

# Efficacy and Tolerability of Roflumilast Cream 0.3% in Patients With Chronic Plaque Psoriasis Involvement on the Face, Intertriginous, or Genital Areas: Pooled Results from Phase 3 Trials (DERMIS-1 and DERMIS-2)

Laura K. Ferris,<sup>1</sup> April Armstrong,<sup>2</sup> James Del Rosso,<sup>3</sup> Zoe D. Draelos,<sup>4</sup> Melinda Gooderham,<sup>5</sup> Mark Lebwohl,<sup>6</sup> Kim A. Papp,<sup>7</sup> Jennifer Soung,<sup>8</sup> Linda Stein Gold,<sup>9</sup> David Krupa,<sup>10</sup> Robert C. Higham,<sup>10</sup> Patrick Burnett,<sup>10</sup> David R. Berk<sup>10</sup>

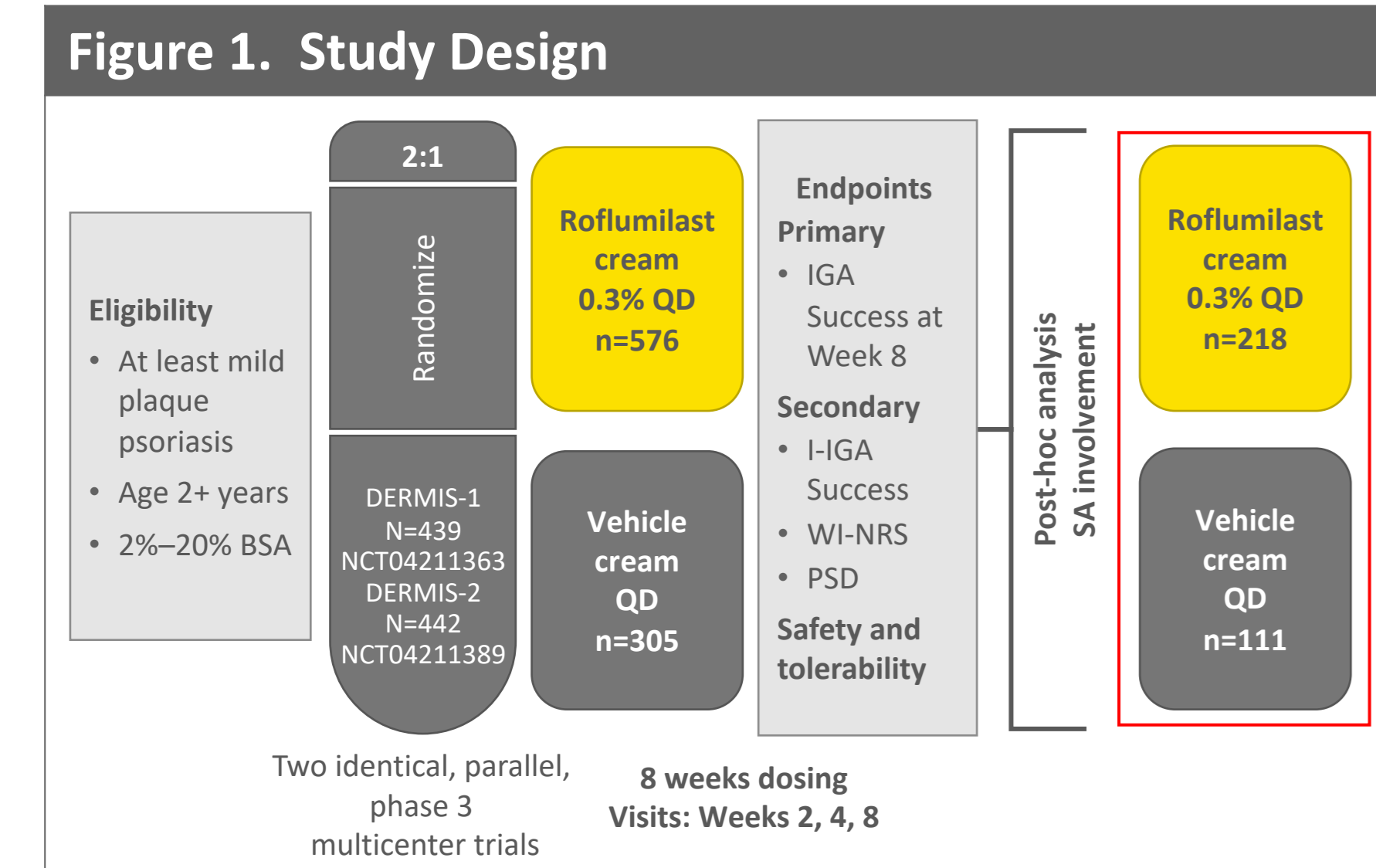
<sup>1</sup>University of Pittsburgh, Department of Dermatology, Pittsburgh, PA, USA; <sup>2</sup>Keck School of Medicine, Department of Dermatology, University of Southern California Los Angeles, CA, USA; <sup>3</sup>JDR Dermatology Research Center, LLC, Las Vegas, NV, USA; <sup>4</sup>Dermatology Consulting Services, High Point, NC, USA; <sup>5</sup>SKIN Centre for Dermatology, Probity Medical Research and Queen's University, Peterborough, ON, Canada; <sup>6</sup>Icahn School of Medicine at Mount Sinai, New York, NY, USA; <sup>7</sup>Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada; <sup>8</sup>Southern California Dermatology, Santa Ana, CA, USA; <sup>9</sup>Henry Ford Medical Center, Detroit, MI, USA; <sup>10</sup>Arcutis Biotherapeutics, Inc., Westlake Village, CA, USA

