Novel Tretinoin 0.05% lotion for the once-daily treatment of moderate-to-severe acne vulgaris: Assessment of safety and tolerability in subgroups

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Background

- Topical tretinoin has been extensively studied in clinical trials, and its essential role in the treatment of acne vulgaris (acne) established through evidence-based guidelines
- However, there is a common perception that their use is associated with significant cutaneous irritation, and the potential to cause or exacerbate postinflammatory hyperpigmentation (PIH) in those patients especially vulnerable (i.e., Hispanics and African Americans)
- A new lotion formulation of tretinoin has recently been developed leveraging polymerized emulsion technology with the aim to improve both efficacy and tolerability (Figure 1).

Objective

- To evaluate safety, and tolerability of a novel tretinoin 0.05% lotion in moderate-to-severe acne in a number of subpopulations. .

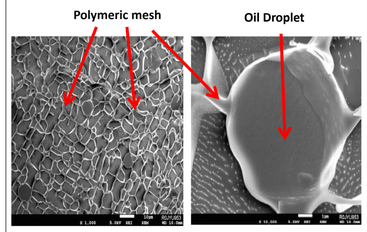
Methods

- A total of 1640 patients, 9-58 years of age were randomized to receive a novel tretinoin 0.05% lotion or vehicle in two double-blind, placebo-controlled 12-week, 2-arm, parallel group studies evaluating safety and efficacy
- CeraVe® hydrating cleanser and CeraVe® moisturising lotion (L'Oreal, NY) were provided for optimal moisturization/cleaning of the skin
- Cutaneous safety (erythema and scaling) and tolerability (itching, burning and stinging) were assessed using a scale of 0 (none) to 3 (severe)
- Safety was evaluated through reported adverse events (AEs), which were summarized by treatment group, severity, and relationship to study treatment
- A number of subpopulations were investigated to provide additional insights.

Results

- Across the two studies, tretinoin 0.05% lotion was considered safe and very well tolerated
- The most commonly reported treatment-related AEs were of low incidence and included application site reactions, and skin related events attributed to the known properties of tretinoin (Table 2)
- Only application site pain (3.1%), dryness (3.7%) and erythema (1.4%) were reported by >1% or patients
- Skin reactions (such as scaling, burning and stinging) were rare, mild and transient
- Treatment-related AEs were particularly rare (≤2%) in the Hispanic subpopulation and males, and significantly less than in the non-Hispanic (P<0.001) and female (P=0.008) subpopulations see Tables 2 and 3
- In all subgroups, severity of cutaneous safety and tolerability scores remained below 0.5 (where 1=mild) over the course of the studies and were generally lower than baseline severity
- In those patients where PIH may be more of a concern than the acne which proceeds it, there was no evidence to suggest that treatment with tretinoin 0.05% lotion caused or exacerbated PIH.

Figure 1: Cryo scanning electron microscopy (SEM) imaging of lotion formulation



1000X Magnification Lotion Vehicle — 10000X Magnification Lotion Vehicle

Table 1: Treatment-Emergent and Related Adverse Event (AE) Characteristics through Week 12 (Pooled Data – Safety Population)

	Tretinoin 0.05% Lotion (N=767)	Vehicle Lotion (N=783)
Patients reporting any TEAE	180 (23.5%)	151 (19.3%)
Patients reporting any SAE	7 (0.9%)	4 (0.5%)
Patients who died	0 (0.0%)	0 (0.0%)
Patients who discontinued due to TEAE	12 (1.6%)	0 (0.0%)
Severity of AEs reported		
Mild	105 (13.7%)	95 (12.1%)
Moderate	67 (8.7%)	46 (5.9%)
Severe	8 (1.0%)	10 (1.3%)
Relationship to study drug (% by patient)		
Related	62 (8.1%)	15 (1.9%)
Unrelated	118 (15.4%)	136 (17.4%)
Treatment Related AEs reported by ≥1% patients		
Application site pain	24 (3.1%)	3 (0.4%)
Application site dryness	28 (3.7%)	1 (0.1%)
Application site erythema	11 (1.4%)	1 (0.1%)

Table 2: Treatment-Emergent and Related Adverse Event (AE) Characteristics through Week 12 (Pooled Data – Safety Population). Effect of gender

	Tretinoin 0.05% Lotion MALE PATIENTS (N=363)	Tretinoin 0.05% Lotion FEMALE PATIENTS (N=404)
Patients reporting any TEAE	79 (21.8%)	101 (25.0%)
Patients reporting any SAE	2 (0.6%)	5 (1.2%)
Patients who died	0 (0.0%)	0 (0.0%)
Patients who discontinued due to TEAE	2 (0.6%)	10 (2.5%)
Severity of AEs reported		
Mild	47 (12.9%)	58 (14.4%)
Moderate	27 (7.4%)	40 (9.7%)
Severe	5 (1.4%)	3 (0.7%)
Relationship to study drug (% by patient)		
Related	19 (5.2%)	43 (10.6%)
Unrelated	60 (16.5%)	58 (14.4%)
Treatment Related AEs reported by ≥1% patients*		
Application site pain	8 (2.2%)	16 (3.9%)
Application site dryness	6 (1.7%)	22 (5.4%)
Application site erythema	4 (1.1%)	7 (1.7%)
Application site irritation	2 (0.6%)	5 (1.2%)
Application site pruritus	1 (0.3%)	6 (1.5%)

Table 3: Treatment-Emergent and Related Adverse Event (AE) Characteristics through Week 12 (Pooled Data – Safety Population). Effect of ethnicity

	Tretinoin 0.05% Lotion HISPANIC PATIENTS (N=345)	Tretinoin 0.05% Lotion NON-HISPANIC PATIENTS (N=421)
Patients reporting any TEAE	47 (13.6%)	67 (17.7%)
Patients reporting any SAE	2 (0.6%)	2 (0.5%)
Patients who died	0 (0.0%)	0 (0.0%)
Patients who discontinued due to TEAE	3 (0.9%)	0 (0.0%)
Severity of AEs reported		
Mild	36 (10.4%)	42 (11.1%)
Moderate	9 (2.6%)	19 (5.0%)
Severe	2 (0.6%)	6 (1.6%)
Relationship to study drug		
Related	15 (4.3%)	7 (1.8%)
Unrelated	32 (9.3%)	60 (15.8%)
Treatment Related AEs reported by ≥1% patients*		
Application site pain	7 (2.0%)	17 (4.0%)
Application site dryness	5 (1.4%)	23 (5.5%)
Application site erythema	4 (1.2%)	7 (1.7%)
Application site pruritus	2 (0.6%)	5 (1.2%)

Conclusion

This novel tretinoin 0.05% lotion developed using polymerized emulsion technology provides a highly favorable safety and tolerability profile in moderate-to-severe acne patients.

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