

Assessment of the Vehicle for Roflumilast Cream Compared to a Commercially Marketed, Ceramide-Containing Moisturizing Cream in Patients With Mild Eczema

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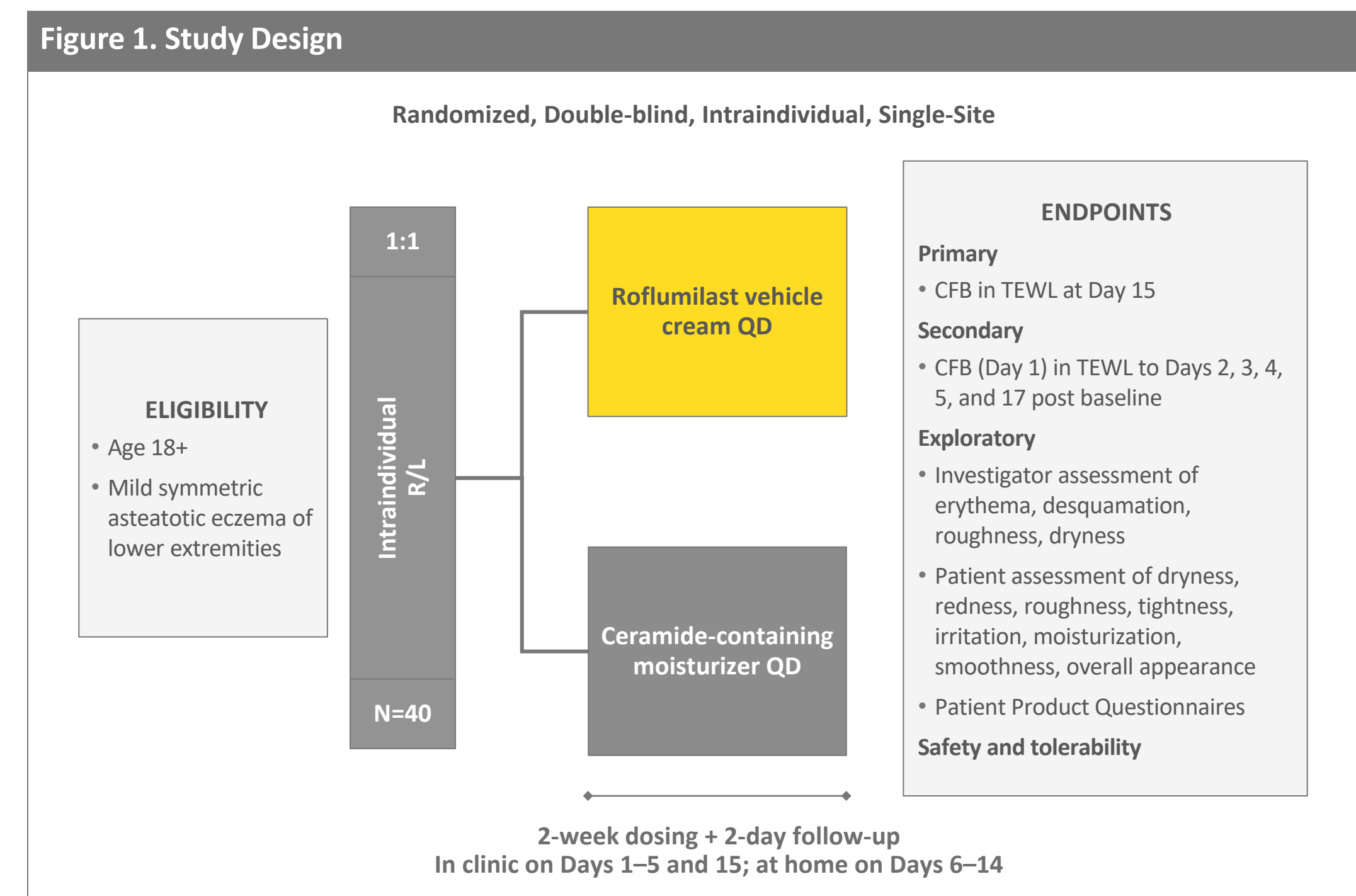
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INTRODUCTION

