ARQ-151, Roflumilast Cream, Improved Chronic Plaque Psoriasis in Phase 2b Study

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Disclosures

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Treatment of Chronic Plaque Psoriasis

Background

- High-potency corticosteroids and vitamin D derivatives are the main treatments, but have long-term tolerability issues
  - Sensitive areas such as the face and intertriginous areas require additional considerations
- PDE-4 activity is elevated in psoriatic skin relative to healthy skin, and inhibition of PDE-4 results in downregulation of inflammatory cytokines TNFα, IFNϒ, IL-17, and IL-23[1,2]
- Roflumilast cream (ARQ-151) is a potent, selective PDE-4 inhibitor under clinical investigation
  - Demonstrates ~25- to >300-fold higher potency than currently available PDE-4 inhibitors[3]

PDE-4: phosphodiesterase-4.

[1]Pincelli C, et al. *J Drugs Dermatol* 2018;17:835-840. [2]Li H, et al. *Front Pharmacol* 2018;9:1048. [3]Dong C, et al. *J Pharmacol Exp Ther* 2016;358:413-422.

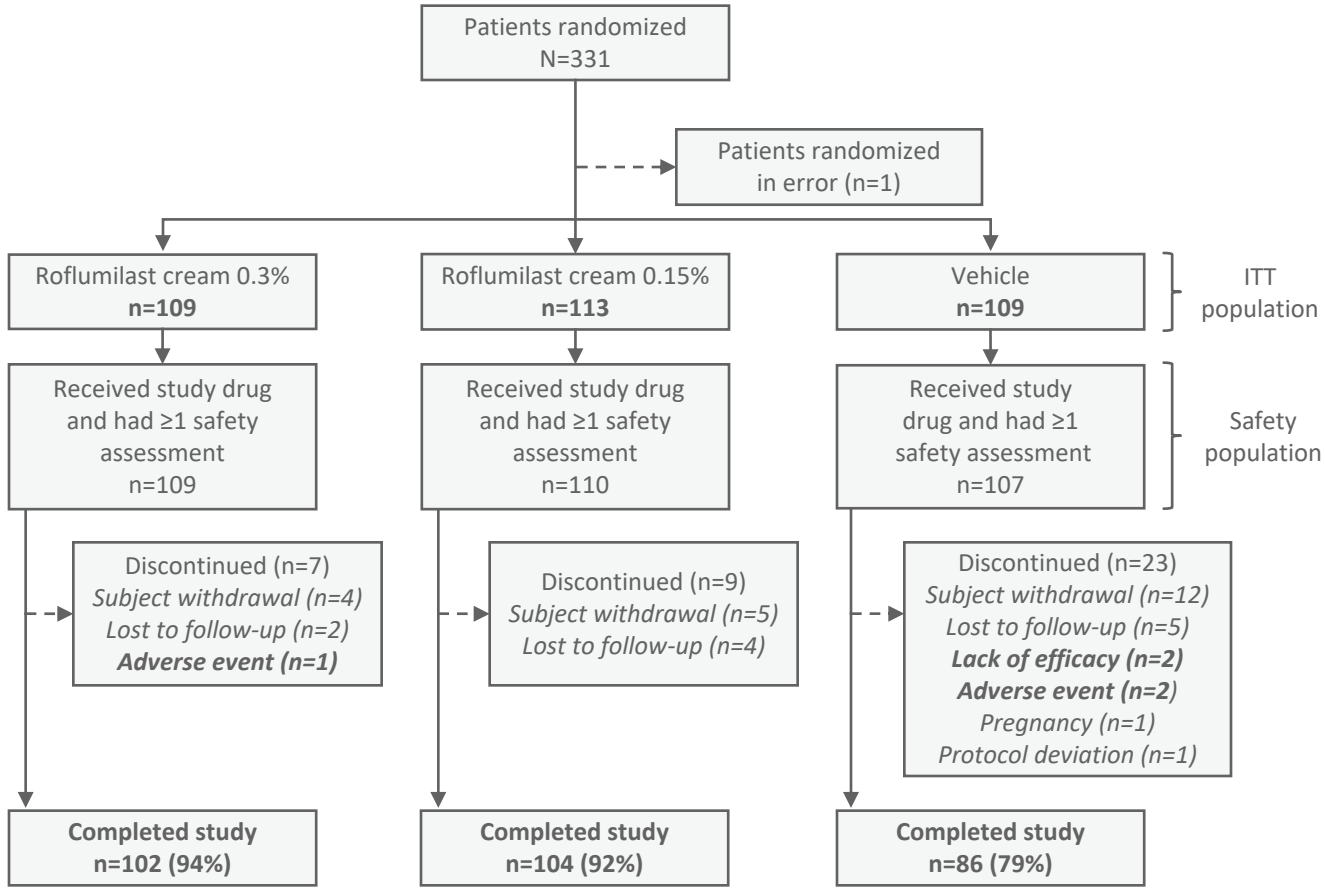
Safety and Efficacy of Topical Once-Daily Roflumilast Cream in Subjects With Chronic Plaque Psoriasis: Objective and Methods