## INTRODUCTION

- Patients with psoriasis involving special areas, such as the face, intertriginous, and genital areas, may have a disproportionately greater negative impact on their quality of life than patients without psoriasis involvement in those areas<sup>1</sup>
- Chronic use of current topical treatment options in these areas is limited due to risk of local skin side effects or limitations on duration of use<sup>2</sup>
- Roflumilast is a selective and highly potent phosphodiesterase 4 (PDE4) inhibitor with greater affinity for PDE4 than apremilast or crisaborole and approximately 25- to >300-fold more potent based on in vitro assays<sup>3</sup>
  - Topical roflumilast is being investigated as a once-daily, nonsteroidal treatment for long-term management of various dermatologic conditions, including atopic dermatitis, seborrheic dermatitis, and chronic plaque psoriasis (approved by the US Food and Drug Administration July 29, 2022)
- Efficacy, safety, and tolerability of roflumilast cream 0.3% in psoriasis have been demonstrated in a phase 2b study in patients with psoriasis; the individual phase 3 DERMIS-1 and DERMIS-2 results were previously reported<sup>4,5</sup>
- Here, we report the pooled results from 2 phase 3, randomized, double-blind, vehicle-controlled, multicenter trials of once-daily roflumilast cream 0.3% in patients with psoriasis (DERMIS-1 and DERMIS-2), presenting subgroup analyses of patients with involvement of special areas (SAs: defined as the face, and/or intertriginous, and/or genital areas)

## METHODS

- DERMIS-1 and DERMIS-2 were 2 identical, phase 3, randomized, double-blind, vehicle-controlled, 8-week studies of once-daily roflumilast cream 0.3% in patients (≥2 years of age) with psoriasis (body surface area [BSA] affected: 2%–20%; Figure 1)
- The primary efficacy endpoint was Investigator Global Assessment (IGA) Success at Week 8, which was defined as achievement of Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline



IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline. BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: intertriginous IGA; PSD: Psoriasis Symptoms Diary; QD: once daily; SA: special areas (SA: defined as the face, and/or intertriginous, and/or genital areas); WI-NRS: Worst Itch Numeric Rating Scale.

