Presentation #D3T01.4C

Efficacy and Safety of Ruxolitinib Cream in Patients With Cutaneous Lichen Planus: Results From a Phase 2, Randomized, Vehicle-Controlled Study

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Presenting Author Disclosures

- Aaron R. Mangold has served as a consultant for Argenyx, Boehringer Ingelheim, Bristol Myers Squibb, Clarivate, Incyte Corporation, Janssen, Nuvig, Pfizer (institution receives funds), Regeneron (institution receives funds), Soligenix, and Tourmaline Bio; has received grant support from AbbVie, Argenx, Corbus, Eli Lilly, Incyte Corporation, Kyowa, Merck, Miragen, Palvella, Pfizer, Priovant, and Regeneron; has received royalties from Adelphi Values and Clarivate; and has patents for methods and materials for assessing and treating cutaneous squamous cell carcinoma (provisional PCT/US2023/078902), use of oral Janus kinase inhibitors in lichen planus (PCT/US2024/020149), and topical ruxolitinib for treating lichen planus (PCT/US2021/053149, 2023-520085, 21805700.8)

Ruxolitinib Cream for Cutaneous LP

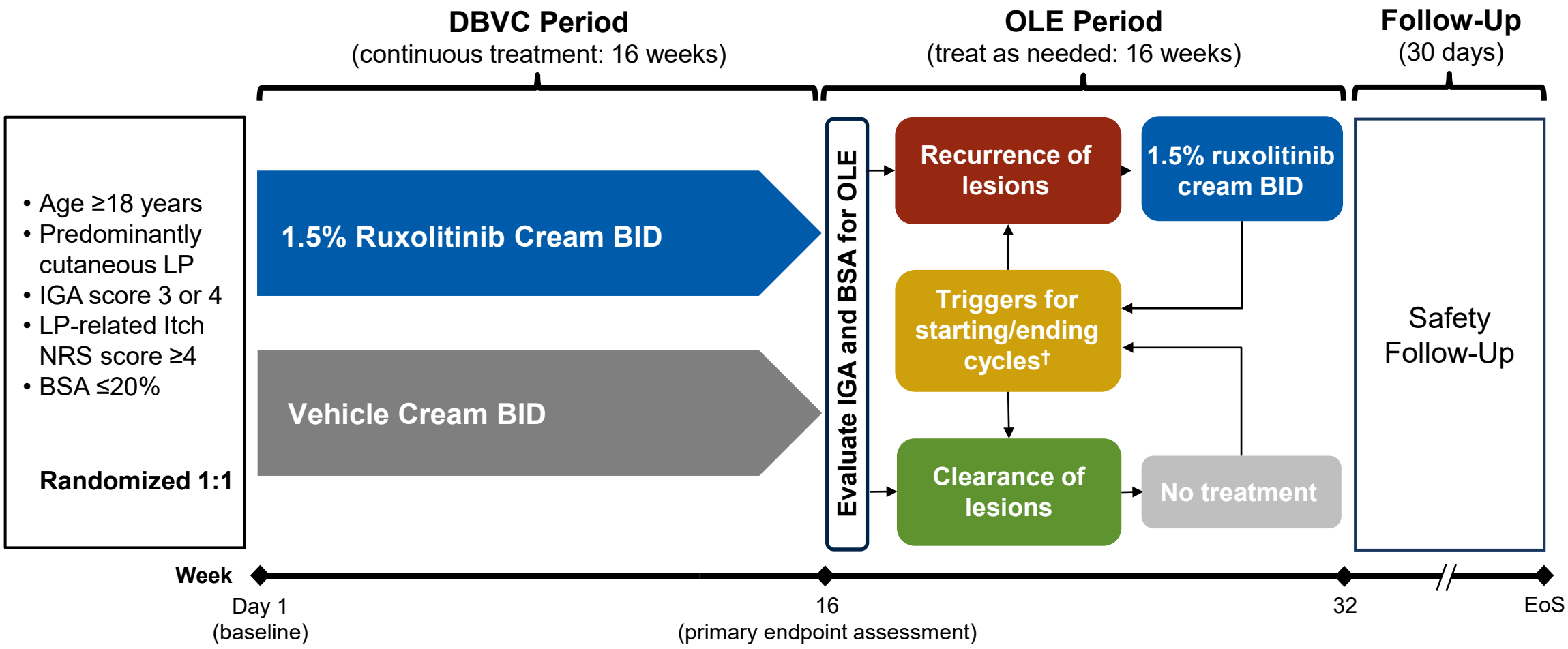
- LP is a chronic, highly pruritic, immune-mediated inflammatory disease that affects the skin and other tissues[1]
  - LP pathogenesis involves increased susceptibility of keratinocytes to CD8+ T-cell autoimmune cytotoxicity in a process mediated by interferon-γ and JAKs[1,2]
- Ruxolitinib cream is a JAK1/JAK2 inhibitor designed for topical administration
  - Proof of concept in LP was previously demonstrated in a single-arm, open-label trial of 12 patients with cutaneous LP[3]