- In atopic dermatitis (AD) and many other inflammatory skin conditions, the skin barrier is damaged and patients frequently report that topical medications used to treat AD induce stinging, itching, irritation, and burning¹
- This may be due, in part, to the properties of dermatologic topical preparations employing penetration-enhancing vehicles designed to maximize delivery and absorption of the drug by damaging the stratum corneum
- Damaging the skin to increase drug penetration and enhance drug delivery can worsen disease and inhibit epidermal repair
- Topical roflumilast is a selective and highly potent phosphodiesterase-4 inhibitor being investigated for dermatological conditions, including AD²⁻⁴
- The vehicle for roflumilast cream is uniquely formulated at physiological skin pH (5.5), without propylene glycol, polyethylene glycol, ethanol, or fragrances, and with both 50% water and an ultra-mild emulsifier that is expected to result in no functional surfactant activity in clinical use
- In this study, we investigated properties of the vehicle for roflumilast cream, which did not contain active ingredient (roflumilast), compared with one of the leading, currently marketed, dermatologist-recommended, ceramide-containing moisturizers applied to patients with mild asteatotic eczema of the lower extremities once-daily for 15 days

METHODS

- This was a single-site, randomized, double-blinded, intraindividual study
- Male and female adult (aged ≥18 years) patients with mild, symmetric asteatotic eczema of the lower extremities were enrolled (Figure 1)
- The primary efficacy endpoint was the change in transepidermal water loss (TEWL) from baseline to Day 15
- Before treatment application, patients underwent a 1-minute TEWL measurement from both legs at a predetermined target site 6 inches above the ankle on the mid-anterior shin
- Research center staff then applied the assigned blinded study products (the vehicle for roflumilast cream and the ceramide-containing moisturizer, randomized to leg) to patients' lower legs
- Patients returned to the research center at least 4 hours after the initial visit and on Days 2, 3, 4, 5, 15, and 17 for TEWL measurements from both legs, product application (Days 2–5 and 15), investigator assessments, and patient assessments
- On Day 5, patients received a study diary and the study products
- Patients applied the assigned product to each leg every morning Days 6 through 14
- Patients completed a product questionnaire on Days 1 and 15 immediately after product application
- On Day 1, the product questionnaire contained 4 questions each rated on a 5-point scale (1=good; 5=poor):
 - How would you rate how the product spreads on your skin?
 - How would you rate how quickly the product absorbs into your skin?
 - How would you rate the feel of your skin after apply product to your skin?
 - How would you rate the smell of the product after you apply product to your skin?
- The questionnaire on Day 15 consisted of a single question answered on a 5-point scale (1=likely; 5=unlikely):
 - If allowed to do so, how likely would you be to continue using this product to treat your dry skin?



CFB: change from baseline; L: left lower leg; QD: once daily; R: right lower leg; TEWL: transepidermal water loss.

RESULTS

- A total of 40 patients participated (Table 1)
- Baseline disease characteristics were similar for the legs treated with roflumilast cream vehicle and legs treated with moisturizer (Table 2)

Table 1. Baseline Demographics

	Patients (n=40)
Age in years, mean	52
Age in years, median	54
Gender, n (%)	
Male	8 (20)
Female	32 (80)
Race, n (%)	
White	29 (72.5)
Black or African-American	11 (27.5)
Ethnicity, n (%)	
Not Hispanic/Latino	40 (100)
Fitzpatrick skin type, n (%)	
Fitzpatrick I–III	29 (72.5)
Fitzpatrick IV–VI	11 (27.5)