## RESULTS

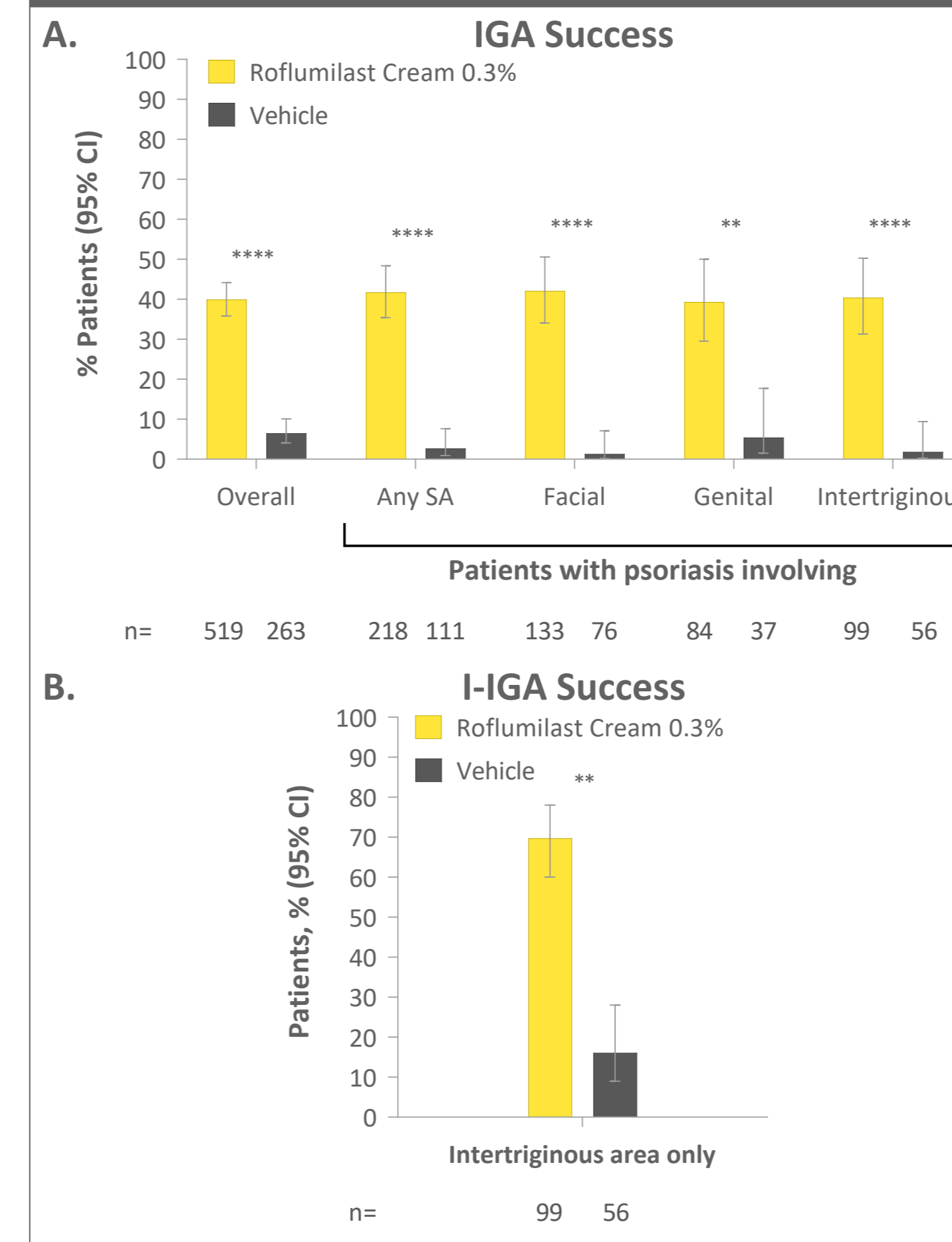
- Baseline disease characteristics and demographics were similar across treatment groups (Table 1)
- Significantly more roflumilast-treated patients achieved the primary endpoint, IGA Success at Week 8 (Figure 2)
  - Across the subgroups at Week 8, a greater percentage of patients in the roflumilast group achieved IGA Success compared with that of the vehicle group
  - More patients in the roflumilast group also had an IGA status of Clear or Almost Clear across subgroups at Week 8 (Figure 3)
- More roflumilast-treated patients who had a baseline score ≥4 on the Worst Itch Numeric Rating Scale (WI-NRS) had a 4-point improvement at Week 8 across subgroups (Figure 4)
- The least square mean percent change from baseline in Psoriasis Symptoms Diary (PSD) scores was greater after roflumilast treatment than with vehicle treatment at Week 8 across subgroups (Figure 5)