Objective:
To evaluate efficacy and safety of ruxolitinib cream in patients with cutaneous LP from a phase 2, randomized, double-blind, vehicle-controlled study (NCT05593432)

JAK, Janus kinase; LP, lichen planus.

1. Boch K, et al. *Front Med (Lausanne)*. 2021;8:737813. 2. Shao S, et al. *Sci Transl Med.* 2019;11(511):eaav7561. 3. Brumfiel CM, et al. *J Invest Dermatol*. 2022;142(8):2109-2116.

Study Design



BID, twice daily; BSA, body surface area; DBVC, double-blind vehicle-controlled; EoS, end of study; IGA, Investigator's Global Assessment; OLE, open-label extension; NRS, numerical rating scale.

† At study visits, the investigator confirmed whether the patient required continuation of therapy (IGA ≥1) or could (re)enter no-treatment cycle (IGA=0). Within a treatment cycle, patients stopped treatment 3 days after all LP signs and symptoms resolved. Patients were discontinued from study treatment if disease extent exceeded 20% affected BSA.

Primary and Secondary Endpoints

- Primary
  - IGA-TS at Week 16
    - IGA score of 0 (clear) or 1 (almost clear) with ≥2-grade improvement from baseline
- Secondary
  - IGA-TS over time
  - Itch NRS4 over time
  - Time to Itch NRS4
  - Skin Pain NRS change from baseline
- Safety
  - Frequency and severity of adverse events

IGA for Cutaneous LP

Grade	Severity
0	Clear
1	Almost clear
2	Mild
3	Moderate
4	Severe

IGA-TS, IGA treatment success; Itch NRS4, ≥4-point improvement in Itch NRS score from baseline.

