Impact of Age on Efficacy and Safety of Fixed-Dose Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel in Participants with Moderate-to-Severe Acne

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SYNOPSIS

- Acne affects patients of all ages, but there are age-related differences in clinical presentation and efficacy and safety of acne treatments[1]
- Topical clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% (CAB) gel is the only fixed-dose, triple-combination formulation approved for the treatment of acne, and is indicated for use in patients aged ≥12 years[2]
- In three clinical studies of participants with moderate-to-severe acne, once-daily CAB gel demonstrated superior efficacy to vehicle and component dyads, with good safety and tolerability[3,4]

OBJECTIVE

- This post hoc analysis was performed to evaluate the efficacy and safety of CAB in pediatric, adolescent, and adult participants

METHODS

- In a phase 2 (NCT03170388) and two phase 3 (NCT04214652, NCT04214639) studies, participants aged ≥9 years with moderate-to-severe acne were randomized to once-daily CAB or vehicle gel; data for participants randomized to the component dyad gels (phase 2 study) are not shown here
- Endpoints included percentage of participants achieving treatment success (defined as ≥2-grade reduction from baseline in Evaluator's Global Severity Score [EGSS] and clear/almost clear skin) and least-squares mean percent change from baseline in inflammatory/noninflammatory lesion counts at week 12
- Treatment-emergent adverse events (TEAEs) and cutaneous safety (Investigator-assessed) and tolerability (participant-reported) were also assessed
- Pooled data for participants randomized to CAB or vehicle across all three studies were analyzed for participants categorized by age: 9-24 years (pediatric and adolescent) or ≥25 years (adult)
  - These ages were chosen as acne in patients aged 18-24 years is more similar to adolescents than adults, and age 25 is often used to define "adult acne"[1,5]

RESULTS

Participants

- The pooled population comprised 657 participants in two age group: aged 9-24 years (CAB: n=297; vehicle: n=218) and aged ≥25 years (n=91; n=51)
- The majority of participants were female and White, and most had moderate acne (EGSS 3) at baseline (**Table 1**)

Efficacy

- At week 12, approximately half of CAB-treated participants in both age groups achieved treatment success versus less than one fourth with vehicle (*P*<0.01, both; **Figure 1**)
- Treatment with CAB resulted in >70% reductions from baseline in inflammatory and noninflammatory lesions in both age groups at week 12, versus 45%-62% with vehicle (*P*≤0.001, all; **Figure 2**)
- The only significant difference between CAB-treated participants in the two age groups across the efficacy endpoints was for treatment success at week 8 (*P*<0.05)
- Images of acne improvements in adolescent and adult participants treated with CAB are shown in **Figure 3**

Safety

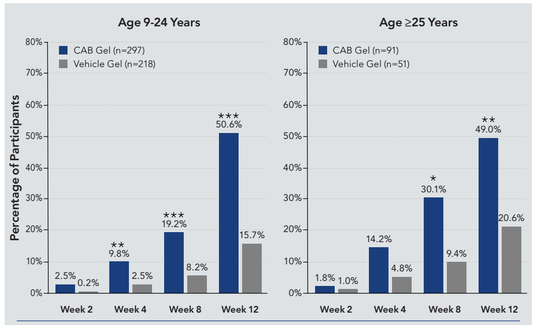
- No notable age-related trends in safety or tolerability were observed (**Table 2**; **Figure 4**)
- Most TEAEs with CAB were of mild-moderate severity, with no age-related trends (**Table 2**)
- Transient increases in the severity of cutaneous safety/tolerability assessments with CAB did not substantially differ between the age groups, with mean scores beginning to normalize by week 4 (**Figure 4**)

TABLE 1. Baseline Demographics and Characteristics (ITT Population, Pooled Participants)