**Table 1. Baseline Demographics and Disease Characteristics**

n (%)	Roflumilast Cream 0.3% (n=576)	Vehicle (n=305)
<b>Age in years, mean (SD)</b>	47.2 (14.6)	47.9 (15.0)
<b>Sex, n (%)</b>		
Male	365 (63.4)	196 (64.3)
Female	211 (36.6)	109 (35.7)
<b>Race, n (%)</b>		
American Indian or Alaska Native	4 (0.7)	2 (0.7)
Asian	41 (7.1)	20 (6.6)
Black or African American	21 (3.6)	17 (5.6)
Native Hawaiian or Other Pacific Islander	5 (0.9)	1 (0.3)
White	474 (82.3)	250 (82.0)
Not reported	9 (1.6)	5 (1.6)
Other	19 (3.3)	9 (3.0)
More than 1 race	3 (0.5)	1 (0.3)
<b>IGA score, n (%)</b>		
2 (mild)	101 (17.5)	44 (14.4)
3 (moderate)	426 (74.0)	240 (78.7)
4 (severe)	49 (8.5)	21 (6.9)
<b>Psoriasis-affected BSA, mean % (SD)</b>	6.7 (4.6)	7.6 (4.9)
<b>I-IGA score, n (%)</b>		
1 (almost clear)	7 (1.2)	2 (0.7)
2 (mild)	58 (10.1)	29 (9.5)
3 (moderate)	54 (9.4)	33 (10.8)
4 (severe)	4 (0.7)	1 (0.3)
<b>PASI, mean score (SD)</b>	6.4 (3.2)	6.9 (3.6)
<b>WI-NRS, mean score (SD)</b>	5.7 (2.7)	5.9 (2.8)
<b>WI-NRS score ≥4, n (%)</b>	447 (77.6)	231 (75.7)

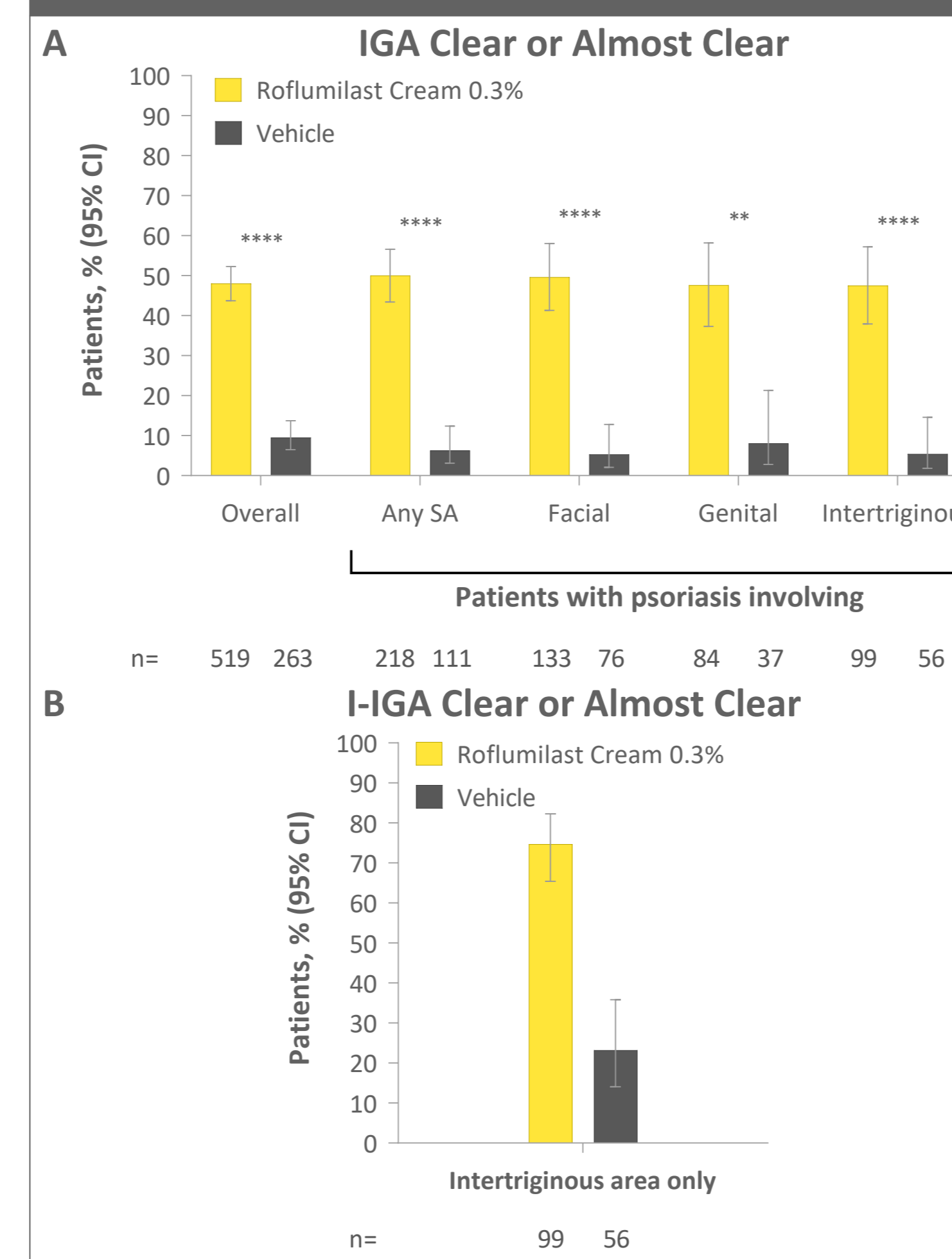
BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: intertriginous IGA; PASI: Psoriasis Area Severity Index; WI-NRS: Worst Itch Numeric Rating Scale; SD: standard deviation.

