Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel for Acne: Pooled Analysis by Age and Sex

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SYNOPOSIS

- Acne clinical presentation and response to treatment may differ between males and females as well as between pediatric/postadolescent (≤24 years) and adult (≥25 years) patients[1-5]
- Clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel (CAB) is the only fixed-dose, triple-combination topical treatment for acne
- In clinical trials of participants with moderate to severe acne, CAB demonstrated superior efficacy to vehicle and component dyads combination gels, with good safety and tolerability[6-8]

OBJECTIVE

- To evaluate the impact of age and sex on the efficacy and safety of CAB gel

METHODS

- In one phase 2 and two phase 3 double-blind, 12-week studies, participants with moderate to severe acne were randomized to once-daily CAB or vehicle
  - CeraVe® hydrating cleanser and CeraVe® moisturizing lotion (L'Oreal, NY) were provided as needed for optimal skin moisturization/cleaning
- Data were pooled and analyzed post hoc for participants categorized by age and sex: females 9-24 or ≥25 years and males 9-24 or ≥25 years
- Endpoints included treatment success (≥2-grade reduction from baseline in Evaluator's Global Severity Score [EGSS] and a score of 0 [clear] or 1 [almost clear]) and least squares mean percent change from baseline in inflammatory (IL) and noninflammatory (NIL) lesions
- Treatment-emergent adverse events (TEAEs) and cutaneous safety/tolerability were also assessed

RESULTS

Participants

- The pooled participant population (N=657) included 395 females (9-24 years, n=274; ≥25 years, n=121) and 262 males (9-24 years, n=241; ≥25 years, n=21; **Table 1**)
  - A greater percentage of participants ≥25 years were Black/African American
  - Baseline lesion counts were similar across all age/sex subgroups, though in both age groups a greater percentage of male participants had severe acne than females
- Treatment compliance was high (>90%) in all subgroups (**Table 1**)

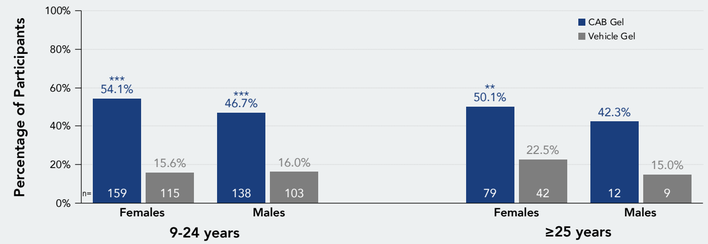
Efficacy

- Rates of treatment success at week 12 were greater for participants treated with CAB vs vehicle in all age/sex subgroups; differences vs vehicle were statistically significant ($P<0.01$) for all groups except males ≥25 years (due to the low number of participants in this group; **Figure 1**)
  - In both younger and older age groups, treatment success rates were higher for females treated with CAB than males (54.1% and 54.1% vs 42.3% and 46.7%, respectively)
- At week 12, all participants treated with CAB had >75% IL reductions from baseline (**Figure 2**)
  - Reductions were significantly greater than with vehicle for all groups ($P\leq0.01$) except males ≥25 years
- Participants treated with CAB in all age/sex subgroups had ≥70% NIL reductions from baseline to week 12, significantly greater than with vehicle ($P<0.05$, all; **Figure 3**)
- IL and NIL reductions with CAB were significantly greater than with vehicle as early as week 2 for all participants 9-24 years and week 4 for females ≥25 years ($P\leq0.05$, all)
- Images of participants treated with CAB from each subgroup are shown in **Figure 3**

Safety and Tolerability

- TEAEs were primarily mild to moderate in severity, with rates generally similar across CAB-treated groups (**Table 2**; lower rates among males ≥25 years reflect low number of participants)
  - The most common treatment-related TEAEs were typical of topical treatments for acne
- Discontinuation rates due to a TEAE were low (<4% in all subgroups), and there were no severe TEAEs related to treatment
- Of the participants treated with CAB, >80% had a rating of 0 (none) for scaling, hypopigmentation, itching, burning, and stinging at both baseline and at week 12 (data not shown)
  - Transient increases in scaling, burning, and stinging at week 2 resolved back to baseline levels by week 8
  - Mean scores for all cutaneous safety and tolerability assessments were ≤0.6 at all study visits (1=mild)

FIGURE 1. Treatment Success[a] at Week 12 (ITT Population, Pooled)