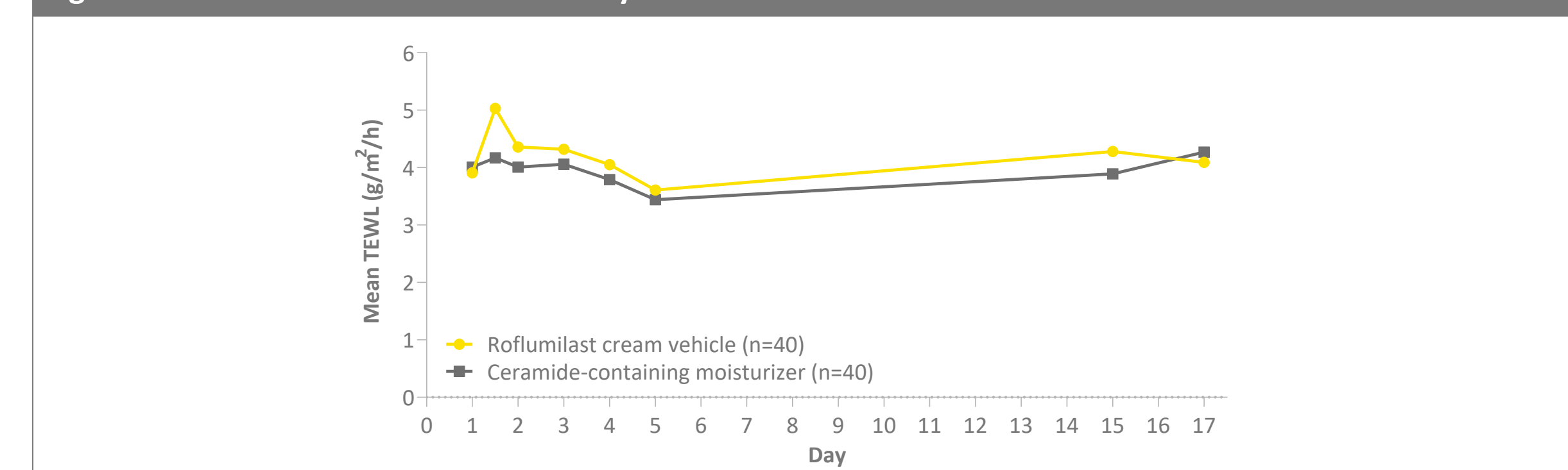
Table 2. Baseline Disease Characteristics

	Roflumilast Cream Vehicle (n=40)	Ceramide-Containing Moisturizer (n=40)
TEWL, in g/m ² /h, mean	3.91	4.01
Investigator efficacy, ^a mean		
Erythema	2.55	2.55
Desquamation	2.60	2.60
Roughness	2.60	2.60
Dryness	2.63	2.63
Patient efficacy, ^a mean		
Dryness	3.18	3.15
Redness	2.18	2.23
Roughness	3.08	3.05
Tightness	2.63	2.68
Irritation	2.73	2.68
Lack of moisturization	3.28	3.30
Lack of smoothness	3.08	3.13
Overall skin appearance problems	3.05	3.03

^a Assessed on 5-point scales (0=none; 4=severe). TEWL: transepidermal water loss.

- The primary efficacy endpoint was met for roflumilast cream vehicle
- No statistically significant change from baseline in TEWL at Day 15 and no skin barrier damage was demonstrated
- Mean TEWL was similar between roflumilast cream vehicle and ceramide-containing moisturizer on Days 1–17 (Figure 2)