**Figure 2. Percent of Patients With Involvement in SAs Achieving IGA Success (A) and I-IGA Success (B) at Week 8**



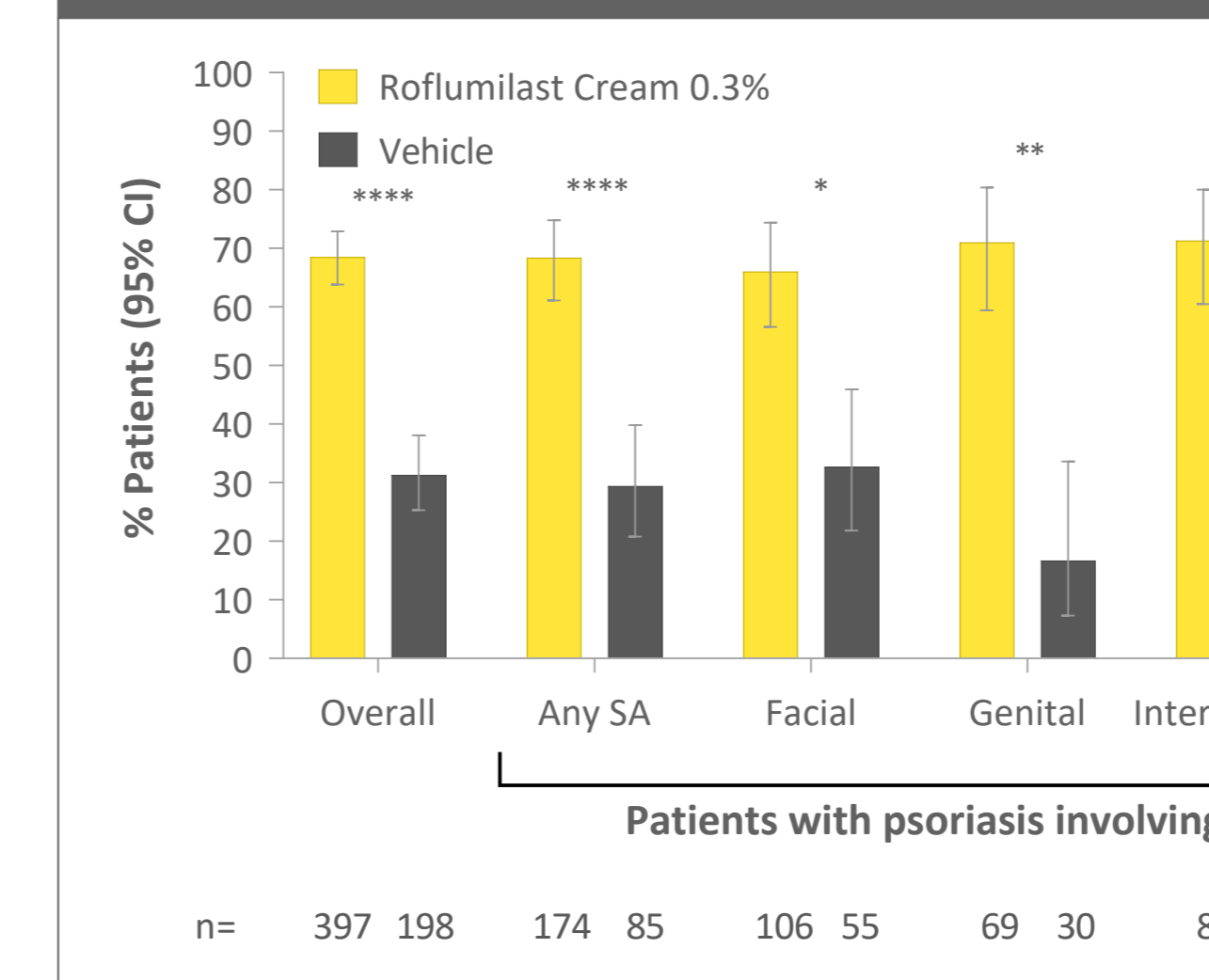
\*P<0.05; \*\*P<0.01; \*\*\*P<0.001; \*\*\*\*P<0.0001. IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline; I-IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline evaluated in intertriginous areas only. CI: confidence interval; IGA: Investigator Global Assessment; I-IGA: intertriginous IGA; SA: special areas.