Patient Demographics and Baseline Disease Characteristics

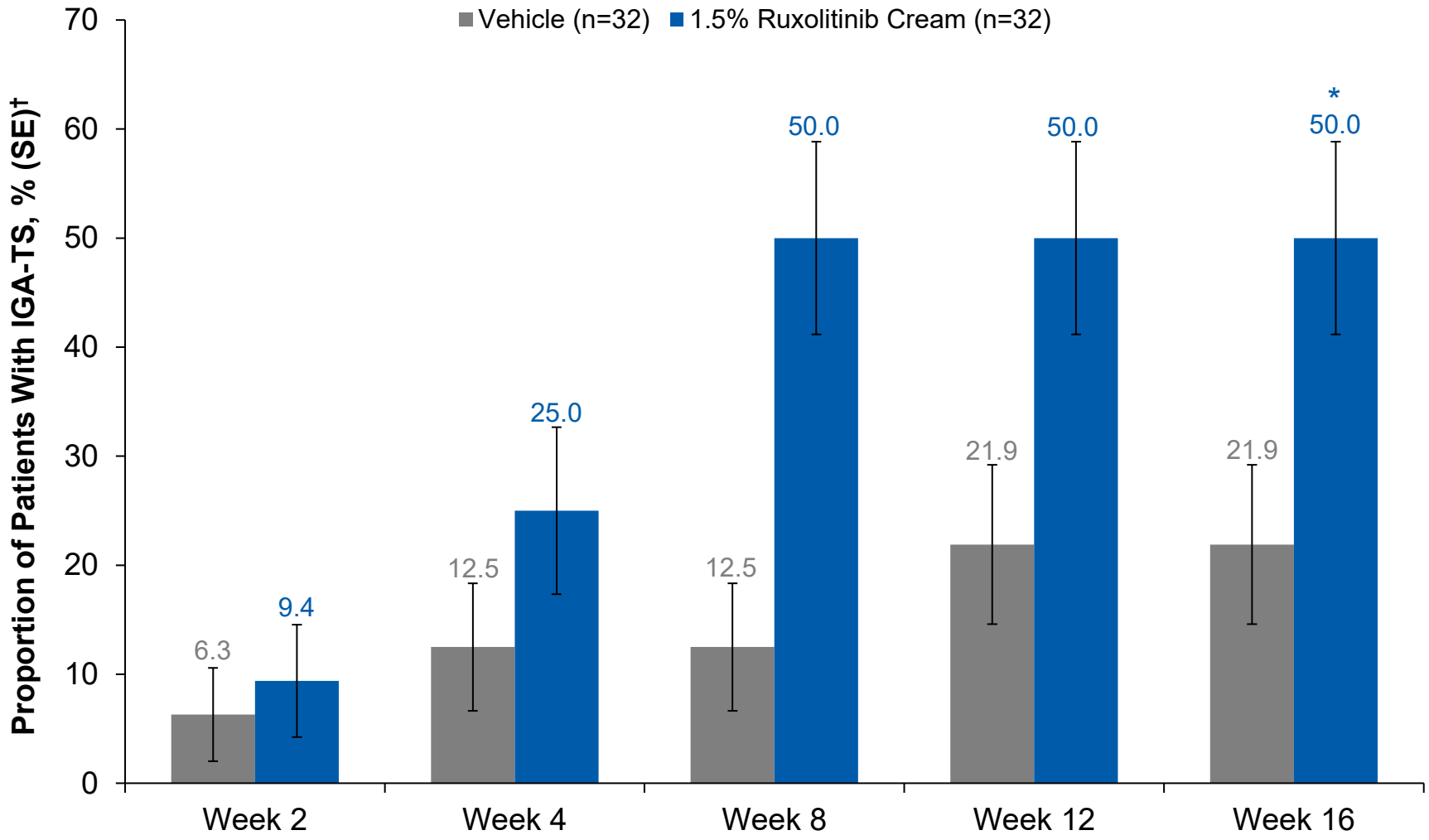
Intent-to-Treat Population

Characteristic	Vehicle Cream (n=32)	1.5% Ruxolitinib Cream (n=32)	Total (N=64)
Age, median (range), y	57.5 (26–77)	56.0 (18–78)	57.0 (18–78)
Female, n (%)	24 (75.0)	22 (68.8)	46 (71.9)
Race, n (%)			
White	19 (59.4)	21 (65.6)	40 (62.5)
Black	9 (28.1)	9 (28.1)	18 (28.1)
Asian	2 (6.3)	2 (6.3)	4 (6.3)
Duration of disease, median (range), y	5.1 (0.1–32.8)	4.9 (0.1–41.9)	4.9 (0.1–41.9)
Prior treatment, n (%)	27 (84.4)	31 (96.9)	58 (90.6)
Affected BSA, mean (SD), %	3.3 (3.2)	4.5 (4.8)	3.9 (4.1)
Baseline IGA score, n (%)			
3 (moderate)	31 (96.9)	29 (90.6)	60 (93.8)
4 (severe)	1 (3.1)	3 (9.4)	4 (6.3)
Baseline Itch NRS score, mean (SD)†	6.4 (1.7)	6.6 (1.5)	6.5 (1.6)
Baseline Skin Pain score, mean (SD)‡	4.5 (2.6)	4.9 (2.3)	4.7 (2.5)

† Vehicle, n=31; 1.5% ruxolitinib cream, n=32; total, n=63.
‡ Vehicle, n=31; 1.5% ruxolitinib cream, n=31; total, n=62.

Achievement of IGA Treatment Success

DBVC Period (Nonresponder Imputation)



Primary Endpoint at Week 16‡

1.5% Ruxolitinib Cream vs Vehicle	
ΔIGA-TS (SE)	29.4 (11.2)
95% CI	7.55–51.33
Odds Ratio (95% CI)	4.04 (1.32–12.38)
P value	0.0129

