Fixed-Dose Clindamycin Phosphate 1.2%, Benzoyl Peroxide 3.1%, and Adapalene 0.15% Gel for Moderate-to-Severe Acne: Phase 2 Study of the First-Triple-Combination Drug

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Objective To evaluate the efficacy, safety, and tolerability of IDP-126 in participants with moderate-to-severe acne

Methods In a phase 2, double-blind, multinational, 12-week study (NCT03170388), participants aged ≥9 years with moderate-to-severe acne were randomized (1:1:1:1) to once-daily IDP-126 gel, vehicle gel, or 1 of 3 component dyad combination gels.

Results A total of 741 participants were enrolled (men:60%, women:40%; mean age:15.8 years). Baseline demographics were well balanced across treatment groups. The efficacy and safety profiles of IDP-126 demonstrated its overall efficacy and safety, with no new safety signals identified.

Conclusion Overall, the efficacy, safety, and tolerability of IDP-126 as a fixed-dose triple-combination clindamycin phosphate 1.2%/BPO 3.1%/adapalene 0.15% gel (IDP-126) in a polymorphic dispersion system showed superior efficacy to vehicle gel and three fixed-dose combinations over 12 weeks in this phase 2 study of adult, adolescent, and pediatric participants with moderate-to-severe acne.

IDP-126 was also safe and well tolerated with low rates of discontinuations.

Synopsis The pathogenesis of acne is multifactorial, involving follicular proliferation of Cutibacterium acnes, increased sebum production, inflammation, and abnormal keratinization. Effective treatment requires pharmacologic targeting of one or more of these pathophysiologic mechanisms. There are numerous prescription oral and topical treatments for acne such as benzoyl peroxide (BPO), retinoids, antibiotics, and hormonal therapies. Combining three acne treatments (an antibiotic, an antibacterial, and retinoid) in a once-daily topical polymorphic dispersion formulation may provide greater efficacy and tolerability than single or dyad treatments.

This is the first study of clindamycin phosphate 1.2%/BPO 3.1%/adapalene 0.15% (IDP-126) gel, which once approved will be the first triple-combination, fixed-dose topical acne treatment.

SYNOPSIS

The pathogenesis of acne is multifactorial, involving follicular proliferation of Cutibacterium acnes, increased sebum production, inflammation, and abnormal keratinization. Effective treatment requires pharmacologic targeting of one or more of these pathophysiologic mechanisms. There are numerous prescription oral and topical treatments for acne such as benzoyl peroxide (BPO), retinoids, antibiotics, and hormonal therapies. Combining three acne treatments (an antibiotic, an antibacterial, and retinoid) in a once-daily topical polymorphic dispersion formulation may provide greater efficacy and tolerability than single or dyad treatments.

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METHODS

In a phase 2, double-blind, multinational, 12-week study (NCT03170388), participants aged ≥9 years with moderate-to-severe acne were randomized (1:1:1:1) to once-daily IDP-126 gel, vehicle gel, or 1 of 3 component dyad combination gels.

The Evaluator’s Global Severity Score (EGSS) was scored as follows (clear) = Normal, clear skin/no evidence of acne, 1 (almost clear) = Rare, noninflammatory lesions, with rare noninflammatory papules; 2 (mild) = Some noninflammatory lesions, with few inflammatory lesions, 3 (moderate) = Noninflammatory lesions predominate, with multiple inflammatory lesions: comedones and papules/pustules, c1 nodulocystic lesions; 4 (severe) = Inflammatory lesions more apparent, many comedones/papules/pustules, c2 nodulocystic lesions.

Ceramide hydrating cleanser and Ceramide moisturizing lotion (C24, NY) were provided as needed for optimal moisturization/clearing of the skin.

Endpoints were treatment success at week 12 (12-scaled reduction from baseline in EGSS and/or almost clear skin and lesions) and mean changes from baseline to week 12 in inflammatory/noninflammatory lesions.

Treatment-emergent adverse events (TEAEs) and cutaneous safety and tolerability (via 4-point scale where 0=none and 3=severe) were also assessed.

RESULTS

Participants A total of 741 participants were enrolled (men:60%, women:40%; mean age:15.8 years). Most participants were female and White, and most had moderate to severe disease (EGSS ≥3) at baseline (Table 1).

Treatment compliance across treatment groups was ≥93%.

Efficacy At week 12, over half of participants achieved treatment success with IDP-126 vs ~30% or less with vehicle gel and component dyads (P<0.001, all; Figure 1).

IDP-126 also demonstrated significantly greater absolute reductions in the number of inflammatory and noninflammatory lesions versus vehicle or dyads (P<0.001, all) compared to baseline (Figure 2).

Images depicting acne improvements in IDP-126-treated participants are shown in Figure 3.

Safety TEAEs rates were higher with IDP-126 and BPO/adapalene vs clindamycin/adapalene, or vehicle at week 12 (Table 2).

Most TEAEs were mild-to-moderate severity (data not shown).

With IDP-126, there was no severe scaling, erythema, hypopigmentation, or itching, and <1% of participants had severe hyperpigmentation, burning, or stinging (Table 2).

CONCLUSIONS

Once-daily treatment with the novel fixed-dose triple-combination clindamycin phosphate 1.2%/BPO 3.1%/adapalene 0.15% gel (IDP-126) in a polymorphic dispersion system showed superior efficacy to vehicle gel and three fixed-dose combinations over 12 weeks in this phase 2 study of adult, adolescent, and pediatric participants with moderate-to-severe acne.

IDP-126 was also safe and well tolerated with low rates of discontinuations.

Overall, the efficacy and safety profiles of IDP-126 demonstrate its potential as a new treatment option in the acne armamentarium.

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