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

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SYNOPSIS

- Combination therapies targeting multiple processes of acne pathogenesis are recommended for most acne patients[1]
- Clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel (CAB; Cabtreo®; Ortho Dermatologics) is the first triple-combination, fixed-dose topical acne treatment approved by the US Food and Drug Administration, and is indicated in patients aged 12 years and older[2]
- CAB demonstrated superior efficacy to vehicle and component dyads, with good safety/tolerability in a phase 2[3] and two phase 3 studies[4] of moderate-to-severe acne
- Clinical presentation and sequelae of acne can vary by race; as such, strategies to improve outcomes in patients with skin of color include the use of treatments that address multiple pathogenic factors of acne and consideration of drug tolerability[5]

OBJECTIVE

- To better understand the efficacy and safety of CAB gel in patients with darker skin phototypes, this post hoc analysis included participants who self-identified as 'Black or African American' (hereafter referred to as Black)

METHODS

- Data were pooled from a phase 2 (NCT03170388; N=741) and two phase 3 (NCT04214652, NCT04214639; N=183, N=180), double-blind, randomized, 12-week studies
  - Eligible participants aged ≥9 years with moderate-to-severe acne were randomized to receive 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
- Post hoc analyses were conducted in Black participants treated with CAB or vehicle gel; results from the dyad arms in the phase 2 study were not included due to the low number of Black participants
- 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
- Treatment-emergent adverse events (TEAEs) and cutaneous safety and tolerability were also assessed

RESULTS

Participants

- Of 657 participants randomized to CAB or vehicle gel, 104 (15.8%) self-identified as Black (n=64 CAB, n=40 vehicle)
- Of Black participants, 76% were female, 94% were not Hispanic/Latino, the average age was 23.1 years, and 89% had moderate acne at baseline (EGSS=3)

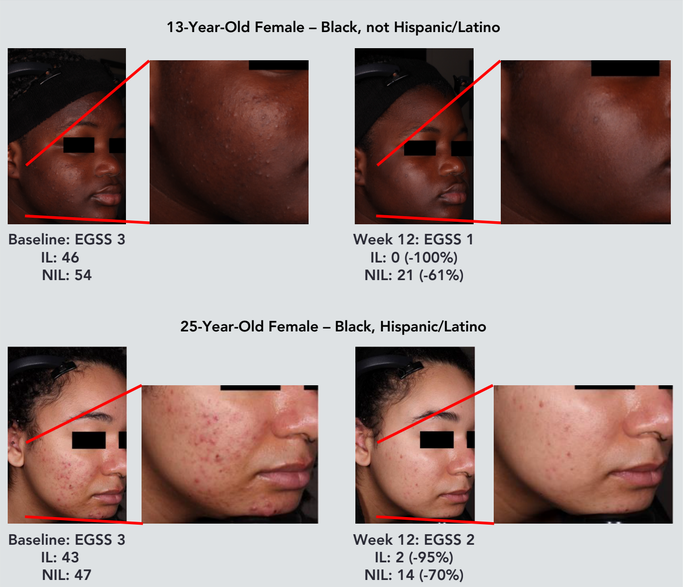
Efficacy

- Images showing acne improvement in CAB-treated participants are shown in **Figure 1**
- At week 12, 31.5% of Black participants treated with CAB achieved treatment success, compared to 17.3% with vehicle (*P*=0.12)
- Inflammatory lesion reductions with CAB at week 12 were significantly greater than with vehicle (-69.0% vs -53.6%, *P*<0.01; **Figure 2A**)
- Noninflammatory lesion reductions at week 12 were numerically greater with CAB than with vehicle (-58.3% vs -51.9%, *P*=0.32; **Figure 2B**)

Safety

- The rate of TEAEs with CAB treatment in Black participants was generally lower than in the overall study populations (23.4% vs 24.6-36.2%)[3,4]
- Most TEAEs were mild-to-moderate, and there were no discontinuations due to AEs (**Table 1**)
- Mean scores for all cutaneous safety and tolerability assessments following CAB treatment were ≤0.6 (1=mild) at all study visits, similar to the overall study populations (<0.7)[3,4]
  - As expected, transient increases in scaling, itching, burning, and stinging between weeks 2 and 8 occurred with CAB treatment but returned close to baseline values by week 12 (data not shown)
- Further, the average value of the worst (highest) cutaneous safety/tolerability score at any time post-baseline was <1 (**Figure 3**)

FIGURE 1. Acne Improvements at Week 12 With CAB



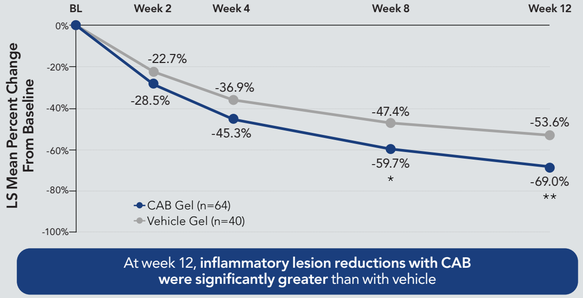
Individual results may vary.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; EGSS, Evaluator's Global Severity Score (0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe); IL, inflammatory lesions; NIL, noninflammatory lesions.