Objective

- Evaluate the safety and efficacy of 2 doses of roflumilast cream versus vehicle

Methods

- Parallel-group, randomized, double-blind, vehicle-controlled Phase 2b Study
- Adult subjects (≥18 years) with chronic plaque psoriasis (IGA ≥2)
- Roflumilast cream 0.3%, 0.15%, or vehicle; QD for 12 weeks
- Primary endpoint: IGA status of 'clear' or 'almost clear' (score 0 or 1) at Week 6
- Secondary endpoint: For subjects with I-IGA ≥2 at baseline, I-IGA success at each time point



ClinicalTrials.gov NCT03638258

BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: Intertriginous IGA; ITT: intent-to-treat; QD: once daily.

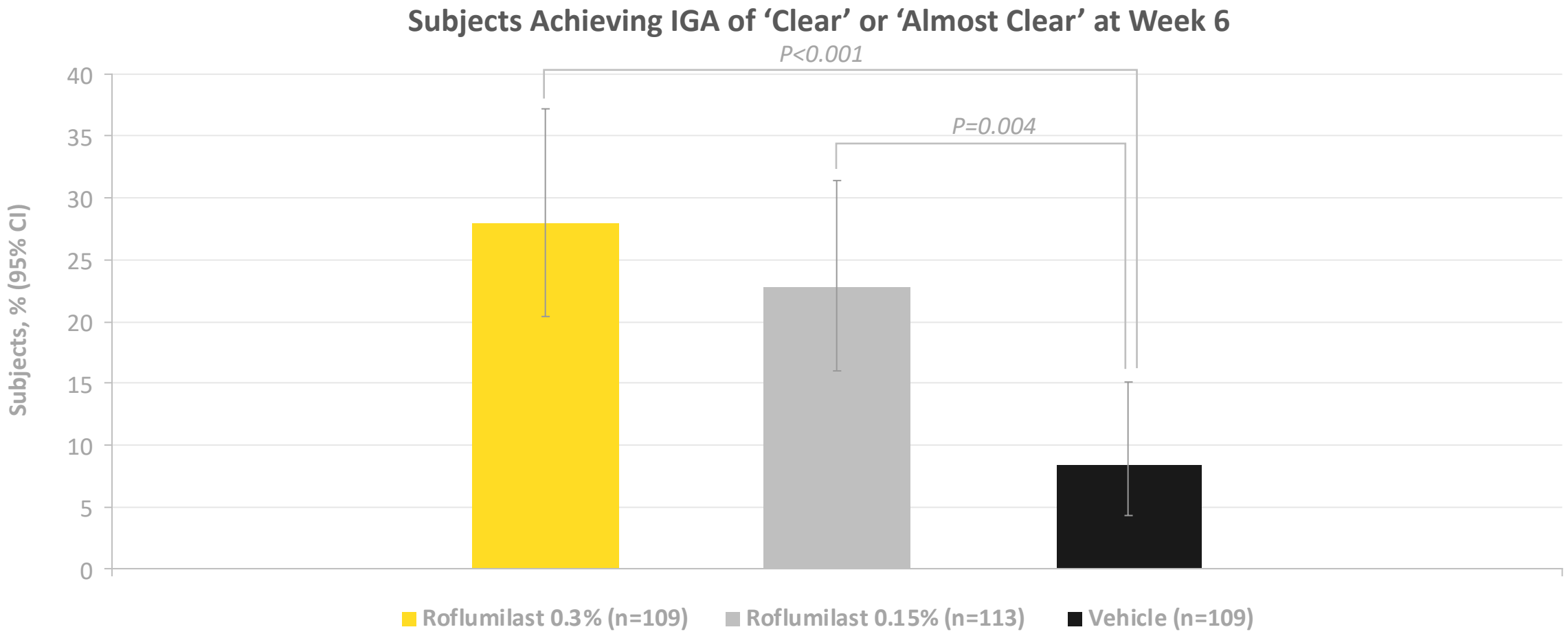
Baseline Characteristics

	Roflumilast 0.3% (n=109)	Roflumilast 0.15% (n=113)	Vehicle (n=109)
Age, mean years (SD)	51.7 (14.1)	54.4 (14.2)	55.5 (13.5)
Sex, male, n (%)	56 (51.4)	62 (54.9)	67 (61.5)
Race, n (%)			
White	82 (75.2)	95 (84.1)	92 (84.4)
Black	12 (11.0)	10 (8.8)	7 (6.4)
Multiple/other	15 (13.8)	8 (7.1)	10 (9.2)
Psoriasis-affected BSA, mean % (SD)	6.3 (4.0)	6.4 (3.9)	6.4 (3.6)
IGA score, n (%)			
2 (mild)	17 (15.6)	18 (15.9)	11 (10.1)
3 (moderate)	84 (77.1)	83 (73.5)	89 (81.7)
4 (severe)	8 (7.3)	12 (10.6)	9 (8.3)