**Figure 3. Percent of Patients With Involvement in SAs Achieving IGA Status of Clear or Almost Clear (A) and I-IGA Clear or Almost Clear (B) at Week 8**



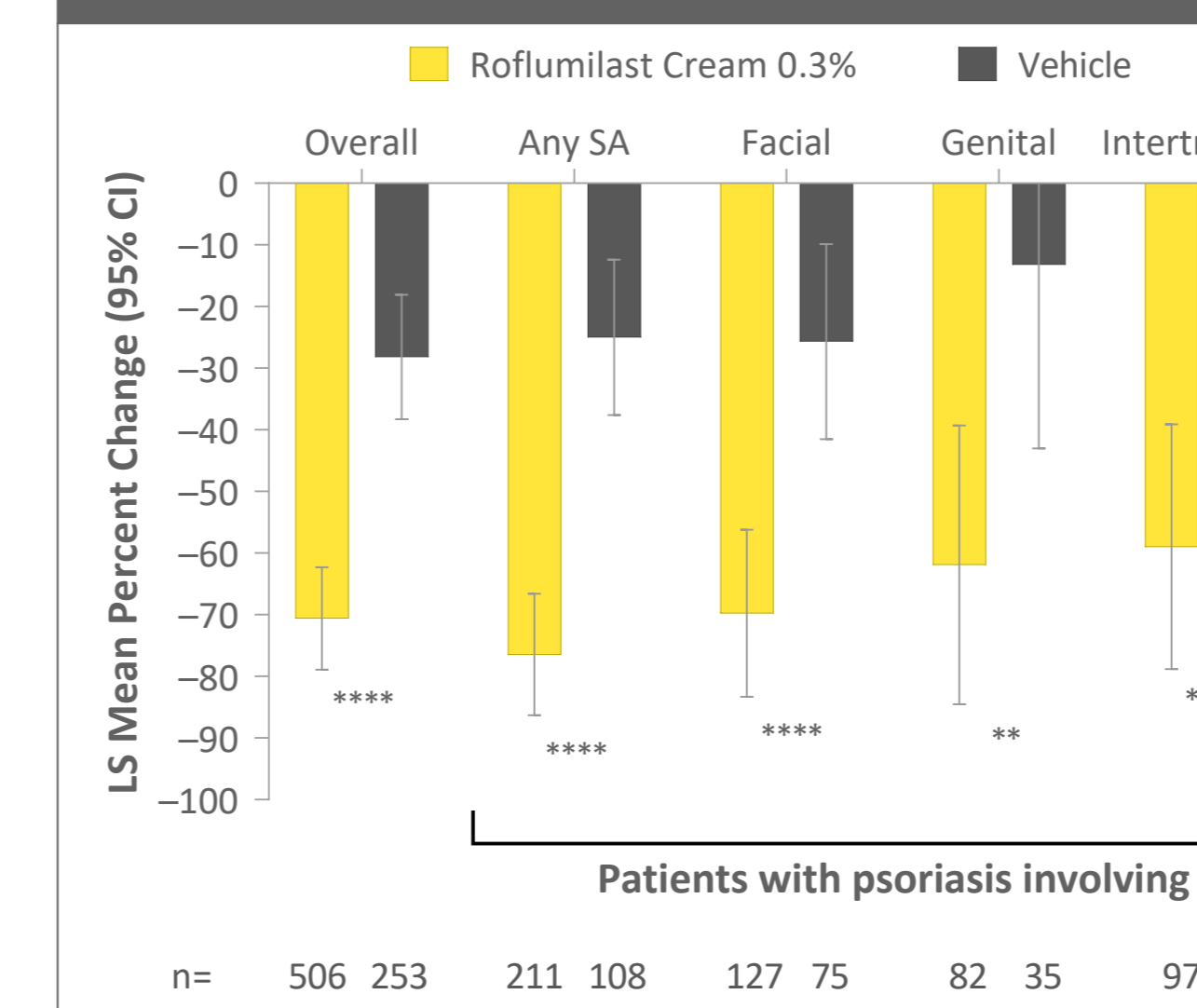
\*P<0.05; \*\*P<0.01; \*\*\*P<0.001; \*\*\*\*P<0.0001. I-IGA Clear or Almost Clear IGA status evaluated in intertriginous areas only. CI: confidence interval; IGA: Investigator Global Assessment; I-IGA: intertriginous IGA; SA: special area.

