A Phase 3, Randomized, Double-Blind, Vehicle-Controlled, Multicenter, Parallel Group Trial Investigating the Efficacy and Safety of Clobetasol Propionate Cream, 0.025% in the Treatment of Moderate to Severe Plaque Psoriasis for 14 Days

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SYNOPSIS

- Topical corticosteroids continue to play a vital role in the management of numerous inflammatory skin conditions.
- However, the management of potential side effects remains a challenge, especially when introducing molecules with a higher potency.
- An alternative concentration of clobetasol propionate cream 0.025% (Impoyz®) formulated with diethylene glycol monoethyl ether (Transcutol P®), a drug solubility and permeation enhancer, demonstrated a lower degree of systemic exposure compared to the traditional 0.05% concentration of clobetasol propionate cream.[1]
- This study reports the efficacy and safety of clobetasol propionate cream 0.025% formulated with diethylene glycol monoethyl ether in adult patients with moderate to severe plaque psoriasis.

OBJECTIVE

- To study the efficacy and safety of a lower-concentration clobetasol propionate cream, 0.025% formulated with diethylene glycol monoethyl ether compared to vehicle for the topical treatment of adult moderate to severe plaque psoriasis.

METHODS

Trial Design and Patients

- This study was a randomized, multicenter, double-blind, vehicle-controlled trial performed across 27 sites in the United States.
- Eligible patients included males or females at least 18 years old with moderate to severe plaque psoriasis (stable for a minimum of 3 months) involving ≥3% body surface area (BSA) with an Investigators Global Assessment (IGA) score of 3 (moderate) or 4 (severe).
- Patients were randomized (2:1) to treatment with clobetasol propionate, 0.025 cream or vehicle cream, twice daily for 14 consecutive days.

Efficacy and Safety Endpoints

- The primary efficacy endpoint was the proportion of subjects with treatment success at Day 15 — defined as an IGA score of 0 (clear) or 1 (almost clear) and at least a 2-grade reduction from baseline.
- Secondary efficacy endpoints included the proportion of subjects with treatment success at the Day 8 visit and the percent change in affected BSA from baseline to the Day 15 visit.
- The primary safety assessment included evaluation by the site investigator for local cutaneous adverse events at all visits beyond baseline.

Statistical Analysis

- For analysis of the primary efficacy endpoint, a Cochran-Mantel-Haenszel (CMH) test for general association, stratified by analysis center, was performed to assess the difference in proportion of subjects with treatment success at Day 15 between the treatment and vehicle groups.
  - Significance testing for percent change in BSA from baseline was performed using a 2-way analysis of variance (ANOVA).
  - Proportion of subjects with treatment success at Day 8 was analyzed using a CMH test.
- Safety outcomes were assessed for the entire population of subjects who received at least 1 confirmed dose of study product and provided any post-baseline safety information. No imputations were made for missing safety data.
- All statistical analyses were performed using SAS Version 9.1.3 statistical software (Cary, NC).

RESULTS

Demographics

- Two hundred ninety subjects were screened for potential inclusion. Of these, 265 were randomized: 176 to the clobetasol group and 89 to the vehicle group.
  - Overall, 260 (98.1%) subjects completed the study, 175 (99.4%) in the clobetasol propionate group and 85 (95.5%) in the vehicle group.
- Demographic and disease characteristics were relatively equally distributed between the 2 groups (Table 1).
  - The only statistically significant difference between the groups was the proportion of subjects age 65 or older (P=.047).

Table 1. Baseline Demographic Characteristics

	Randomization Group			
	Clobetasol Propionate, 0.025% Cream (n=176)	Vehicle Cream (n=89)	Total (N=265)	P-value[a]
Gender (n, %)				0.343[b]
Male	111 (63.1%)	51 (57.3%)	162 (61.1%)	
Female	65 (36.9%)	38 (42.7%)	103 (38.9%)	
Mean Age ± SD	49.5 ± 13.6	50.6 ± 15.9	49.8 ± 14.4	0.377[c]
Age (n, %)				0.047[b]
< 65 Years	152 (86.4%)	70 (78.7%)	222 (83.8%)	
65 Years or Older	24 (13.6%)	19 (21.3%)	43 (16.2%)	
Baseline IGA (n, %)[d]				0.892[b]
0 (Clear)	0 (0)	0 (0)	0 (0)	
1 (Almost Clear)	0 (0)	0 (0)	0 (0)	
2 (Mild)	0 (0)	0 (0)	0 (0)	
3 (Moderate)	142 (80.7%)	72 (80.9%)	214 (80.8%)	
4 (Severe)	34 (19.3%)	17 (19.1%)	51 (19.2%)	
Mean BSA (%) % +/- SD[d]	8.7 ± 10.2	9.2 ± 11.3	8.8 ± 10.6	0.436[c]

[a]P value for significance testing for differences between clobetasol propionate, 0.025% and vehicle groups
[b]Cochran-Mantel-Haenszel test for general association, adjusted for site
[c]Two-Way Analysis of Variance (ANOVA)
[d]At baseline
BSA = Body Surface Area; IGA = Investigator's Global Assessment

Improvement in Treatment Success

- A significantly greater proportion of patients in the clobetasol propionate group experienced treatment success at Day 15 (30.1%) compared to patients who received vehicle (9.0%; P<.001; Figure 1).
  - Treatment success was defined as an IGA score of 0 (clear) or 1 (almost clear).
- The proportion of patients with treatment success at Day 8 was significantly greater in the clobetasol propionate, 0.025% group compared to the vehicle group (14.2% vs 1.1%, P<.001; Figure 1).