	Roflumilast 0.3% (n=109)	Roflumilast 0.15% (n=113)	Vehicle (n=109)
PASI, mean score (SD)	7.7 (3.6)	8.0 (3.9)	7.6 (3.1)
WI-NRS, mean score (SD)	6.1 (2.7)	5.6 (3.1)	5.9 (2.9)
WI-NRS score ≥6, n (%)	71 (65.1)	62 (54.9)	64 (58.7)
PSD, mean total score (SD)	68.9 (41.2)	69.6 (46.2)	75.1 (42.6)
Intertriginous Area			
I-IGA score ≥2, n (%)			
2 (mild)	6 (37.5)	12 (66.7)	7 (41.2)
3 (moderate)	8 (50.0)	3 (16.7)	8 (47.1)
4 (severe)	1 (6.3)	1 (5.6)	2 (11.8)

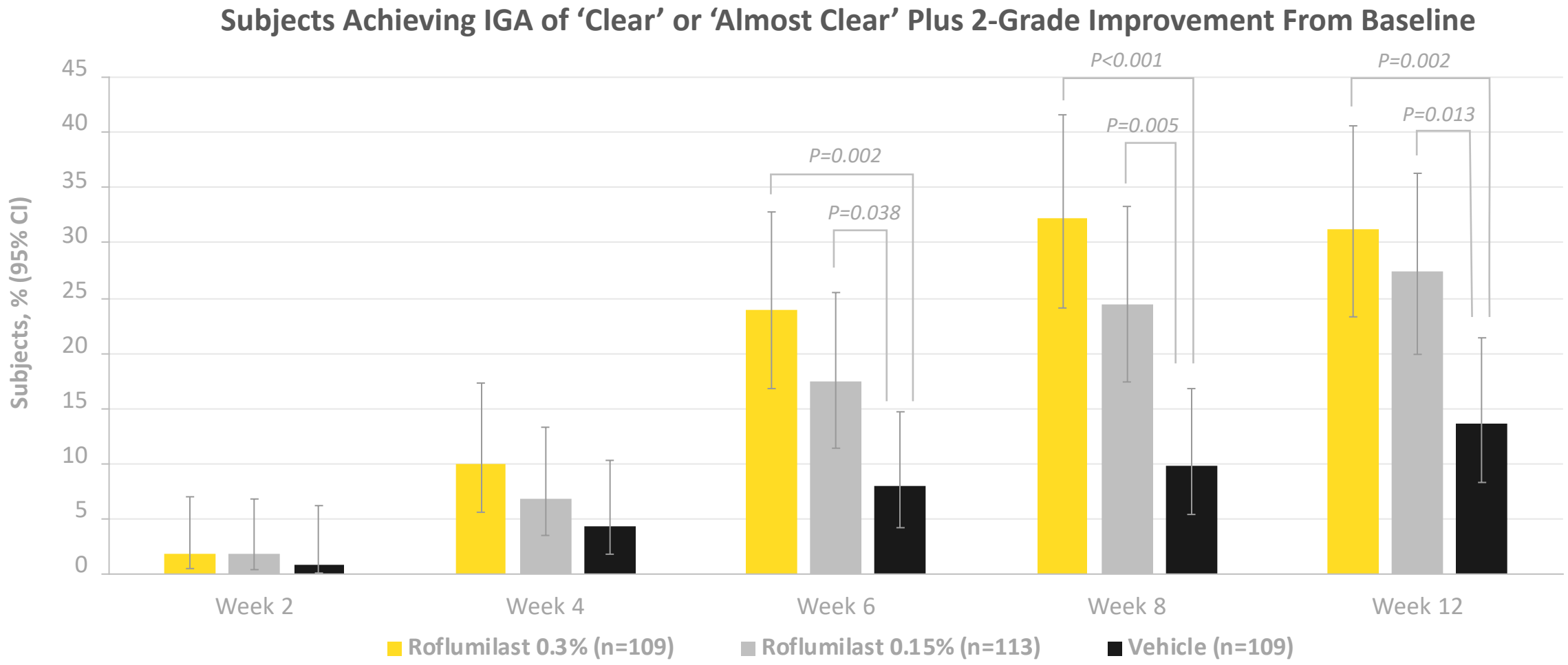
Data are presented for intent-to-treat population. BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: Intertriginous Investigator Global Assessment; PASI: Psoriasis Area and Severity Index; PSD: Psoriasis Symptom Diary; SD: standard deviation; WI-NRS: Worst Itch Numeric Rating Scale.

