

Electronic Supplementary material for the manuscript titled:

Triple Combination Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% for Acne: Efficacy and Safety from a Pooled Phase 3 Analysis

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eTable 1. Evaluator's global severity score

Grade	Value	Severity
Clear	0	Normal, clear skin with no evidence of acne
Almost clear	1	Rare noninflammatory lesions present, with rare noninflamed papules (papules must be resolving/may be hyperpigmented, not pink-red)
Mild	2	Some noninflammatory lesions present, few inflammatory lesions (papules/pustules only; no nodulocystic lesions)
Moderate	3	Noninflammatory lesions predominate, multiple inflammatory lesions: several/many comedones and papules/pustules, and 0-1 nodulocystic lesions
Severe	4	Inflammatory lesions more apparent, many comedones and papules/pustules, there may be 0-2 nodulocystic lesions

eTable 2. Efficacy endpoints at week 12 (ITT population; pooled)

	CAB Gel (n=242)	Vehicle Gel (n=121)	Treatment Difference (95% CI)	P-value
Co-primary endpoints				
Treatment success ^a , %	50.0	22.6	-	<0.001
Absolute change from baseline, mean (SD)				
Inflammatory lesions	-29.0 (9.5)	-21.0 (9.4)	-8.07 (-10.11, -6.03)	<0.001
Noninflammatory lesions	-35.3 (15.0)	-22.7 (14.6)	-12.66 (-15.87, -9.45)	<0.001
Secondary endpoints^b				
Percent change from baseline, mean (SD)				
Inflammatory lesions	-77.9 (25.6)	-57.9 (24.9)	-19.99 (-25.40, -14.58)	<0.001
Noninflammatory lesions	-73.0 (29.9)	-48.2 (29.2)	-24.78 (-31.22, -18.34)	<0.001
≥2-grade reduction in EGSS, %	56.2	23.8	-	<0.001

^aDefined as the proportion of participants achieving a ≥ 2-grade reduction from baseline in EGSS and a score of 0 (clear) or 1 (almost clear).

^bPercent changes in inflammatory and noninflammatory lesions at weeks 4 and 8 (additional secondary endpoints) are displayed in Figure 4.

Multiple imputation with the Markov Chain Monte Carlo method used to impute missing values.

Summary statistics represent average values, obtained from averaging the summary statistics generated from each imputed dataset. Negative values represent decrease from baseline.

CI, confidence interval; EGSS, Evaluator's Global Severity Score; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; SD, standard deviation.

eTable 3. Co-primary endpoints and select secondary endpoints at week 12 in participants aged 9-25 years^a (ITT population, pooled)

	CAB Gel (N=191)	Vehicle (N=94)	Treatment Difference (95% CI)	P-value
Inflammatory lesion counts—Absolute change from baseline at week 12				
LS Mean (LS SD) ^b	-29.4 (9.65)	-20.9 (10.02)	-8.55 (-11.00, -6.11)	<0.001 ^c
Median	-29.0	-22.0	-	-
Min to Max	-69 to -1	-49 to 22	-	-
Noninflammatory lesion counts—Absolute change from baseline at week 12				
LS Mean (LS SD) ^b	-36.3 (15.08)	-22.1 (15.36)	-14.19 (-17.99, -10.40)	<0.001 ^c
Median	-34.6	-25.0	-	-
Min to Max	-101 to 1	-71 to 35	-	-
EGSS reduction of ≥2 grade from baseline and achieving clear or almost clear at week 12				
Success, %	48.2	22.0	26.2 (15.2, 37.2) ^e	<0.001 ^d
Failure, %	51.8	78.0		
Inflammatory lesion counts—Percent change from baseline at week 12				
LS Mean (LS SD) ^b	-77.9 (25.38)	-56.8 (26.27)	-21.01 (-27.40, -14.61)	<0.001 ^c
Median	-85.0	-60.0	-	-
Min to Max	-100 to -3	-100 to 50	-	-
Noninflammatory lesion counts—Percent change from baseline at week 12				
LS Mean (LS SD) ^b	-72.9 (29.51)	-46.3 (30.26)	-26.57 (-34.10, -19.04)	<0.001 ^c
Median	-75.8	-53.5	-	-
Min to Max	-100 to 2	-100 to 76	-	-
EGSS reduction of ≥2 grade from baseline at week 12				
Success, %	54.2	23.8	30.4 (19.3, 41.6) ^e	<0.001 ^d
Failure, %	45.8	76.2	-	-

^aMultiple imputation with the Markov Chain Monte Carlo method used to impute missing values.

^bLeast squares means, standard deviations, difference in least squares means and associated 95% confidence interval from an analysis of covariance with factors of treatment group and analysis center and the respective baseline lesion count as a covariate. Negative least squares means values represent decrease from baseline.

^cP-values were obtained from a ranked analysis of covariance with factors of treatment group and analysis center and the respective baseline lesion count as a covariate.

^dEstimates and P-value from a logistic regression (using Firth's Penalized Likelihood) with factors of treatment group and analysis center.

^eTreatment difference and corresponding 95% confidence interval based on the reported percentage successes.

CI, confidence interval; EGSS, Evaluator's Global Severity Score; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; LS, least squares; Max, maximum; Min, minimum; SD, standard deviation.

eTable 4. Summary of Acne-QoL questionnaire responses (ITT population)

Domain	CAB Gel (n=214)		Vehicle Gel (n=111)	
	Mean	SD	Mean	SD
Self-Perception				
Baseline	21.6	9.4	20.7	8.4
Week 12	30.2	5.9	26.1	6.9
Role-Emotional				
Baseline	21.7	8.8	21.4	7.5
Week 12	29.3	5.6	25.1	6.7
Role-Social				
Baseline	20.4	7.3	20.4	7.0
Week 12	25.6	4.3	23.6	5.6
Acne Symptoms				
Baseline	20.1	5.7	20.1	5.5
Week 12	27.6	4.2	24.9	5.3

No imputation of missing values. A higher score at week 12 indicates improvement.

Range of possible scores are 5-35 for self-perception, role-emotional, and acne symptoms and 4-28 for role-social.

Acne-QoL, Acne-specific Quality of Life; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; SD, standard deviation.

eTable 5. All related TEAEs reported in any treatment group through week 12 (safety population)

Participants, n (%)	CAB Gel (n=242)	Vehicle Gel (n=121)
Application site pain	31 (12.8)	1 (0.8)
Application site dryness	7 (2.9)	0
Erythema	6 (2.5)	0
Application site irritation	5 (2.1)	0
Application site exfoliation	4 (1.7)	0
Xerosis	3 (1.2)	1 (0.8)
Application site dermatitis	3 (1.2)	0
Application site erythema	3 (1.2)	0
Application site pruritus	2 (0.8)	0
Application site burn	1 (0.4)	0
Application site paraesthesia	1 (0.4)	0
Dry skin	1 (0.4)	0
Swelling face	1 (0.4)	0
Paraesthesia	1 (0.4)	0

CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; TEAE, treatment-emergent adverse event.