clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% (CAB; Cabtreo™ [Ortho Dermatologics]) polymeric dispersion gel—the first fixed-dose, triple-combination topical product approved for acne—has demonstrated good efficacy, safety, and tolerability in participants with moderate-to-severe acne[9,10]

OBJECTIVE

- To assess the impact of age on efficacy, safety, and tolerability in females with moderate-to-severe acne

METHODS

- In one phase 2 (N=741; NCT03170388) and two identically designed phase 3 (N=183; N=180; NCT04214639; NCT04214652), double-blind, randomized, 12-week studies, participants aged ≥9 years with moderate-to-severe acne were randomized to receive once-daily CAB or vehicle gel
  - The phase 2 study included three additional dyad randomization arms (data not shown)
  - Coprimary endpoints comprised inflammatory and noninflammatory lesion counts and treatment success (≥2-grade reduction from baseline in Evaluator's Global Severity Score and score of 'clear' or 'almost clear')
  - Treatment-emergent adverse events (TEAEs) and cutaneous safety (Investigator-assessed) and tolerability (participant-assessed) were also evaluated
- Pooled data from these studies were analyzed post hoc from female participants categorized by age: 9-24 years and ≥25 years

RESULTS

Participants

- The pooled population comprised a total of 395 females: aged 9-24 years (n=274); aged ≥25 years (n=121)
  - Most participants were White and Non-Hispanic, and the majority had moderate (EGGS 3) acne at baseline (**Table 1**)

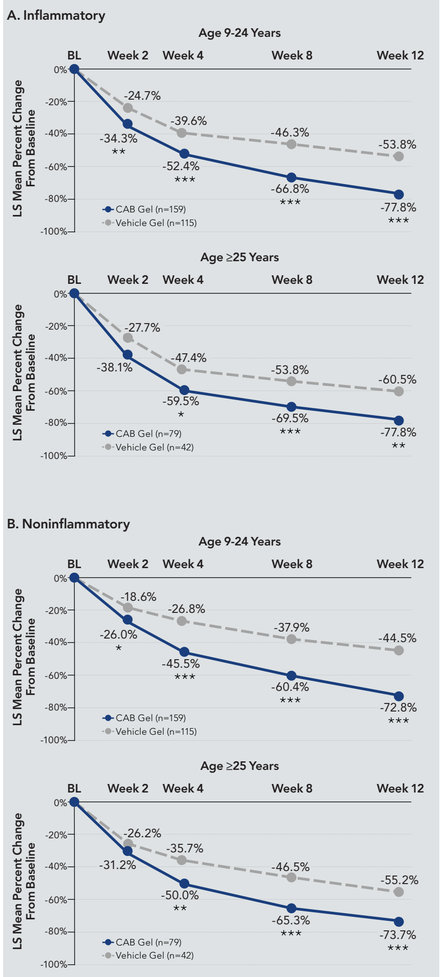
Efficacy

- At week 12 in both age groups, least-squares mean percent reductions from baseline were >70% with CAB for inflammatory and noninflammatory lesions, significantly greater than with vehicle gel (*P*<0.01, all; **Figure 1**)
- Half of CAB-treated females in both age groups achieved treatment success at week 12 versus less than one-quarter with vehicle (*P*<0.01, both; **Figure 2**)
- Images showing acne improvements in CAB-treated females are shown in **Figure 3**

Safety and Tolerability

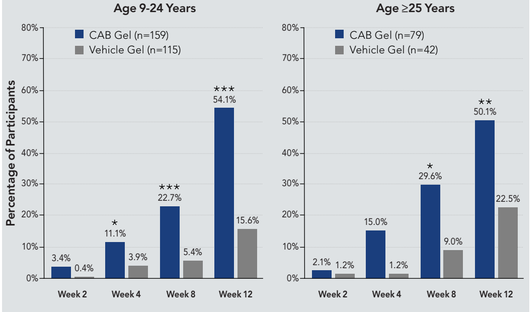
- No notable age-related trends in safety or tolerability were observed (**Table 2; Figure 4**)
- Most TEAEs were mild-to-moderate in severity, with rates similar to the overall pooled phase 2 and 3 populations (overall CAB [n=383]: 30.5%; **Table 2**)
- Transient increases in the severity of cutaneous safety/tolerability assessments with CAB did not substantially differ between the older and younger females, with scores beginning to normalize by week 4 (**Figure 4**)

FIGURE 1. Mean Percent Change from Baseline in Lesion Counts by Visit in Females by Age Group (Pooled ITT Population)



*P<0.05; **P<0.01; ***P≤0.001 vs vehicle.
Values have been adjusted for multiple imputation.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat; LS, least squares.

FIGURE 2. Treatment Success[a] at Week 12 in Females by Age Group (Pooled ITT Population)



*P<0.05; **P<0.01; ***P<0.001 vs vehicle.
[a]At least 2-grade reduction from baseline in Evaluator's Global Severity Score and clear/almost clear skin.
Values have been adjusted for multiple imputation.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat.