Primary Endpoint of IGA ‘Clear’ or ‘Almost Clear’ at Week 6 Was Met for Both Roflumilast Cream Doses



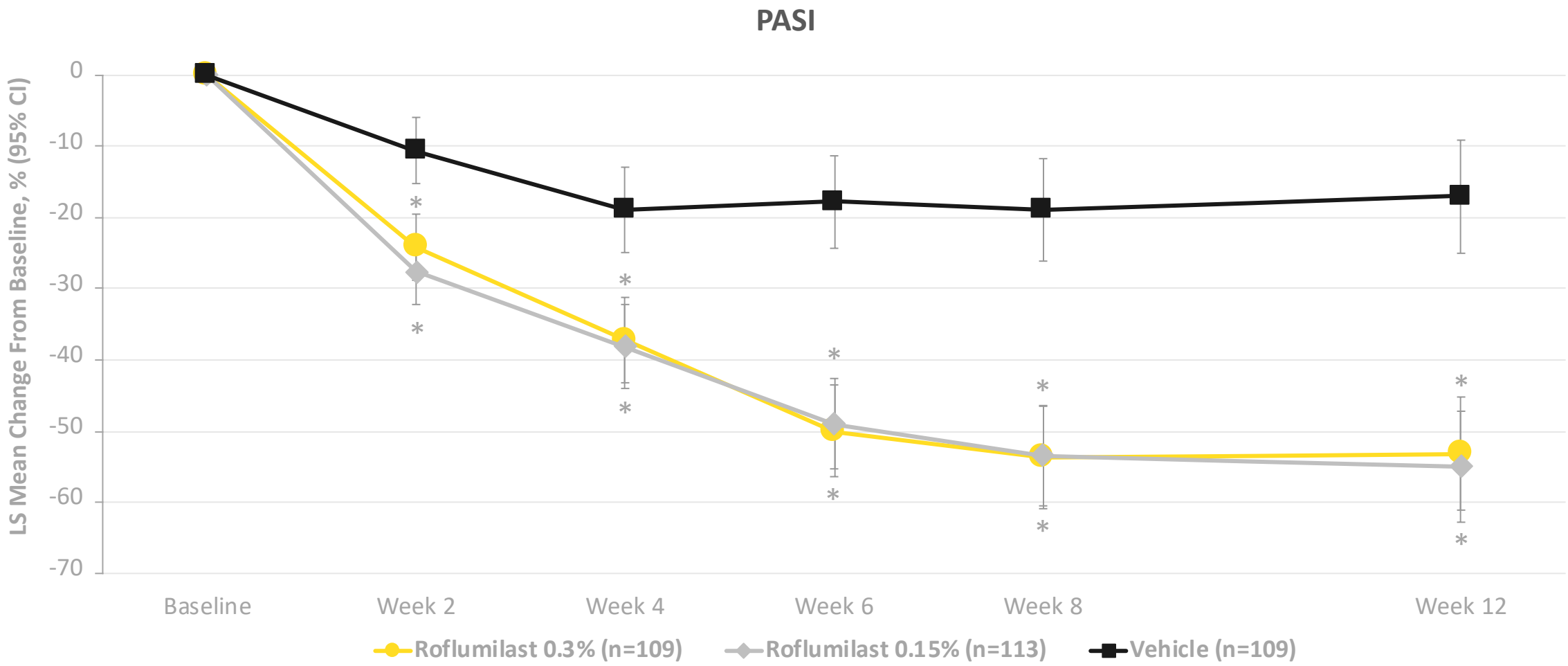
Data are presented for intent-to-treat population. CI: confidence interval; IGA: Investigator Global Assessment.

Roflumilast Cream Improved Severity of Chronic Plaque Psoriasis as Measured by IGA Success



Data are presented for intent-to-treat population. CI: confidence interval; IGA: Investigator Global Assessment.