**Figure 4. Percentage of Patients Achieving WI-NRS Success at Week 8**



\*P<0.05; \*\*P<0.01; \*\*\*P<0.001; \*\*\*\*P<0.0001. WI-NRS Success = ≥4-point improvement in patients with baseline WI-NRS score ≥4. CI: confidence interval; WI-NRS: Worst Itch Numeric Rating Scale.

**Figure 5. LS Mean Percent Change in PSD at Week 8**



\*P<0.05; \*\*P<0.01; \*\*\*P<0.001; \*\*\*\*P<0.0001. CI: confidence interval; LS: least square; PSD: Psoriasis Symptoms Diary.

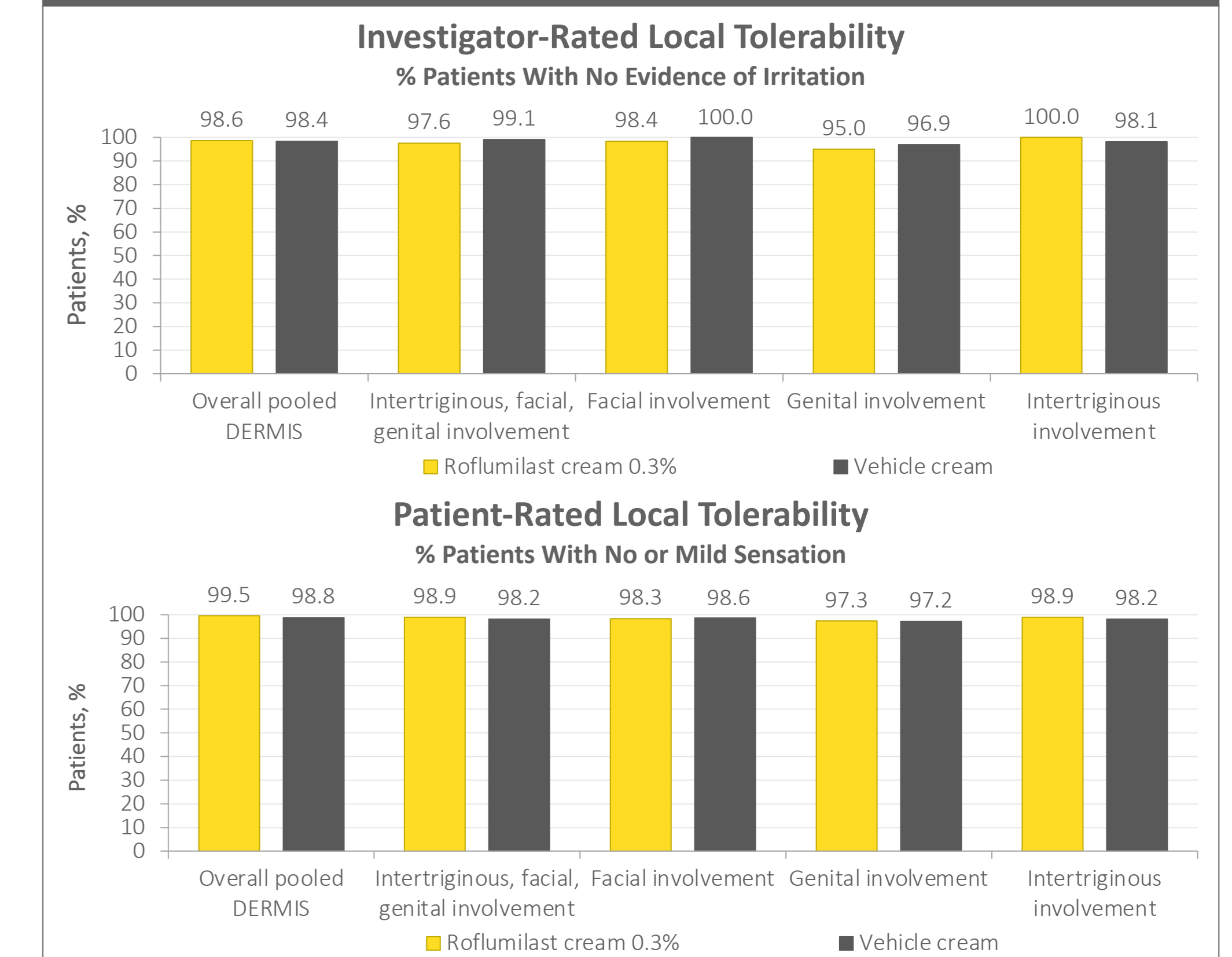
## SAFETY

- In patients with involvement in SA, local tolerability was highly favorable as reported by patient and investigator assessment of irritation, burning, and stinging (Figure 6)
  - ≥97.6% of patients had no evidence of irritation at Week 8 on investigator-rated assessments
  - ≥97.2% reported no warmth/tingling sensation or mild sensation at Week 8 on patient-rated assessments

## CONCLUSIONS

- Roflumilast cream 0.3% provided improvement across multiple efficacy endpoints versus vehicle cream while demonstrating favorable safety and tolerability in patients with chronic plaque psoriasis involving intertriginous, and/or face, and/or genital areas in 2 phase 3 trials
- The local tolerability profile as assessed by both patients and investigators was favorable
- The subgroup analysis of the pooled results of the phase 3 DERMIS-1 and DERMIS-2 trials showed that once-daily roflumilast cream 0.3% demonstrated efficacy and tolerability in patients with psoriasis involvement in difficult-to-treat areas

**Figure 6. Investigator- and Patient-Rated Local Tolerability at Week 8**



Patient-rated tolerability: 0 = None (no sensation), 1 = Mild (slight warm, tingling sensation), 2 = Moderate (definite warm, tingling sensation), 3 = Severe (hot, tingling/stinging sensation).

- Overall incidence of treatment-emergent adverse events (TEAEs), serious AEs, and TEAEs leading to discontinuation was low with similar rates between roflumilast and vehicle across both studies