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

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

	Participants Aged 9-24 Years				Participants Aged ≥25 Years			
	Female		Male		Female		Male	
Characteristic	CAB Gel (n=159)	Vehicle (n=115)	CAB Gel (n=138)	Vehicle (n=103)	CAB Gel (n=79)	Vehicle (n=42)	CAB Gel (n=12)	Vehicle (n=9)
Age, mean (SD), y	17.2 (3.7)	17.5 (3.7)	16.1 (2.4)	16.9 (2.6)	30.8 (5.0)	32.4 (5.8)	32.7 (6.8)	31.0 (7.3)
Age, median (range), y	16 (10-24)	17 (11-24)	16 (12-24)	17 (12-24)	29 (25-48)	30 (25-45)	30.5 (26-46)	27.0 (26-47)
Ethnicity, Hispanic/Latino, n (%)	39 (24.5)	26 (22.6)	27 (19.6)	23 (22.3)	21 (26.6)	6 (14.3)	3 (25.0)	2 (22.2)
Race, n (%)								
White	116 (73.0)	82 (71.3)	102 (73.9)	82 (79.6)	43 (54.4)	23 (54.8)	6 (50.0)	6 (66.7)
Black/African American	27 (17.0)	17 (14.8)	14 (10.1)	7 (6.8)	20 (25.3)	15 (35.7)	3 (25.0)	1 (11.1)
Asian	8 (5.0)	7 (6.1)	13 (9.4)	10 (9.7)	8 (10.1)	3 (7.1)	2 (16.7)	2 (22.2)
Other[a]	8 (5.0)	9 (7.8)	9 (6.5)	4 (3.9)	8 (10.1)	1 (2.4)	1 (8.3)	0
Inflammatory lesion count, mean (SD)	36.4 (9.0)	38.0 (9.0)	40.2 (11.5)	39.7 (10.6)	36.3 (5.7)	33.4 (3.2)	33.8 (4.9)	36.9 (8.5)
Noninflammatory lesion count, mean (SD)	53.3 (20.6)	50.5 (16.9)	51.2 (19.4)	50.7 (19.8)	44.1 (9.8)	44.4 (11.9)	41.8 (7.8)	40.0 (4.1)
Evaluator's Global Severity Score, n (%)								
3 – Moderate	145 (91.2)	104 (90.4)	115 (83.3)	88 (85.4)	70 (88.6)	42 (100.0)	10 (83.3)	8 (88.9)
4 – Severe	14 (8.8)	11 (9.6)	23 (16.7)	15 (14.6)	9 (11.4)	0	2 (16.7)	1 (11.1)
Compliance, %[b]	136 (90.7)	104 (96.3)	125 (94.0)	92 (94.8)	64 (90.1)	38 (92.7)	10 (90.9)	9 (100.0)

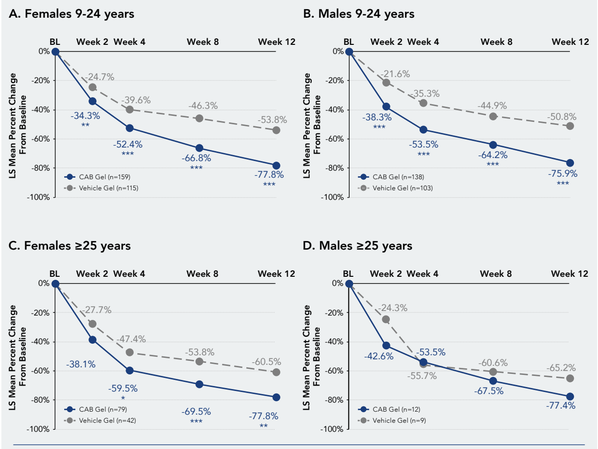
[a]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Not Reported/Multiple.
[b]A participant was considered compliant with the dosing regimen if they did not miss >5 consecutive days dosing and applied 80-120% of expected applications while participating in the study.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; SD, standard deviation.

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

	Participants Aged 9-24 Years				Participants Aged ≥25 Years			
	Female		Male		Female		Male	
Participants, n (%)	CAB Gel (n=156)	Vehicle (n=114)	CAB Gel (n=137)	Vehicle (n=102)	CAB Gel (n=78)	Vehicle (n=42)	CAB Gel (n=12)	Vehicle (n=9)
Reporting any TEAE	53 (34.0)	15 (13.2)	40 (29.2)	15 (14.7)	23 (29.5)	2 (4.8)	1 (8.3)	0
Discontinued due to a TEAE[a]	4 (2.6)	1 (0.9)	4 (2.9)	1 (1.0)	3 (3.8)	0	0	0
Related	29 (18.6)	2 (1.8)	27 (19.7)	1 (1.0)	19 (24.4)	1 (2.4)	1 (8.3)	0
Most common treatment-related TEAEs[b]								
Application site pain	16 (10.3)	1 (0.9)	17 (12.4)	1 (1.0)	8 (10.3)	0	1 (8.3)	0
Erythema	1 (0.6)	0	4 (2.9)	0	1 (1.3)	0	1 (8.3)	0
Application site dryness	5 (3.2)	0	6 (4.4)	0	5 (6.4)	0	0	0
Application site exfoliation	6 (3.8)	1 (0.9)	1 (0.7)	0	2 (2.6)	0	0	0
Application site pruritus	2 (1.3)	0	0	0	3 (3.8)	0	0	0
Application site erythema	1 (0.6)	0	1 (0.7)	0	3 (3.8)	0	0	0
Xerosis	0	0	0	0	3 (3.8)	1 (2.4)	0	0
Application site irritation	4 (2.6)	0	2 (1.5)	0	2 (2.6)	0	0	0