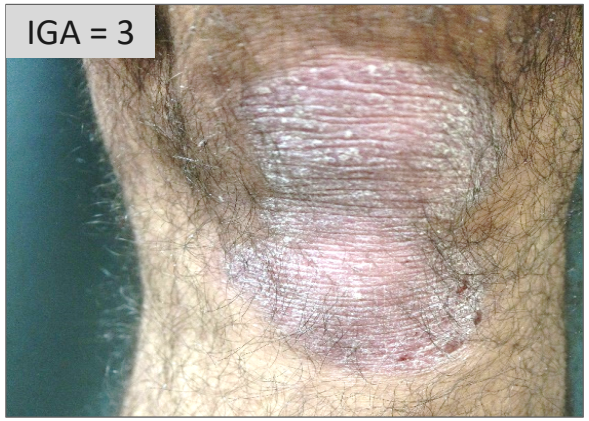
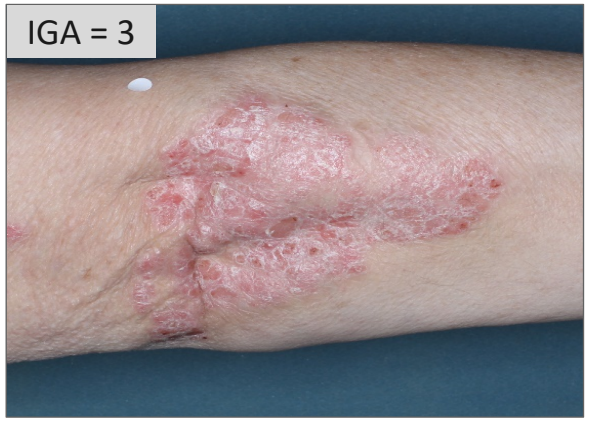
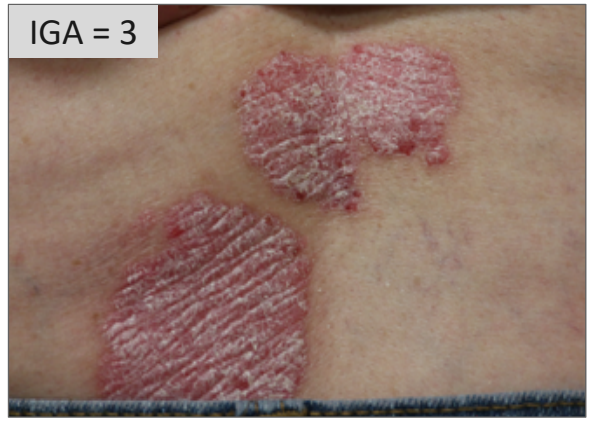
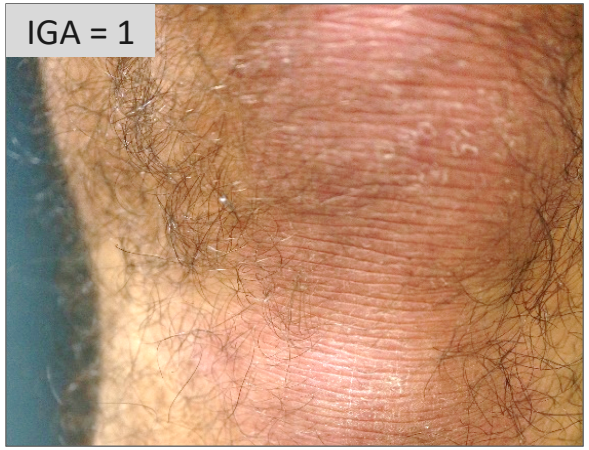
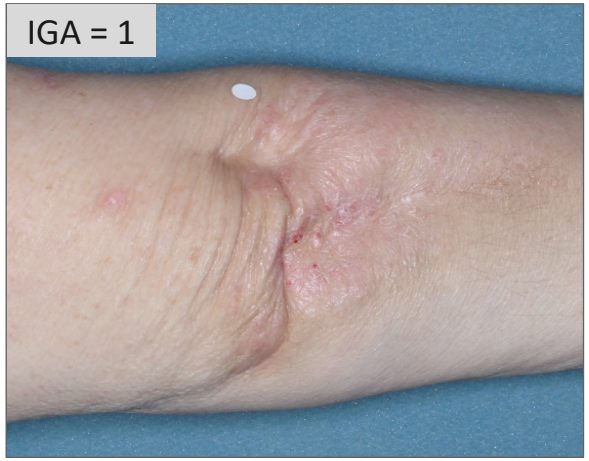
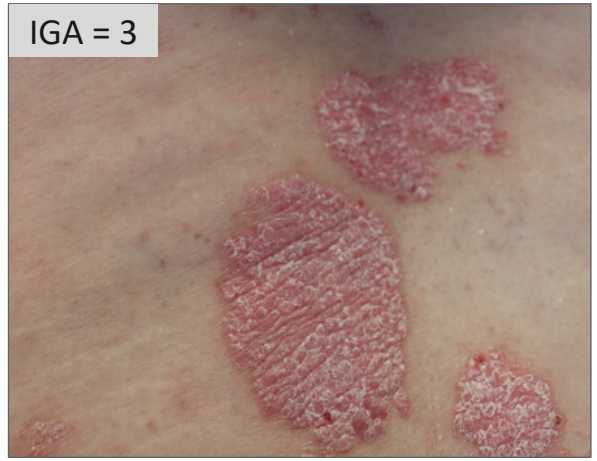
Roflumilast Cream Led to Early Improvement in Chronic Plaque Psoriasis Area and Severity Index