TABLE 1. Demographics and Baseline Characteristics in Females by Age Group (Pooled ITT Population)

	Age 9-24 Years		Age ≥25 Years	
	CAB Gel (n=159)	Vehicle Gel (n=115)	CAB Gel (n=79)	Vehicle Gel (n=42)
Age, mean (SD), y	17.2 (3.7)	17.5 (3.7)	30.8 (5.0)	32.4 (5.8)
Age, median (range), y	16 (10-24)	17 (11-24)	29 (25-48)	30 (25-45)
Ethnicity, Hispanic/Latino, n (%)	39 (24.5)	26 (22.6)	21 (26.6)	6 (14.3)
Race, n (%)				
White	116 (73.0)	82 (71.3)	43 (54.4)	23 (54.8)
Black or African American	27 (17.0)	17 (14.8)	20 (25.3)	15 (35.7)
Asian	8 (5.0)	7 (6.1)	8 (10.1)	3 (7.1)
Other[a]	8 (5.0)	9 (7.8)	8 (10.1)	1 (2.4)
Inflammatory lesion count, mean (SD)	36.4 (9.0)	38.0 (9.0)	36.3 (5.7)	33.4 (3.2)
Noninflammatory lesion count, mean (SD)	53.3 (20.6)	50.5 (16.9)	44.1 (9.8)	44.4 (11.9)
Evaluator's Global Severity Score, n (%)				
3 – Moderate	145 (91.2)	104 (90.4)	70 (88.6)	42 (100)
4 – Severe	14 (8.8)	11 (9.6)	9 (11.4)	0

[a]American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander, or not reported/multiple/other.
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 Females by Age Group (Pooled Safety Population)

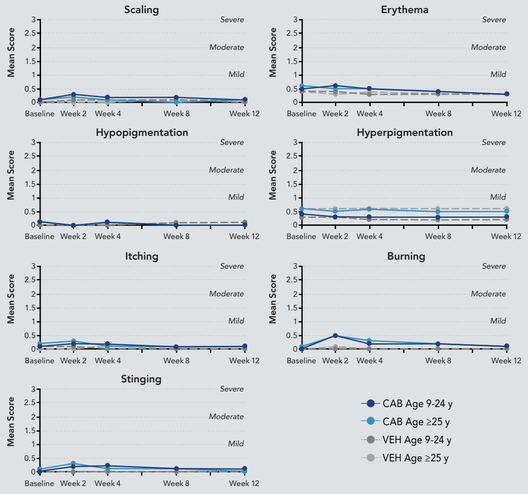
	Age 9-24 Years		Age ≥25 Years	
Participants, n (%)	CAB Gel (n=156)	Vehicle Gel (n=114)	CAB Gel (n=90)	Vehicle Gel (n=51)
TEAEs	53 (34.0)	15 (13.2)	23 (29.5)	2 (4.8)
Related	29 (18.6)	2 (1.8)	19 (24.4)	1 (2.4)
Discontinued drug or study due to AE	4 (2.6)	1 (0.9)	3 (3.8)	0
Most common treatment-related TEAEs[a]				
AS pain	16 (10.3)	1 (0.9)	8 (10.3)	0
AS exfoliation	6 (3.8)	1 (0.9)	2 (2.6)	0
AS dryness	5 (3.2)	0	5 (6.4)	0
Xerosis	0	0	3 (3.8)	1 (2.4)
AS erythema	1 (0.6)	0	3 (3.8)	0
AS pruritus	2 (1.3)	0	3 (3.8)	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.

FIGURE 3. Acne Improvements with CAB in Females Aged 9-24 and ≥25 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. Cutaneous Safety and Tolerability in Females by Age Group (Pooled Safety Population)



Investigator-assessed cutaneous safety (scaling, erythema, hypopigmentation, and hyperpigmentation) and participant-reported tolerability (itching, burning, and stinging) were evaluated via a 4-point scale where 0=none and 3=severe.
N values at baseline: CAB age 9-24 y, n=156; VEH age 9-24 y, n=114; CAB age ≥25 y, n=78; VEH age ≥25 y, n=42.
CAB, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel; VEH, vehicle gel.

CONCLUSIONS

- With greater than 70% lesion reductions and half of participants achieving treatment success by week 12, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel demonstrated good efficacy, safety, and tolerability in both younger and older females with moderate-to-severe acne
- No age-related trends in efficacy or tolerability were observed, suggesting that the innovative, fixed-dose, triple combination gel (approved for use in patients aged 12 and older) is a valuable treatment option for female patients of all ages, including those with more mature skin

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AUTHOR DISCLOSURES

Julie Harper has received honoraria from Aclaris, Almirall, BioPharmX, Cassiopea, Cutanea, Dermira, Foamix, Galderma, LaRoche-Posay, 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. Hilary Baldwin has served as advisor, investigator, and on speakers' bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. Valerie Callender has served as an investigator, consultant, or speaker for Acne Store, Almirall, Aerolase, AbbVie, Allergan Aesthetics, Avava, Avita Medical, Beiersdorf, Cutera, Dermavant, Eirion Therapeutics, Eli Lilly, Galderma, Janssen, Jeune Aesthetics, L'Oréal, Ortho Dermatologics, Pfizer, Prollineum, Regeneron, Scientis, Sente, SkinBetter Science, SkinCeuticals, Symatese, Teoxane, and UpToDate. Michael Gold has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. Heather Woolery-Lloyd is a shareholder for Somabella Laboratories, LLC. She has served as a speaker for Aclaris and Ortho Dermatologics, consultant for Ortho Dermatologics, and received grants/research funding from Allergan, Galderma, Nestle, Pfizer, Endo, LEO Pharma, Eirion, Golgel, and Aclaris. 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.

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