Triple-Combination Fixed-Dose Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% for Moderate-to-Severe Acne: Efficacy and Safety Results From a Pooled Phase 3 Analysis

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SYNOPSIS AND OBJECTIVE

- A three-pronged approach to acne treatment that combines an antibiotic, a retinoid, and an antimicrobial agent in a single formulation may be more efficacious than monotherapy or dual combinations, while potentially reducing antibiotic resistance
- Clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide [BPO] 3.1% polymeric mesh gel (IDP-126) is the first fixed-dose triple-combination acne topical in development
- IDP-126 demonstrated superior efficacy to vehicle and component dyads, with good safety/tolerability, in a phase 2 and two phase 3 studies of moderate-to-severe acne[1,2]
- This post hoc analysis examined efficacy, safety, and impact on quality of life of IDP-126 in data pooled from the phase 3 studies

METHODS

- In two identical phase 3, double-blind, randomized studies (NCT04214639; NCT04214652), participants aged ≥9 years with moderate-to-severe acne were randomized 2:1 to receive IDP-126 or vehicle gel once daily for 12 weeks
  - CeraVe® hydrating cleanser and CeraVe® moisturizing lotion (L'Oreal, NY) were provided as needed for optimal skin moisturization/cleaning
- Endpoints included treatment success (≥2-grade reduction from baseline in Evaluator's Global Severity Score [EGSS] and clear/almost clear skin), least-squares mean percent change from baseline in inflammatory/noninflammatory lesion counts, and the Acne-Specific Quality of Life questionnaire (Acne-QoL)[3]
- Treatment-emergent adverse events (TEAEs) and cutaneous safety and tolerability were also evaluated

RESULTS

Participants

- Of the 363 participants in the pooled population, a majority were female (58.4%) or White (73.6%), with a mean age of 20.3 years
- More than 90% of participants had moderate disease (EGSS=3) at baseline

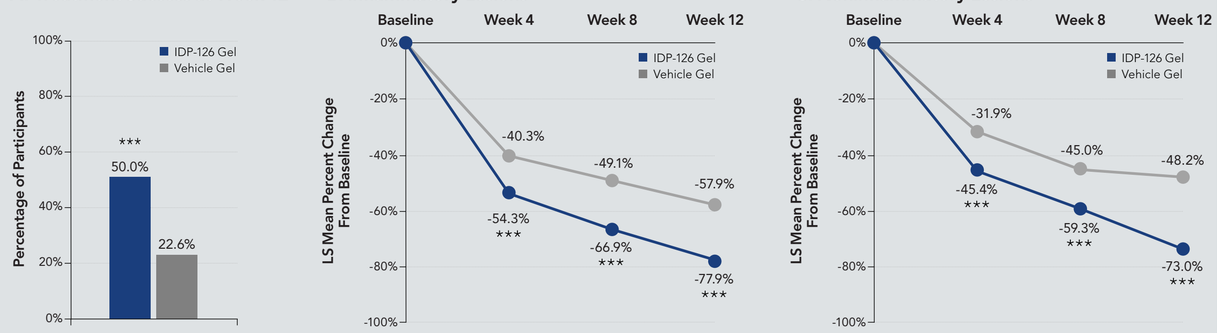
Efficacy and Quality of Life

- At week 12, half of participants treated with IDP-126 achieved treatment success versus less than one quarter treated with vehicle (*P*<0.001; **Figure 1A**)
- At week 12, IDP-126 resulted in >70% reductions in both inflammatory and noninflammatory lesions (*P*<0.001 versus vehicle, both; **Figure 1B, C**)
  - Lesion reductions were significantly greater with IDP-126 versus vehicle as early as week 4
- Acne-QoL improvements from baseline to week 12 were significantly greater with IDP-126 than vehicle across all four domains (**Figure 2**)
- Images of representative IDP-126-treated participants are shown in **Figure 3**

Safety

- TEAEs were generally mild or moderate and more frequent among participants treated with IDP-126 (**Table 1**)
- Rates of discontinuation from study/treatment due to a TEAE were low (<3%)
- Transient increases from baseline in investigator-assessed scaling and erythema and participant-assessed itching, burning, and stinging were observed with IDP-126, but resolved back to or near baseline values by week 12 (data not shown)

FIGURE 1. Treatment Success[a] at Week 12 and Lesion Reductions From Baseline by Study Visit (ITT Population, Pooled)