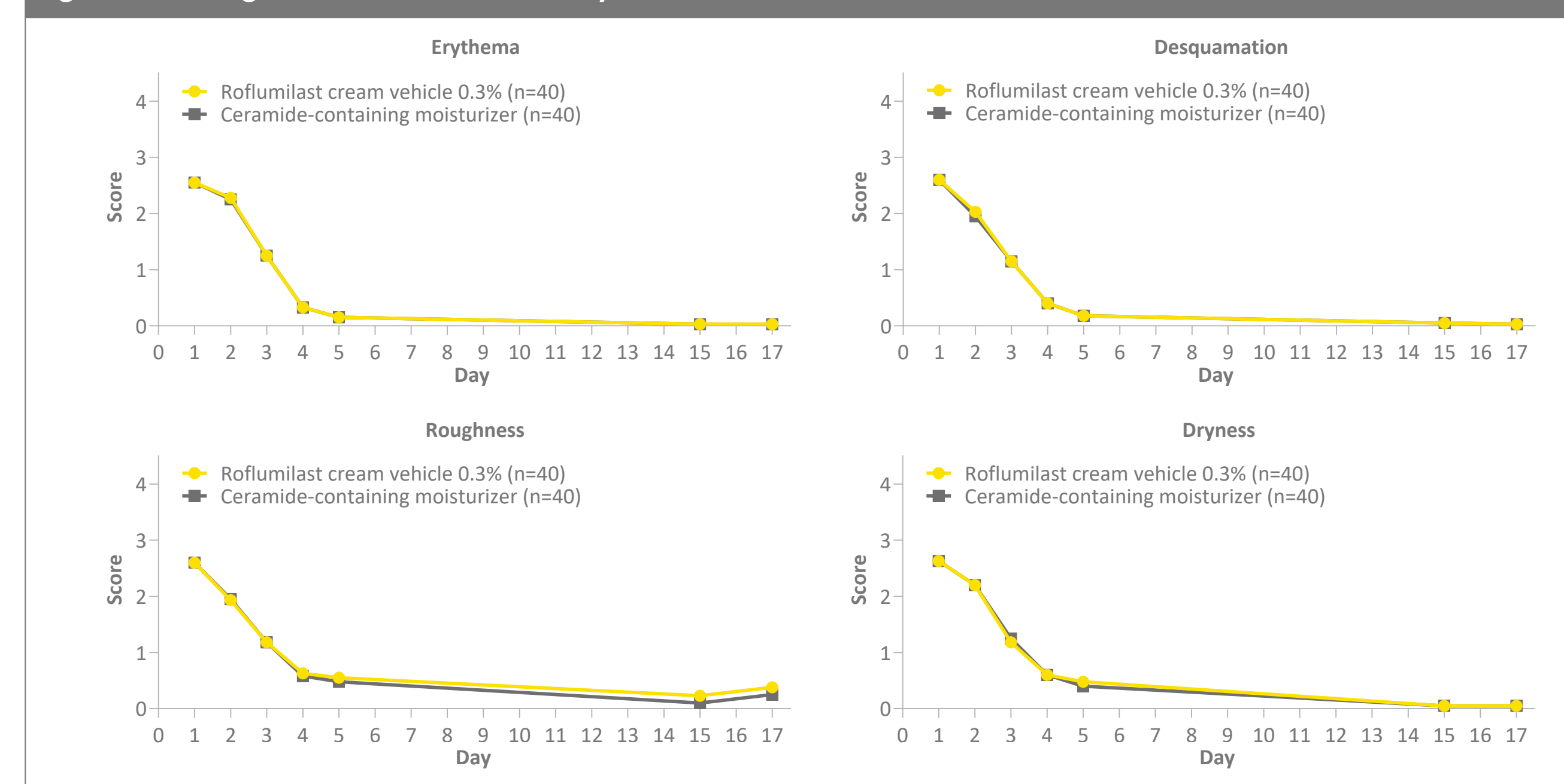
Figure 2. Mean TEWL Over Time From Days 1–17



TEWL: transepidermal water loss.

- Statistically significant and sustained improvements occurred in investigator-assessed erythema, desquamation, roughness, and dryness after the initial application at all timepoints through Day 15 for both roflumilast cream vehicle and the ceramide-containing moisturizer with similar results for both treatments at most timepoints (Figure 3)