- No skin atrophy was seen in the SAs treated with topical roflumilast or vehicle (Table 2)

**Table 2. Overall AEs<sup>6</sup>**

n (%)	Roflumilast Cream 0.3% (n=576)	Vehicle (n=305)
<b>Patients with any TEAE</b>	147 (25.5)	64 (21.0)
<b>Patients with any treatment-related TEAE</b>	23 (4.0)	11 (3.6)
<b>Patients with any SAE</b>	2 (0.3)	2 (0.7)
<b>Patients who discontinued study due to AE</b>	6 (1.0)	4 (1.3)
<b>Most common TEAE (≥1% in the roflumilast group), preferred term</b>		
Diarrhea	18 (3.1)	0
Headache	14 (2.4)	3 (1.0)
Insomnia	8 (1.4)	2 (0.7)
Nausea	7 (1.2)	1 (0.3)
Nasopharyngitis	6 (1.0)	4 (1.3)
Urinary tract infection	6 (1.0)	2 (0.7)
Application-site pain	6 (1.0)	1 (0.3)
Upper respiratory tract infection	6 (1.0)	1 (0.3)

AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

## REFERENCES

- Merola JF, et al. *Dermatol Ther* 2018;34:e12589.
- Elmets CA, et al. *J Am Acad Dermatol* 2021;84:432–470.
- Dong C, et al. *J Pharmacol Exp Ther* 2016;358:413–422.
- Lebwohl MG, et al. *N Engl J Med* 2020;383:229–239.
- Lebwohl MG, et al. 30th Congress of the European Academy of Dermatology and Venerology (EADV) Virtual, September 29–October 2, 2021.
- Lebwohl MG, et al. American Academy of Dermatology (AAD), Boston, MA, March 25–29, 2022.

## ACKNOWLEDGEMENTS

- This study was supported by Arcutis Biotherapeutics, Inc.
- Thank you to the investigators and their staff for their participation in the trial
- We are grateful to the study participants and their families for their time and commitment
- Writing support was provided by Christina McManus, PhD, and Lauren Ramsey, PharmD, Alligent Biopharm Consulting LLC, and funded by Arcutis Biotherapeutics, Inc.

## DISCLOSURES

LKF, AA, JD, ZDD, MG, ML, KAP, JS, and LSG are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; DK, RCH, PB, and DRB are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.