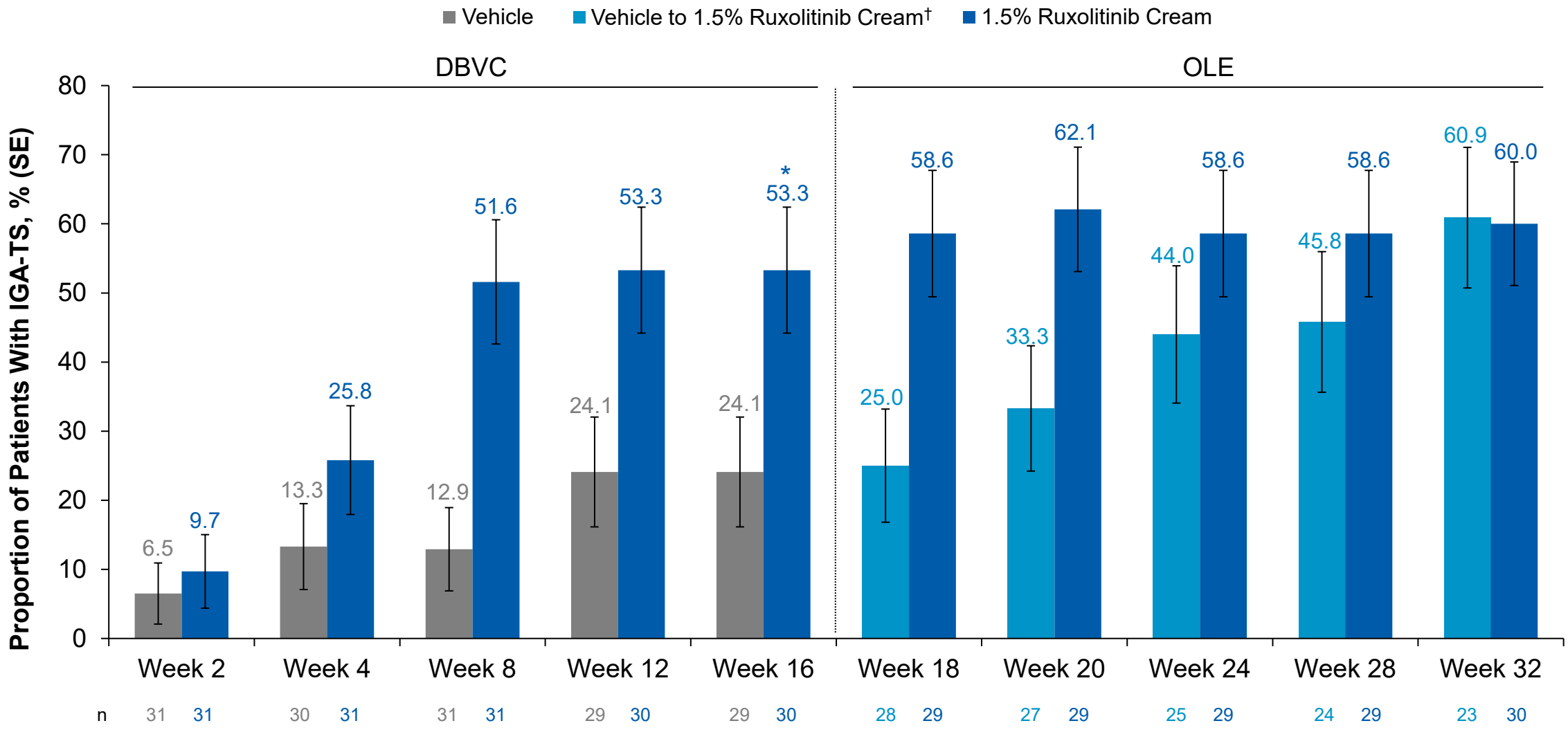
* *P*<0.05 vs vehicle (only assessed at Week 16).

† IGA-TS was defined as IGA score of 0 or 1 with ≥2-grade improvement from baseline. Patients with missing post-baseline values were imputed as nonresponders.

‡ Response rate, odds ratio, and *P* value were from a Cochran-Mantel-Haenszel test stratified by baseline IGA score (3 or 4).

Achievement of IGA Treatment Success

DBVC Period and OLE (As Observed)



* *P*<0.05 vs vehicle (Cochran-Mantel-Haenszel test stratified by baseline IGA score [3 or 4]; only assessed at Week 16). † After Week 16, patients applied 1.5% ruxolitinib cream.