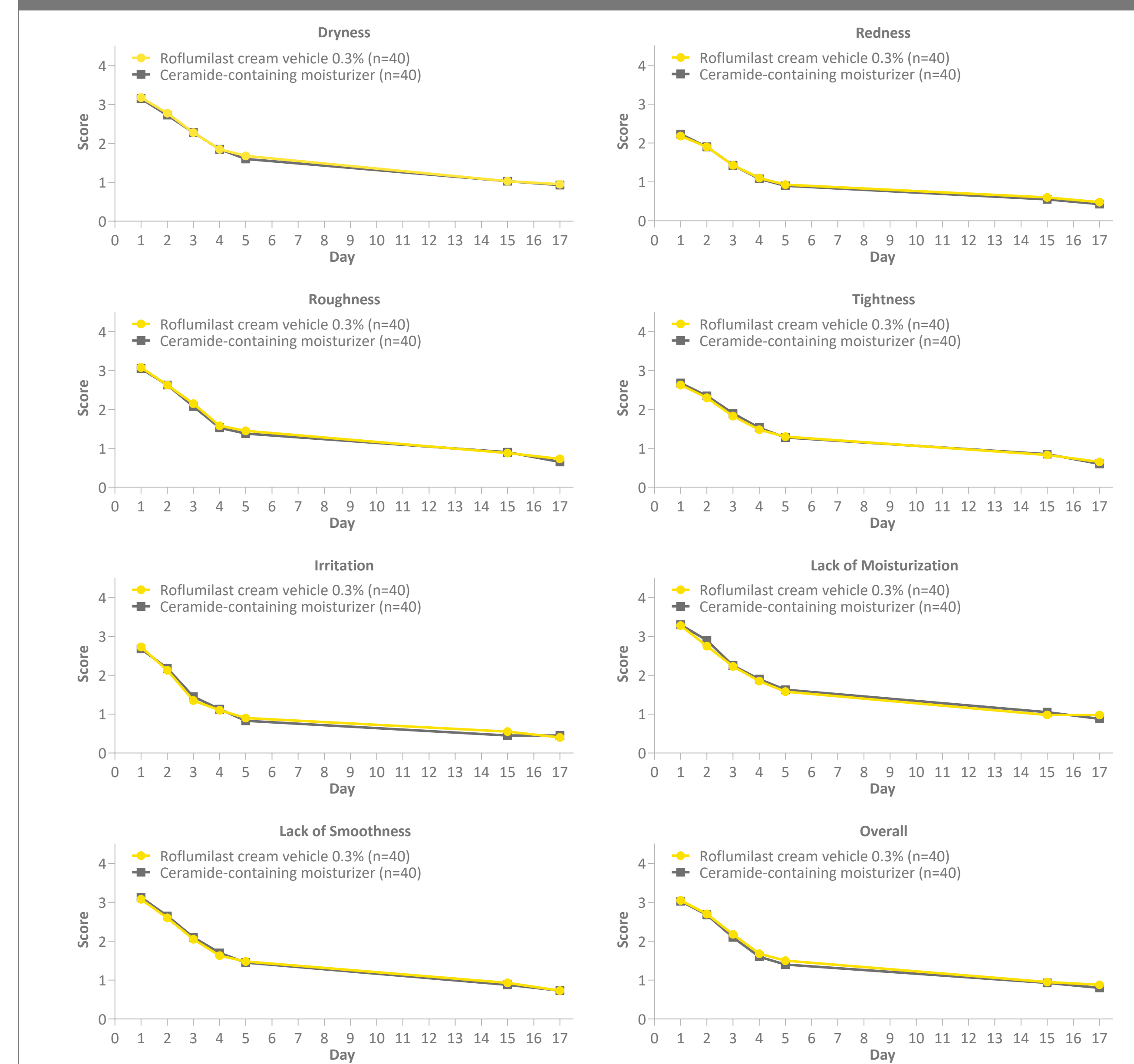
Figure 3. Investigator Assessment of Efficacy



Each measure evaluated on a 5-point scale (0=none; 4=severe). P<0.05 for all comparisons for roflumilast vehicle with ceramide-containing moisturizer.

- Statistically significant improvements also occurred with both treatments in patient-assessed measures of dryness, redness, roughness, tightness, irritation, moisturization, smoothness, and overall skin appearance with no differences between products (Figure 4)