TABLE 1. Summary of Adverse Events Through Week 12 (Safety Population, Pooled)

Participants, n (%)	CAB (n=64)	Vehicle (n=40)
Reporting any TEAE	15 (23.4)	4 (10.0)
Reporting any SAE	1 (1.6)[a]	0
Discontinued study/drug due to AEs	0	0
TEAE Severity		
Mild	10 (15.6)	2 (5.0)
Moderate	3 (4.7)	2 (5.0)
Severe	2 (3.1)	0
Related TEAEs	9 (14.1)	0
Most common treatment-related TEAEs[b]		
Application site pain	6 (9.4)	0
Application site exfoliation	2 (3.1)	0
Application site pruritus	2 (3.1)	0

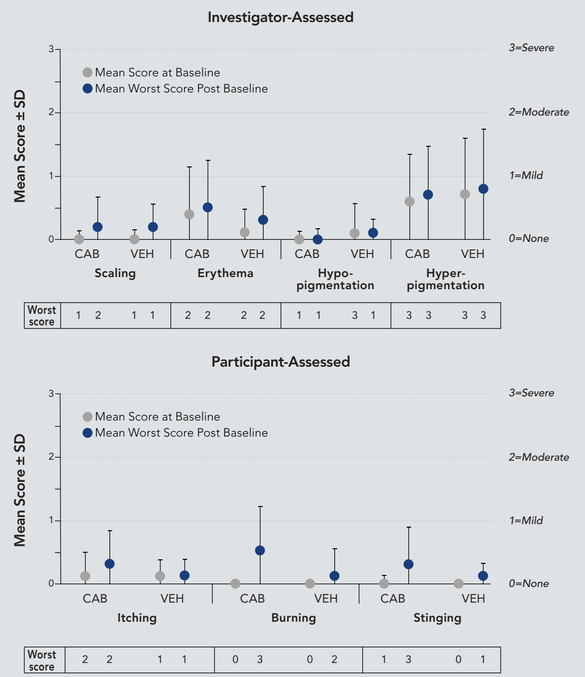
[a]Sickle cell anemia with crisis; not considered related to the study drug.
[b]Reported in ≥2% participants in any treatment group.
AE, adverse event; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

FIGURE 2. Lesion Reductions by Study Visit (ITT Population, Pooled)



*P<0.05, **P<0.01 vs vehicle.
Values have been adjusted for multiple imputation (Markov Chain Monte Carlo method). These studies were not powered for statistical analysis of between-group differences in Black participants.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; LS, least squares.

FIGURE 3. Cutaneous Safety and Tolerability in Black Participants (Safety Population, Pooled)



Mean worst score is the mean of the worst (highest) scores from each participant at any week after baseline.
N values: CAB: BL n=64, Post BL n=63; Vehicle: BL n=40, Post BL n=40.
BL, baseline; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; VEH, vehicle.

CONCLUSIONS

- The innovative fixed-dose, triple-combination CAB gel was well tolerated in Black participants with moderate-to-severe acne, and led to substantial acne reductions
- At week 12, nearly one-third of Black participants achieved treatment success with CAB versus less than one-fifth with vehicle gel
- CAB provided nearly 70% reductions in inflammatory lesions and nearly 60% reductions in noninflammatory lesions at week 12
  - The studies were not powered to detect significant differences between CAB and vehicle gel in this post hoc analysis of Black participants; therefore, *P* values are for informative purposes only
- Most TEAEs associated with CAB treatment were of mild-moderate severity
- Despite the small number of self-identified Black participants in these clinical studies of CAB gel, these post hoc analyses add valuable information to the limited literature describing treatment effects of fixed-dose combination acne treatments in Black individuals

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AUTHOR DISCLOSURES

Valerie Callender has served as an investigator, consultant, or speaker for Acne Store, Almirall, Aerolase, AbbVie, Allergan Aesthetics, Avava, Avita Medical, Beiersdorf, Cutera, Dermavant, Elrion Therapeutics, Eli Lilly, Galderma, Janssen, Jeune Aesthetics, L'Oréal, Ortho Dermatologics, Pfizer, Prollinium, Regeneron, Scientis, Sente, SkinBetter Science, SkinCeuticals, Symatese, Teoxane, and UpToDate. Andrew Alexis has received Grants (funds to institution) from Leo, Amgen, Galderma, Arcutis, Dermavant, AbbVie, Castle; advisory board/consulting from Leo, Galderma, Pfizer, Sanofi-Regeneron, Dermavant, Beiersdorf, Ortho Dermatologics, L'Oreal, BMS, Bausch health, UCB, Arcutis, Janssen, Allergan, Almirall, AbbVie, Amgen, VisualDx, Eli Lilly, Swiss American, Cutera, Cara, EPI, Incyte, Castle, Apogee, Canfield, Alphyn, Avita Medical, Genentech; speaker fees from Regeneron, SANOFI-Genzyme, BMS, L'Oreal, Janssen, J&J; equipment (loan to institution) from Aerolase; and royalties from Wiley-Blackwell and Wolters Kluwer Health. Neal Bhatia has served as advisor, consultant, and investigator for AbbVie, Almirall, Biofrontera, BI, Brickell, BMS, EPI Health, Ferndale, Galderma, inCyte, ISDIN, J&J, Lafloche-Posay, LEO Pharma, Ortho Dermatologics, Regeneron, Sanofi, Sun Pharma, Verrica, and Vyne. Julie Harper has received honoraria from Aclaris, Almirall, BioPharmX, Cassiopea, Cutanea, Dermira, Foamix, Galderma, Lafloche-Posay, Ortho Dermatologics, and Sun Pharma. Hilary Baldwin has served as advisor, investigator, and on speakers' bureau for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma.

ACKNOWLEDGEMENTS: Medical writing support was provided by Kavitha Abiraman, PhD, from Prescott Medical Communications Group, a Citrus Health Group, Inc., company (Chicago, Illinois) with financial support from Ortho Dermatologics; Ortho Dermatologics is a division of Bausch Health US, LLC • *Presented at the 2024 Fall Clinical Dermatology Conference* • *October 24–27, 2024* • *Las Vegas, NV*