	Age 9-24 Years		Age ≥25 Years	
	CAB Gel (n=297)	Vehicle Gel (n=218)	CAB Gel (n=91)	Vehicle Gel (n=51)
Age, mean (SD), y	16.7 (3.2)	17.2 (3.2)	31.1 (5.3)	32.1 (6.1)
Age, median (range), y	16 (10-24)	17 (11-24)	29 (25-48)	30 (25-47)
Sex, female, n (%)	159 (53.5)	115 (52.8)	79 (86.8)	42 (82.4)
Ethnicity, Hispanic/Latino, n (%)	66 (22.2)	49 (22.5)	24 (26.4)	8 (15.7)
Race, n (%)				
White	218 (73.4)	164 (75.2)	49 (53.8)	29 (56.9)
Black or African American	41 (13.8)	24 (11.0)	23 (25.3)	16 (31.4)
Asian	21 (7.1)	17 (7.8)	10 (11.0)	5 (9.8)
Other[a]	17 (5.7)	13 (6.0)	9 (9.9)	1 (2.0)
Inflammatory lesion count, mean (SD)	38.2 (10.4)	38.8 (9.8)	36.0 (5.7)	34.0 (4.7)
Noninflammatory lesion count, mean (SD)	52.3 (20.1)	50.6 (18.3)	43.8 (9.5)	43.6 (11.0)
Evaluator's Global Severity Score, n (%)				
3 – Moderate	260 (87.5)	192 (88.1)	80 (87.9)	50 (98.0)
4 – Severe	37 (12.5)	26 (11.9)	11 (12.1)	1 (2.0)

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

FIGURE 1. Treatment Success[a] Through Week 12 by Age (ITT Population, Pooled Participants)



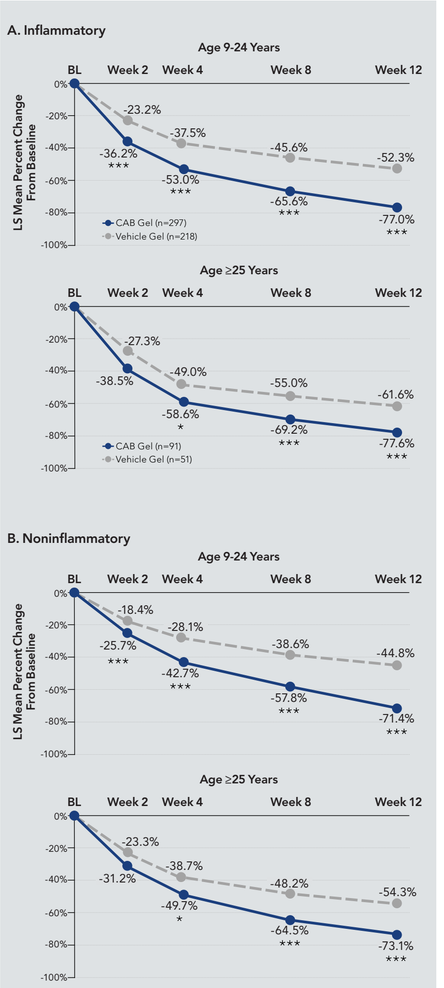
*P<0.05, **P<0.01, ***P≤0.001 vs vehicle.
[a]Treatment success defined as ≥2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 (clear) or 1 (almost clear).
There were no significant differences between active treatment age groups except at week 8 (*P*<0.05).
Values have been adjusted for multiple imputation (MCMC).
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat; MCMC, Markov Chain Monte Carlo.

TABLE 2. Treatment-Emergent Adverse Events Through Week 12 by Age (Safety Population, Pooled Participants)

	Age 9-24 Years		Age ≥25 Years	
Participants, n (%)	CAB Gel (n=293)	Vehicle Gel (n=216)	CAB Gel (n=90)	Vehicle Gel (n=51)
TEAEs	93 (31.7)	30 (13.9)	24 (26.7)	2 (3.9)
Related	56 (19.1)	3 (1.4)	20 (22.2)	1 (2.0)
Serious AEs	1 (0.3)[b]	0	0	0
Discontinued drug or study due to AE	8 (2.7)	2 (0.9)	3 (3.3)	0
Most common treatment-related TEAEs[a]				
AS pain	33 (11.3)	2 (0.9)	9 (10.0)	0
AS dryness	11 (3.8)	0	5 (5.6)	0
Xerosis	0	0	3 (3.3)	1 (2.0)
AS erythema	2 (0.7)	0	3 (3.3)	0
AS pruritus	2 (0.7)	0	3 (3.3)	0