**P<0.001 vs vehicle*

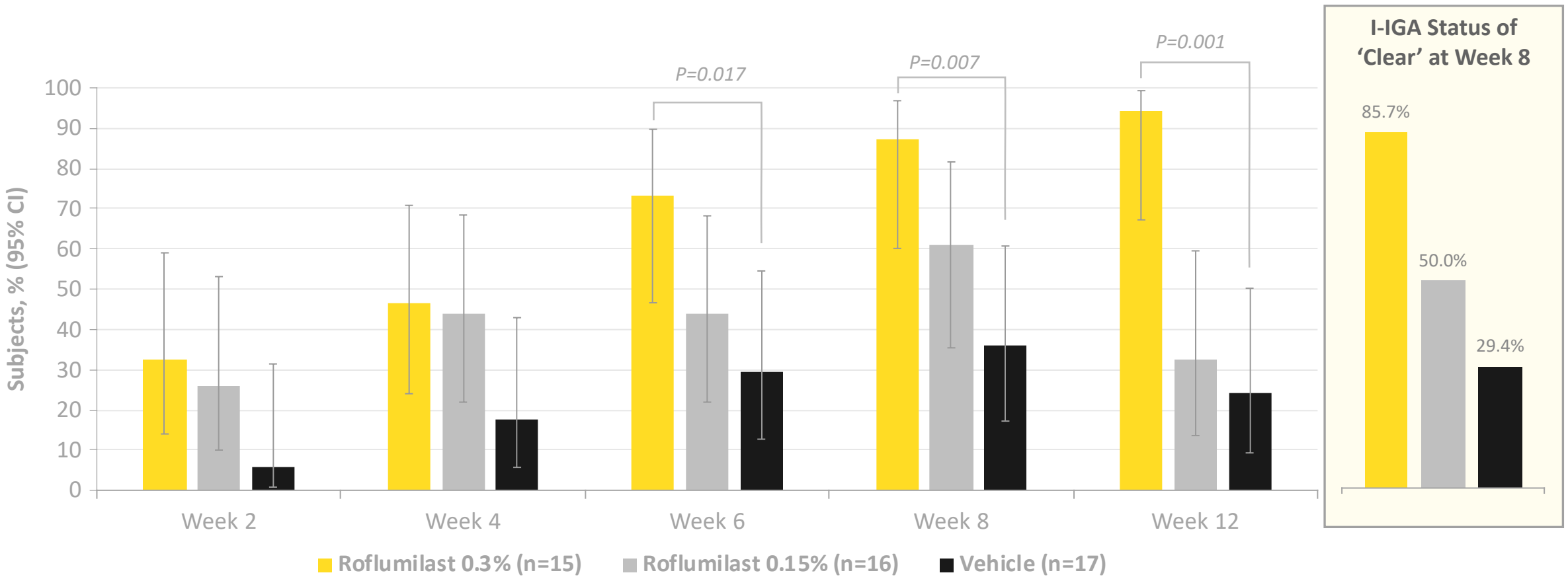
Data are presented for intent-to-treat population. CI: confidence interval; LS: least squares; PASI: Psoriasis Area and Severity Index.