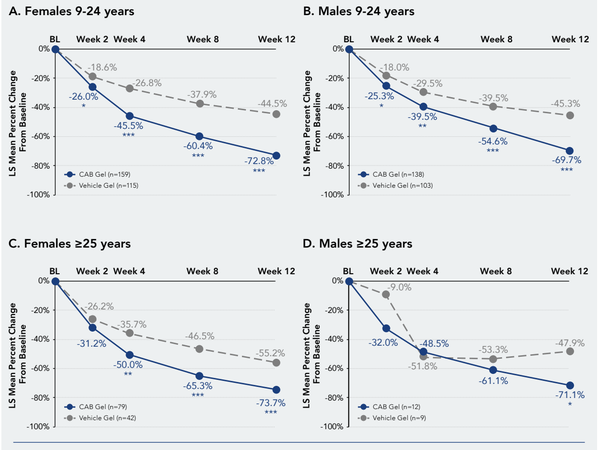
[a]Includes participants who discontinued study drug or prematurely discontinued from the study.
[b]Reported in ≥2% of participants in any treatment group.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; TEAE, treatment-emergent adverse event.

FIGURE 2. Inflammatory Lesion Reductions From Baseline to Week 12 by Age and Sex (ITT Population, Pooled)



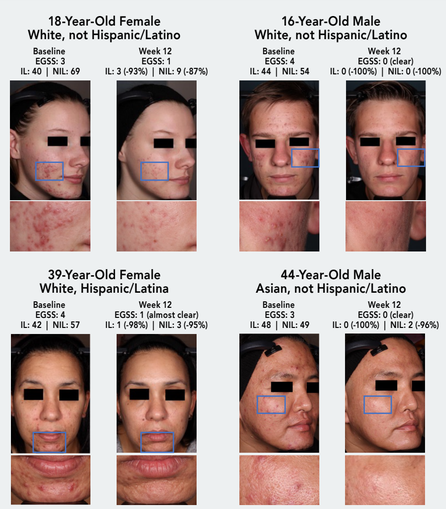
*P<0.05; **P<0.01; ***P≤0.001 vs vehicle.
Values have been adjusted for multiple imputation.
CAB, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%; ITT, intent to treat; LS, least squares.

FIGURE 3. Noninflammatory Lesion Reductions From Baseline to Week 12 by Age and Sex (ITT Population, Pooled)



*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%; ITT, intent to treat; LS, least squares.

FIGURE 4. Acne Improvements With CAB Gel



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

CONCLUSIONS

- Triple-combination CAB gel was efficacious and well tolerated, regardless of age or sex, in participants with moderate to severe acne
  - At week 12, approximately half of female participants and over 43% of male participants achieved treatment success with CAB gel vs less than one fourth with vehicle
  - In all subgroups, CAB gel provided ≥70% reductions from baseline in inflammatory and noninflammatory lesions
- Significant acne improvements early in treatment, good tolerability, and a simplified treatment regimen may foster treatment adherence and greater long-term efficacy[9,10]
- CAB gel is a safe, efficacious, and well-tolerated acne treatment for females and males across age groups

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AUTHOR DISCLOSURES

Julie Harper has received honoraria from Almirall, Cutera, Galderma, LaRoche-Posay, Ortho Dermatologics, and Sun Pharma. 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. Hilary Baldwin has served as advisor, investigator, and on speakers bureau for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. Valerie D 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'Oreal, Ortho Dermatologics, Pfizer, Prollineum, Regeneron, Scientis, Sente, SkinBetter Science, SkinCeuticals, Symatese, Texoane, and UpToDate. Michael Gold has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. 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. Adelaide Hebert has received honoraria from Galderma, LEO Pharma, Almirall, Cassiopea, Ortho Dermatologics, Cutanea, Ferrer, Pfizer, Dermira. The UTHealth McGovern Medical School has received research grants from Cassiopea, Dermira, Ortho Dermatologics. Eric Guenin is an employee of Ortho Dermatologics and may hold stock and/or stock options in its parent company. 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.

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