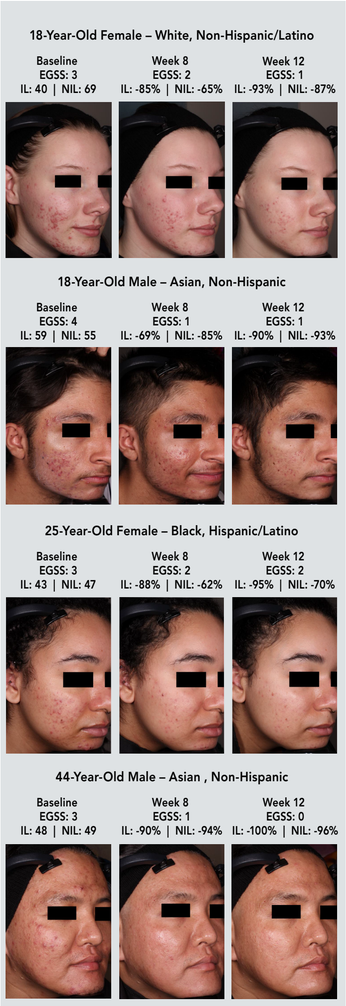
[a]Reported by ≥3% participants in any treatment group.
[b]Sickle cell anemia with crisis; not considered related to study drug.
AE, adverse event; AS, application site; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

FIGURE 2. Least Squares Mean Percent Reductions in Lesion Counts Through Week 12 by Age (ITT Population, Pooled Participants)



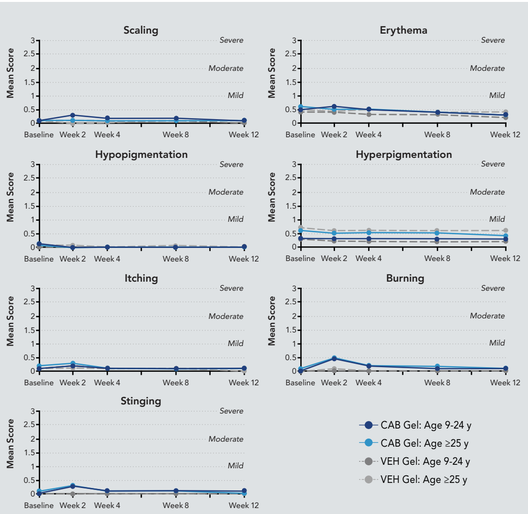
*P<0.05; **P<0.01; ***P≤0.001 vs vehicle.
Values have been adjusted for multiple imputation (MCMC).
BL, baseline; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat; LS, least squares; MCMC, Markov Chain Monte Carlo.

FIGURE 3. Acne Improvements with CAB in Participants 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 Through Week 12 by Age (Safety Population, Pooled Participants)



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=293; VEH age 9-24 y, n=216; CAB age ≥25 y, n=90; VEH age ≥25 y, n=51.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; VEH, vehicle gel.

CONCLUSIONS

- Fixed-dose, triple-combination CAB gel was efficacious and well tolerated in participants with moderate-to-severe acne, regardless of age
- Approximately half of CAB-treated pediatric/adolescent and adult participants achieved clear/almost clear skin, with >70% reductions in lesion counts
- No age-related trends in efficacy or tolerability were observed, suggesting that the innovative CAB gel (approved for use in patients aged ≥12 years) is a valuable treatment option for patients of all ages

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AUTHOR DISCLOSURES

Leon Kircik has served as either a consultant, speaker, advisor or an investigator for Allergan, Almirall, Epi Health, Galderma, Novartis, Ortho Dermatologics, and Sun Pharma. Julie Harper has received honoraria from Aclaris, Almirall, BioPharmX, Cassiopea, Cutanea, Dermira, Foamix, Galderma, LaRoche-Posay, Ortho Dermatologics, and Sun Pharma. Hilary Baldwin has served as advisor, investigator, and on speakers' bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. Lawrence Eichenfield has received honoraria for consulting services from AbbVie, BMS, Almirall, Amgen, Arcutis, Dermata, Dermira, Dermavant, Eli Lilly, Forte Pharma, Galderma, Incyte, J&J, 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. Emil Tanghetti has served as speaker for Novartis, Ortho Dermatologics, Sun Pharma, Lilly, Galderma, AbbVie, and Dermira; served as a consultant/clinical studies for Hologic, Ortho Dermatologics, and Galderma; and is a stockholder for Accure. Emmy Graber has served as a consultant/advisor, research investigator, and/or speaker for Digital Diagnostics, Almirall, Cutera, Hovione, Keratin Biosciences, La Roche Posay, Lipidor AB, Ortho Dermatologics, Sebacia, SolGel, Verrica, and WebMD. 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. Zoe Draelos has received funding from Ortho Dermatologics.

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