Dermal Irritation, Sensitization, and Safety of Fixed-Dose Triple-Combination Clindamycin Phosphate 1.2%/Benzoyl Peroxide 3.1%/Adapalene 0.15% Gel in Healthy Participants

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BACKGROUND AND RATIONALE

- For acne vulgaris, the recommended first-line treatments are topical benzoyl peroxide (BPO) or retinoids as monotherapy, or in combination with each other and/or an antibiotic[1]
- Cutaneous irritation or dermatitis—either irritant (occurs rapidly post-contact) or allergic (a less common, delayed immune-mediated response)—may limit use of BPO or retinoids[2,3]
- IDP-126 polymeric mesh gel (clindamycin phosphate 1.2%/BPO 3.1%/adapalene 0.15%) is the first triple-combination, fixed-dose topical acne product in development and it addresses major acne pathophysiological processes
- In a phase 2 and two phase 3 studies in participants with moderate-to-severe acne, IDP-126 resulted in over 70% reductions of inflammatory and noninflammatory lesions at week 12, with good safety/tolerability[4]

OBJECTIVES

- To assess dermal irritation/sensitization and safety of IDP-126 gel in two phase 1 studies
- To compare irritancy of IDP-126 gel and commercially available BPO 2.5%/adapalene 0.3% gel in one phase 1 study of healthy participants

METHODS

- Two phase 1, randomized, evaluator-blinded, within-participant, dermal safety studies enrolled healthy participants aged ≥18 years (**Figure 1**)
- Patches were applied to participants' upper back multiple times over 6-8 weeks (RIPT) or every 24 hours for 21 days (CIPT; **Figure 1**)
  - Participants in each study received all treatments
- Endpoints comprised sensitization potential (allergic; RIPT only), mean cumulative/total irritation scores, and treatment-emergent adverse events (TEAEs)
  - Clinical grading of irritation consisted of a combination of letter and numerical grades (see table at bottom in **Figure 2**)

RESULTS

Participants

- A total of 279 participants were randomized
- RIPT populations: safety, N=234; cumulative irritancy, n=209; sensitization, n=206
  - A total of 210 participants completed the induction phase and received the challenge phase applications, and 206 (88.0%) completed the study
- CIPT population: safety, N=45
  - A total of 44 participants were included in the irritation analysis, and 42 (93.3%) completed the study
- In both studies, the mean age of participants was ~55 years, and the majority were female (RIPT: 71.4%; CIPT: 77.8%), Black (RIPT/CIPT: ~68%), and non-Hispanic (89.3%; 91.1%), with a Fitzpatrick skin type of IV-VI (65.4%; 80.0%)

Dermal Sensitization and Irritation

- Overall, irritation with IDP-126 was moderate and not clinically significant
- RIPT: No participants had investigator-confirmed sensitization to any treatments
  - As expected, mean cumulative irritation scores were higher with IDP-126 vs vehicle or saline 0.9% (*P*<0.001, both; **Figure 2**)
  - IDP-126 gel, vehicle gel, and saline 0.9% were all classified as not causing clinically significant irritation
- CIPT: IDP-126 had a score of "moderately irritating," but was significantly less irritating than BPO 2.5%/adapalene 0.3% (*P*<0.001; **Figures 2 and 3**)
  - The highest normalized total irritation score was observed for BPO 2.5%/adapalene 0.3% gel, which was significantly greater than IDP-126 (401 vs 264; *P*<0.001; **Figure 3**)

Adverse Events

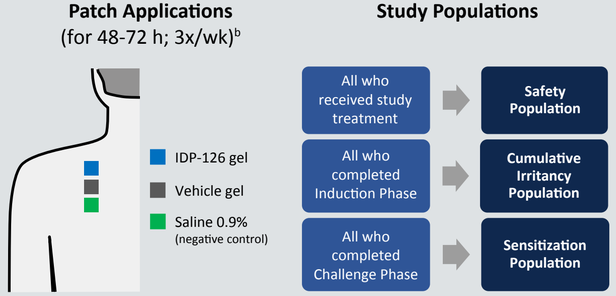
- In both studies, most TEAEs were of mild-moderate severity, and <3% of participants discontinued due to AEs/TEAEs (**Table 1**)
- No TEAEs/serious AEs were related to treatment
- There was no contact dermatitis or discontinuation of patch applications due to irritation

FIGURE 1. Study Designs for the RIPT and CIPT Studies[2,5,6]

Repeat Insult Patch Test (RIPT)

Determines the potential of a topical treatment to induce sensitization (allergic potential) via repeated applications

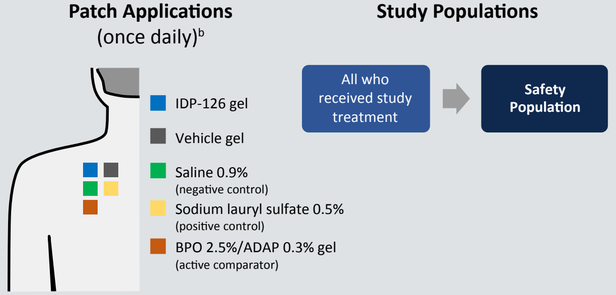
In induction and challenge phases, patches were applied 10 times to left or right upper back over 6-8 weeks. If re-challenge[a] was required, patches were applied 11 additional times.