Reduction in Psoriasis-Affected BSA

- The reduction in mean BSA involvement from baseline to Day 15 was significantly greater in the clobetasol propionate, 0.025% group compared to the vehicle group (-25.1% vs -7.4%, P<.001; Figure 2).

Figure 1. Percentage of Study Participants Achieving Treatment Success

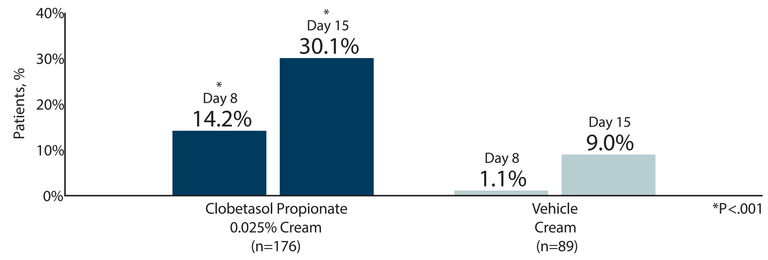
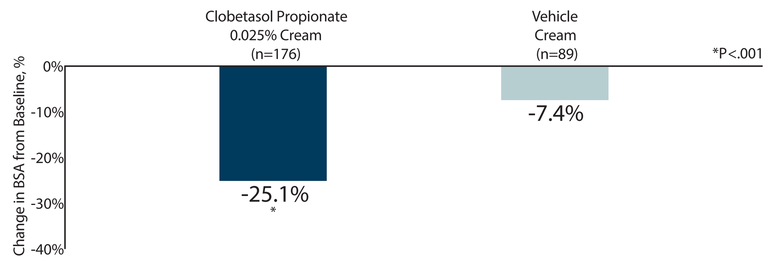


Figure 2. Mean Percent Change in BSA Involvement to Day 15



Safety Endpoints

- In general, the proportion of subjects experiencing local cutaneous adverse events decreased progressively throughout the study period (Table 2).
- At Day 15, the proportion of subjects experiencing atrophy, burning/stinging, pruritus, and fissuring was lower in the clobetasol propionate, 0.025% group compared to the vehicle group.
- The proportion of subjects experiencing striae (0.0% vs 0.6%) and hypopigmentation (1.2% vs 3.5%) were both lower in the vehicle group.
- No subjects in either group exhibited telangiectasia or folliculitis at Day 15.

Table 2. Proportion of Subjects Experiencing Local Cutaneous Signs & Symptoms

Local Cutaneous Signs & Symptoms	Treatment Group	Day 1 (Baseline) n (%)	Day 15 n (%)
Atrophy	Clobetasol propionate, 0.025%	1/176 (0.6%)	1/171 (0.6%)
	Vehicle	2/89 (2.2%)	2/83 (2.4%)
Telangiectasia	Clobetasol propionate, 0.025%	0/176 (0.0%)	0/171 (0.0%)
	Vehicle	1/89 (1.1%)	0/83 (0.0%)
Burning/Stinging	Clobetasol propionate, 0.025%	34/176 (19.3%)	10/171 (5.8%)
	Vehicle	18/89 (20.2%)	9/83 (10.8%)
Pruritus	Clobetasol propionate, 0.025%	91/176 (51.7%)	22/171 (12.9%)
	Vehicle	46/89 (51.7%)	19/83 (22.9%)
Striae	Clobetasol propionate, 0.025%	3/176 (1.7%)	1/171 (0.6%)
	Vehicle	0/89 (0.0%)	0/83 (0.0%)
Hypopigmentation	Clobetasol propionate, 0.025%	5/176 (2.8%)	6/171 (3.5%)
	Vehicle	4/89 (4.5%)	1/83 (1.2%)
Fissuring	Clobetasol propionate, 0.025%	0/176 (0.0%)	0/171 (0.0%)
	Vehicle	3/89 (3.4%)	7/83 (8.4%)
Folliculitis	Clobetasol propionate, 0.025%	0/176 (0.0%)	0/171 (0.0%)
	Vehicle	0/89 (0.0%)	0/83 (0.0%)

CONCLUSIONS

- **The results of this Phase 3 trial indicate that clobetasol propionate, 0.025% cream demonstrates superior efficacy in the treatment of moderate to severe plaque psoriasis compared tp vehicle cream.**
  - Efficacy was demonstrated early, at first post-treatment visit day 8 (14.2% vs 1.6%).
  - Efficacy continued during second week of treatment with more subjects in the clobetasol group achieving treatment success at final visit day 15 (30% vs 9%).
  - Efficacy is notable in that all subjects were diagnosed with moderate to severe plaque psoriasis with baseline IGA's of 3 or 4.
- **The incidence of local cutaneous side effects was low and very similar between subjects treated with clobetasol propionate, 0.025% compared to those who received the vehicle.**

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REFERENCE: 1. Draelos, Z. D., Fowler, J. F., & Cornelison, R. (2018). A Randomized, Parallel Group, Open Label, Multicenter Study to Assess the Potential for Adrenal Suppression and Systemic Drug Absorption Following Multiple Dosing with Clobetasol Propionate Cream (Impoyz™), 0.025% versus Clobetasol Propionate (Temovate®). SKIN The Journal of Cutaneous Medicine, 2(6). https://doi.org/10.25251/skin.2.6.16

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