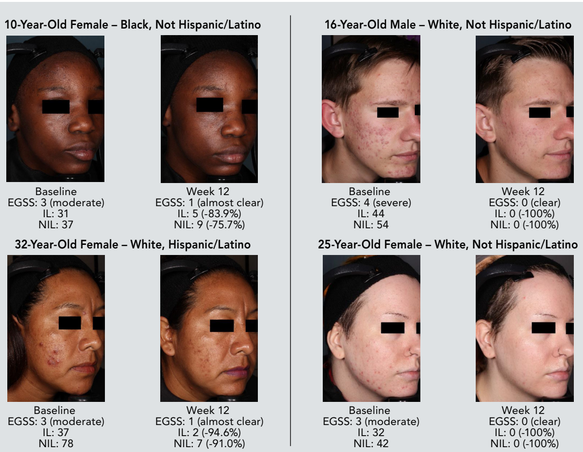


***P<0.001 vs vehicle.
[a]Defined as percentage of participants achieving ≥2-grade reduction from baseline in EGSS and a score of 0 (clear) or 1 (almost clear).
N values were: IDP-126, 242; Vehicle, 121.
Values have been adjusted for multiple imputation.
EGSS was scored as: 0 (clear) = Normal, clear skin/no evidence of acne; 1 (almost clear) = Rare noninflammatory lesions, with rare noninflamed papules; 2 (mild) = Some noninflammatory lesions, with few inflammatory lesions; 3 (moderate) = Noninflammatory lesions predominate, with multiple inflammatory lesions: several/many comedones and papules/pustules, ≤1 nodulocystic lesion; 4 (severe) = Inflammatory lesions more apparent, many comedones/papules/pustules, ≤2 nodulocystic lesions
EGSS, Evaluator's Global Severity Score; IDP-126, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat; LS, least squares.

FIGURE 2. Acne-QoL Improvements at Week 12 (ITT Population, Pooled)

***P<0.001 vs vehicle.
No imputation of missing values.
Horizontal black lines indicate domain scores at baseline for all participants with baseline data: IDP-126, n=242; vehicle, n=121. Arrows indicate changes from baseline for participants with Acne-QoL scores at both baseline and week 12: IDP-126, n=214; vehicle, n=111.
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 questionnaire; IDP-126, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent-to-treat; LS, least squares.

FIGURE 3. Acne Improvements with IDP-126 Gel



Individual results may vary.
EGSS, Evaluator's Global Severity Score; IDP-126, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; IL, inflammatory lesions; NIL, noninflammatory lesions.

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

Participants, n (%)	IDP-126 Gel (n=242)	Vehicle Gel (n=121)
Reporting any TEAE	66 (27.3)	10 (8.3)
Reporting any SAE	0	0
Discontinued study drug due to TEAE[a]	7 (2.9)	0
TEAE severity		
Mild	40 (16.5)	8 (6.6)
Moderate	23 (9.5)	2 (1.7)
Severe[b]	3 (1.2)	0
Treatment-related TEAE severity		
Mild	27 (11.2)	1 (0.8)
Moderate	18 (7.4)	1 (0.8)
Severe	3 (1.2)[c]	0
Treatment-related TEAEs[d]		
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

[a]Prematurely discontinued study drug or study due to an adverse event. Related to study drug (n=1 each): mild erythema; severe application site burn; moderate swelling face, moderate application site pain, moderate erythema, and mild application site exfoliation; moderate application site pain; moderate application site dermatitis; moderate application site irritation. Not related to study drug (n=1): influenza like illness.
[b]All related to study drug.
[c]n=1 each: application site burn (led to study withdrawal); application site pain and application site dryness; application site pain.
[d]Reported in ≥2% of participants in either treatment group.
IDP-126, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- IDP-126, an innovative fixed-dose triple-combination clindamycin phosphate 1.2%/adapalene 0.15%/BPO 3.1% gel, was efficacious, well tolerated, and provided improvement in quality of life in children, adolescents, and adults with moderate-to-severe acne
- Half of participants achieved clear or almost clear skin by 12 weeks, rates not previously seen in clinical studies of other topical acne products

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AUTHOR DISCLOSURES

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. Michael Gold has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. 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. Julie Harper has received honoraria from Aclaris, Almirall, BioPharmX, Cassiopea, Cutanea, Dermira, Foamix, Galderma, LaRoche-Posay, Ortho Dermatologics, and Sun Pharma. James Q. Del Rosso has served as a consultant, investigator, and/or speaker for Ortho Dermatologics, Abbvie, Amgen, Arcutis, Dermavant, EPI Heath, Galderma, Incyte, LEO Pharma, Lilly, MC2 Therapeutics, Pfizer, Sun Pharma, and UCB. Neal Bhatia has served as advisor, consultant, and investigator for AbbVie, Almirall, Biofrontera, BI, Brickell, BMS, EPI Health, Ferndale, Galderma, InCyte, ISDIN, J&J, LaRoche-Posay, LEO Pharma, Ortho Dermatologics, Regeneron, Sanofi, Sun Pharma, Verrica, and Vyne. Hilary Baldwin has served as advisor, investigator, and on speakers' bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. Zoe Draelos received funding from Ortho Dermatologics. Valerie Callender has served as an investigator, consultant, or speaker for Acne Store, Almirall, Aerolase, AbbVie, Allergan Aesthetics, Avava, Avita Medical, Beiersdorf, Cutera, Dermavant, Eli Lilly, Epi Health, Galderma, Janssen, Jeune Aesthetics, L'Oréal, Ortho Dermatologics, Pfizer, Prollineum, Regeneron, Scientis, Sente, SkinBetter science, SkinCeuticals, Symatese, UCB, and UpToDate. Edward Lain has served as investigator, consultant and/or speaker for Ortho Dermatologics, AbbVie, Almirall, Amgen, Arcutis, Dermavant, EPI Health, Galderma, Incyte, LEO Pharma, Novartis, Eli Lilly, Pfizer, Sun Pharma, UCB, Endo International, ChemoCentryx, Biorasi, Sirnaomics, Evelo Biosciences, Concert Pharmaceuticals, Cara Therapeutics, Castle Biosciences, Mindera, Biofrontera, Altasigma, AiViva Biopharma, Anaptys Bio, Bausch Health, Dr Reddy's, Trevi Therapeutics.

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