Roflumilast Cream Improved Severity of Plaque Psoriasis

	Roflumilast 0.3%	Roflumilast 0.15%	Vehicle
Baseline			
Week 8			

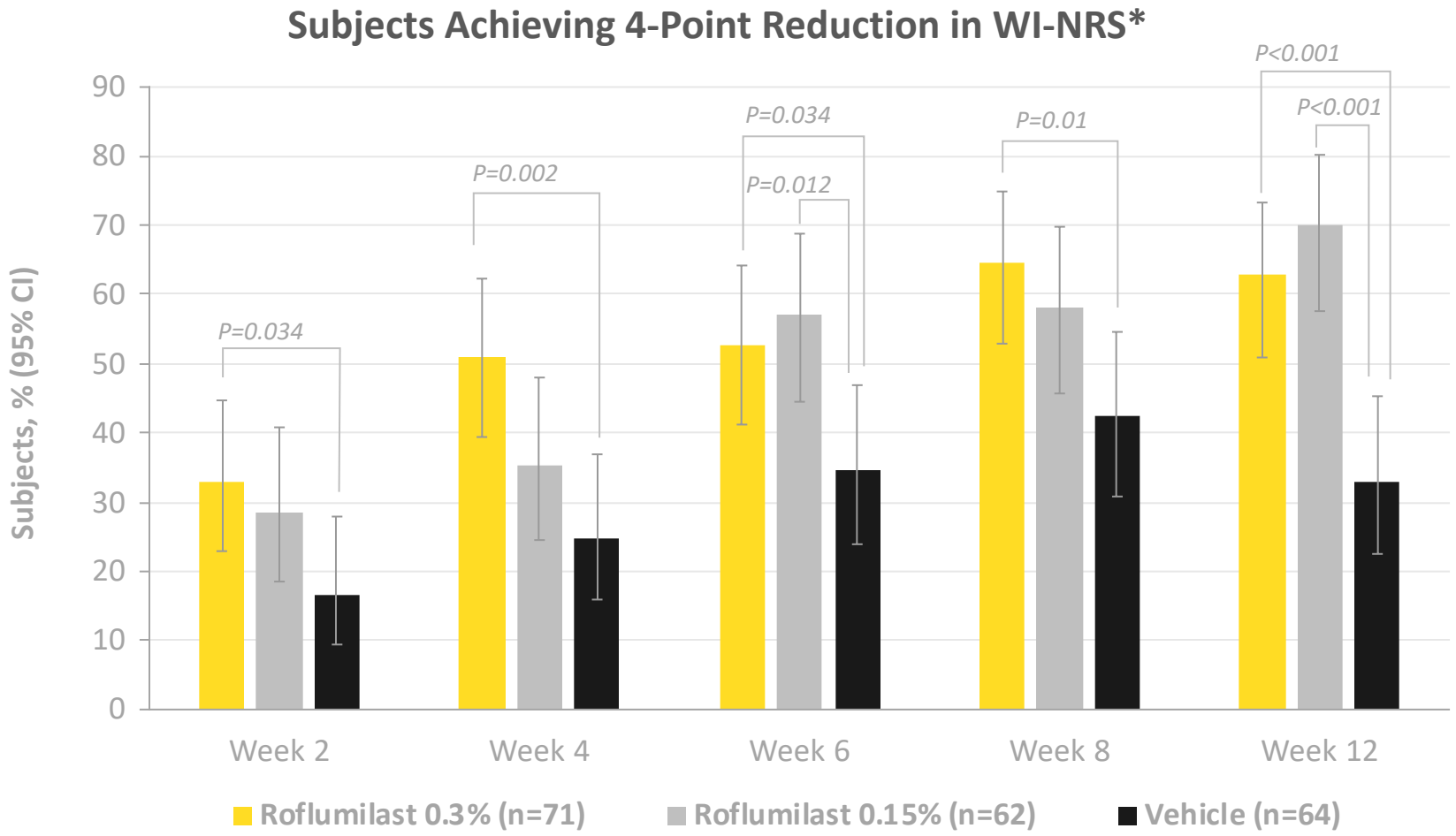
IGA: Investigator Global Assessment.

Most Subjects With Intertriginous Plaques Treated With Roflumilast Cream Achieved I-IGA Success by Week 6 With Continued Improvement Through Week 12



Data are presented for intent-to-treat population. CI: confidence interval; I-IGA: Intertriginous Investigator Global Assessment.

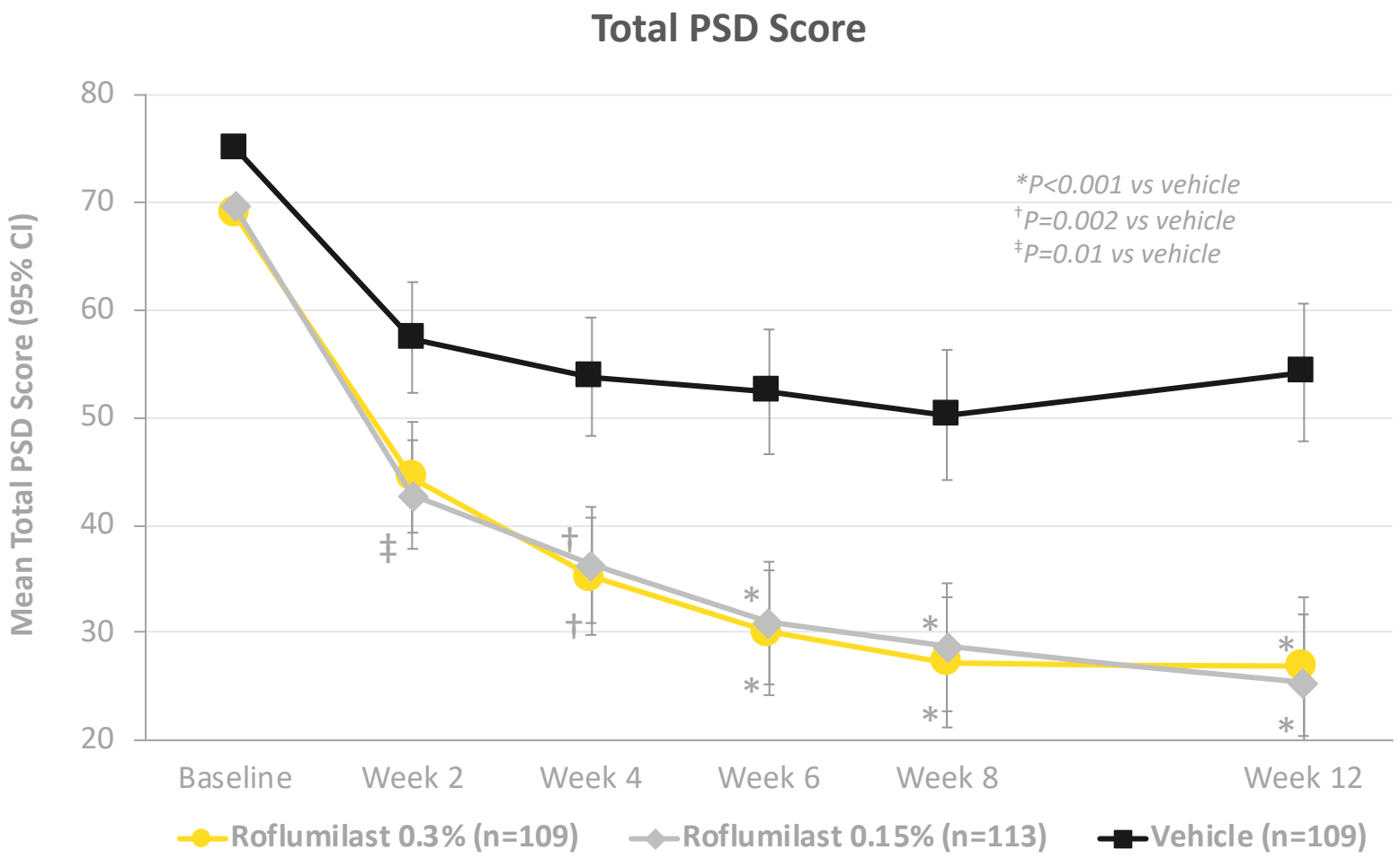
Roflumilast Cream Rapidly Improved Subject-Reported Itch