Cumulative Irritancy Patch Test (CIPT)

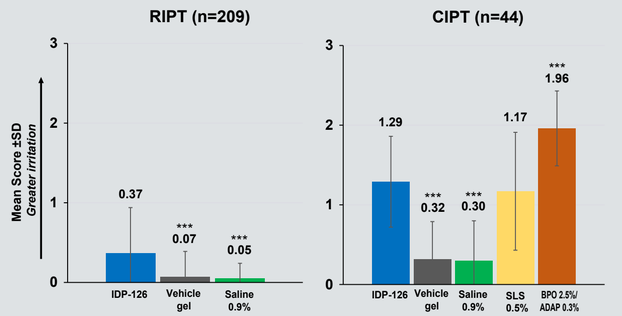
Evaluates a topical treatment's irritancy potential as a result of direct damage to the epidermal cells (without involvement of allergic or immunologic mechanism) via repeated applications

Over 21 days, patches were applied once daily to the left or right upper back for 24h.



[a]Participants were only re-challenged to a study material if there were signs suggestive of contact sensitization observed at any challenge evaluations or at the investigator's discretion.
[b]Treatment patch placement was randomized for each participant.
ADAP, adapalene; BPO, benzoyl peroxide; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%.

FIGURE 2. Mean Cumulative Irritation Scores (RIPT Cumulative Irritancy Population; CIPT Safety Population)



CUMULATIVE IRRITATION SCORE
NUMERICAL GRADE + LETTER GRADE
MAX WORST SCORE = 6

Numerical grade	
0	No evidence of irritation
1	Minimal erythema; barely perceptible
2	Definite erythema, readily visible; or minimal edema; or minimal papular response
3	Erythema, edema, and/or papules; vesicular eruption; or strong spreading reaction

Letter grade (converted to numbers)	
0	Slight glazed appearance
1	Marked glazing
2	Glazing with peeling and cracking
3	Glazing with fissures; film of dried serous exudate; or small petechial erosions

***P<0.001 vs IDP-126 gel.
Saline 0.9%=negative control; SLS 0.5%=positive control; BPO 2.5%/ADAP 0.3%=active comparator.
BPO 2.5%/ADAP 0.3%, benzoyl peroxide 2.5%/adapalene 0.3% gel; CIPT, cumulative irritancy patch test; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel; RIPT, repeat insult patch test; SD, standard deviation; SLS, sodium lauryl sulfate.

FIGURE 3. Normalized Total Irritation Scores (CIPT Safety Population)

To determine irritation classification of each treatment, a normalized total score for each patch was calculated by multiplying the mean total irritation score by a factor of 10

- 0–49 = no significant irritation
- 50–199 = slightly irritating
- 200–449 = moderately irritating
- 450–630 = highly irritating

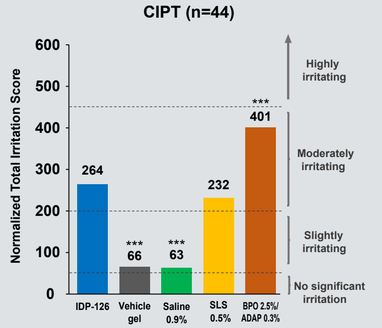


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TABLE 1. Treatment-Emergent Adverse Events (Safety Populations)

n (%)	RIPT (n=234)	CIPT (n=45)
Participants reporting any TEAE	4 (1.7)	1 (2.2)
Participants reporting any SAE[a]	1 (0.4)	1 (2.2)
Participants discontinuing due to AE/TEAE[b]	3 (1.3)	1 (2.2)
Deaths	1 (0.4)[c]	0
Severity of TEAEs		
Mild	2 (0.9)	0
Moderate	1 (0.4)	1 (2.2)
Severe	1 (0.4)	0
Relationship to study drug		
Related	0	0
Unrelated	4 (1.7)	1 (2.2)

[a]None of the participants had SAEs that were considered treatment related.
[b]Discontinuing from the study or study drug; none of the AEs were deemed related to treatment.
[c]Patient died during hospitalization for suspected COVID-19; no proof of death could be obtained.
AE, adverse event; CIPT, cumulative irritancy patch test; RIPT, repeat insult patch test; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- In two phase 1 studies, fixed-dose, triple-combination IDP-126 polymeric mesh gel had moderate irritancy and no confirmed sensitization (ie, allergic potential) in healthy participants
- Additionally, IDP-126 gel demonstrated significantly less irritation versus commercially available, branded BPO 2.5%/adapalene 0.3% gel
- IDP-126 was well tolerated, with most TEAEs of mild-moderate severity
- Overall, IDP-126 demonstrated good safety and tolerability, mirroring the phase 2 and phase 3 study results[4]

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AUTHOR DISCLOSURES

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