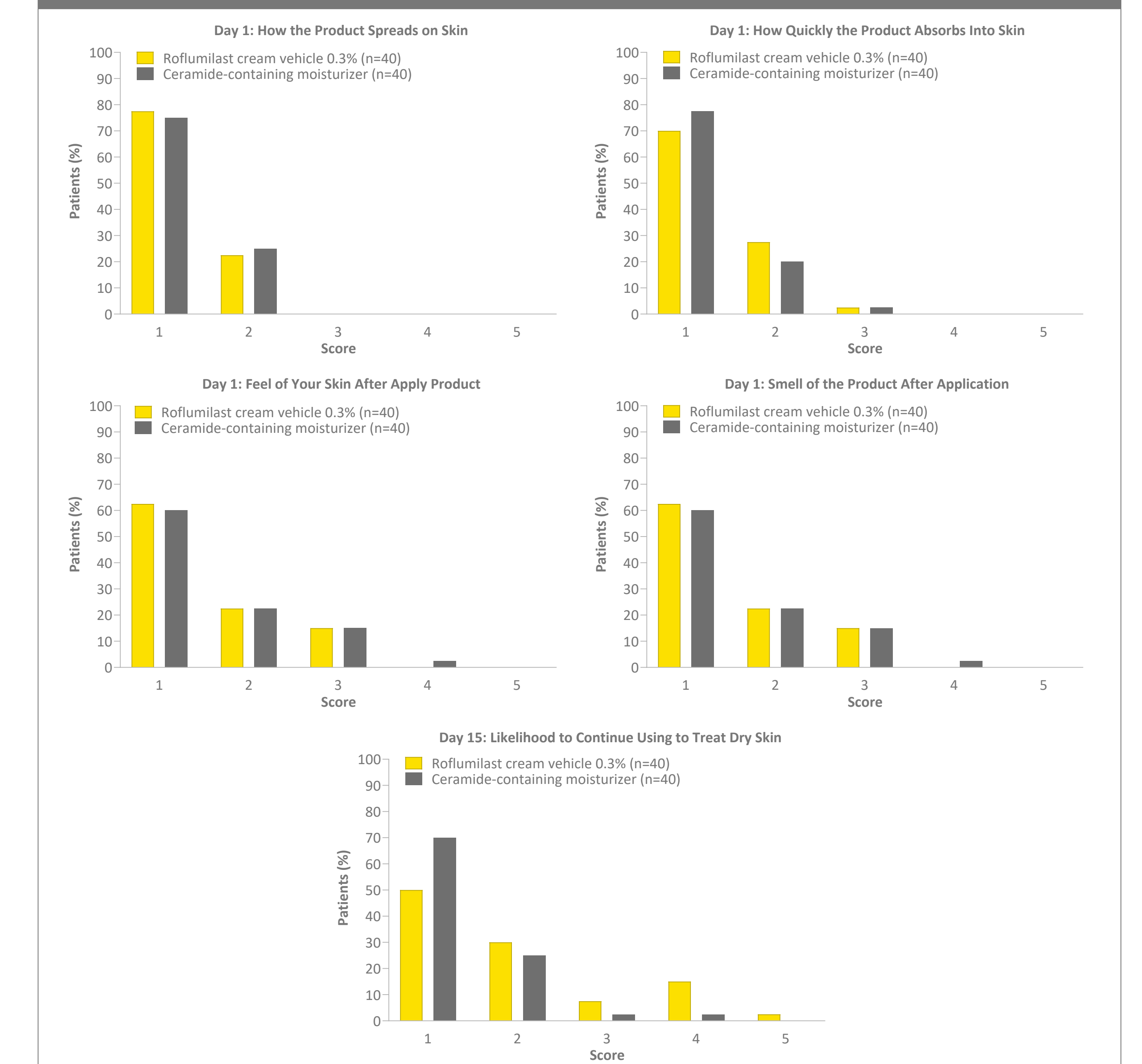
Figure 4. Patient Assessment of Efficacy



Each measure evaluated on a 5-point scale (0=none; 4=severe). P<0.05 for all comparisons for roflumilast vehicle with ceramide-containing moisturizer.

- Patients consistently rated aesthetic properties of roflumilast cream vehicle favorably and comparable with the ceramide moisturizer, and both products were well received (Figure 5)
- On Day 1, the aesthetic properties of roflumilast cream vehicle were consistently rated favorably and were considered comparable with the ceramide moisturizer
- On Day 15, most patients rated both products between likely and somewhat likely to continue using the product to treat their dry skin if allowed to do so
- No adverse events or tolerability issues were reported, including no stinging or burning

Figure 5. Patient Product Questionnaire



Day 1 questions evaluated on a 5-point scale (1=good, 2=somewhat good, 3=neither good nor poor, 4=somewhat poor, 5=poor); Day 15 question evaluated on a different 5-point scale (1=likely, 2=somewhat likely, 3=neither likely nor unlikely, 4=somewhat likely, 5=unlikely).

DISCUSSION

- Topical roflumilast is formulated as a water-based cream with an ultra-mild emulsifier at physiological pH of the skin without commonly used irritating ingredients or fragrances
- Compared with one of the leading, currently marketed, dermatologist-recommended, ceramide-containing moisturizers, the vehicle for roflumilast cream performed generally similar across most assessments in patients with asteatotic eczema
- Roflumilast cream vehicle did not produce any barrier damage since no significant change occurred in the objective measure of barrier function, TEWL, at Day 15
- Roflumilast cream vehicle was very similar to the ceramide-containing moisturizer across all patient and/or investigator assessments of efficacy, tolerability, and aesthetic properties
- These results suggest roflumilast cream vehicle performed as well as the ceramide-containing moisturizing cream among patients with mild asteatotic eczema of the lower extremities

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DISCLOSURES

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