*Subjects with score of ≥6 on WI-NRS at baseline.

Data are presented for intent-to-treat population. CI: confidence interval; WI-NRS: Worst Itch Numeric Rating Scale.

Roflumilast Cream Rapidly Reduced Patient-Reported Burden of Disease



Data are presented for intent-to-treat population. CI: confidence interval; PSD: Psoriasis Symptom Diary.

Most TEAEs Were Mild or Moderate

- Treatment-related AEs were uncommon and were similar across groups
- More subjects discontinued the study due to an AE in the vehicle group vs the roflumilast groups
- Rates of application site pain were low and similar to vehicle
- 97% of AEs were rated mild or moderate
- Rates of gastrointestinal and psychiatric AEs were low and similar between groups
- Proportion of subjects with weight loss was comparable across groups and comparable to weight gain

TEAE, n (%)	Roflumilast 0.3% (n=109)	Roflumilast 0.15% (n=110)	Vehicle (n=107)
Subjects with any TEAE	42 (38.5)	30 (27.3)	32 (29.9)
Subjects with any treatment-related TEAE	7 (6.4)	3 (2.7)	7 (6.5)
Subjects with any SAE[a]	1 (0.9)	1 (0.9)	2 (1.9)
Subjects who discontinued study due to AE[b]	1 (0.9)	0	2 (1.9)
Most common TEAE (>2%)			
Upper respiratory tract infection (including viral)	9 (8.2)	8 (7.3)	4 (3.7)
Nasopharyngitis	4 (3.7)	3 (2.7)	4 (3.7)
Application site pain	2 (1.8)	1 (0.9)	3 (2.8)
Sinusitis	3 (2.8)	0	0
Urinary tract infection	0	3 (2.7)	1 (0.9)

[a]Roflumilast 0.3%: worsening of chest pain in a subject with history of myocardial infarction; roflumilast 0.15%: melanoma (not in treatment area); vehicle group: acute infarction of left basal ganglia, spontaneous miscarriage. [b]Roflumilast 0.3%: onset of worsening psoriasis; vehicle: mood swings, contact dermatitis.

Data are presented for safety population. AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Conclusions

- PDE-4 inhibition is a validated mechanism of action for oral psoriasis therapy, but new for topical psoriasis treatment
- Roflumilast once-daily cream demonstrated significant improvements in psoriasis signs and symptoms
  - Statistically significant increase in IGA 'clear'/'almost clear' and IGA success
  - Improvement in secondary endpoints of subject-reported itch, burden of disease
  - Significant clinical improvement in intertriginous areas: most patients 'clear' at Week 8
- Improvements in efficacy were observed as early as Week 2
- Roflumilast cream was well-tolerated; application site pain similar to vehicle

Roflumilast cream, an investigational once-daily topical PDE-4 inhibitor, achieved improvements in psoriasis signs and symptoms compared with vehicle cream, including in intertriginous areas

IGA: Investigator Global Assessment; PDE-4: phosphodiesterase-4.

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