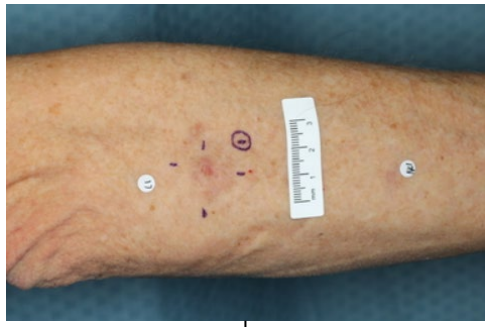
Example Photos

White Male Aged 72 years

Lesion 1, cross-polarized light

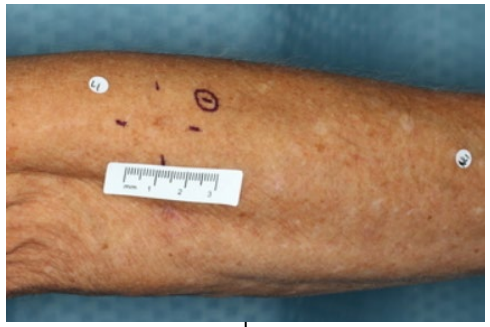
IGA=3

Baseline



IGA=1

8



IGA=0

16

Week

4

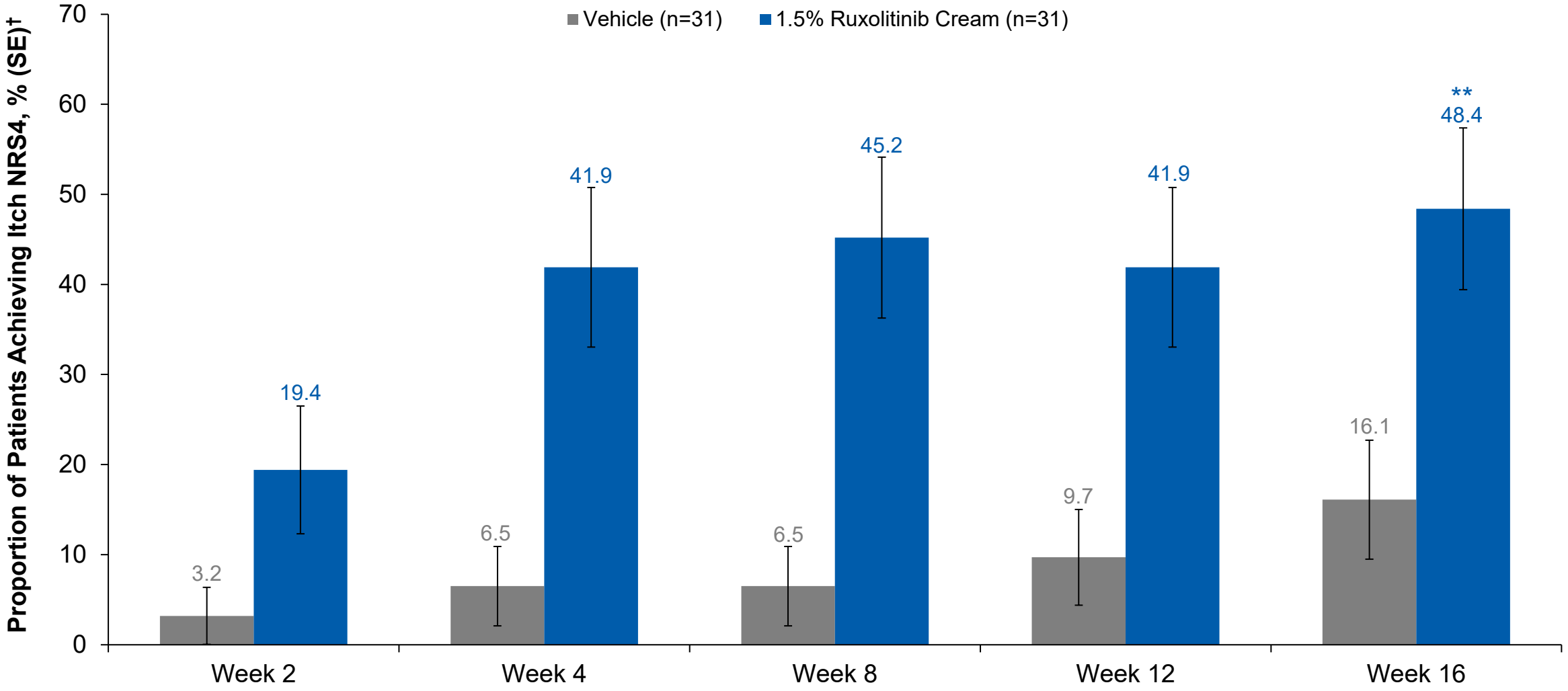
IGA=2

12

IGA=0

Achievement of Itch NRS4

DBVC Period (Nonresponder Imputation)

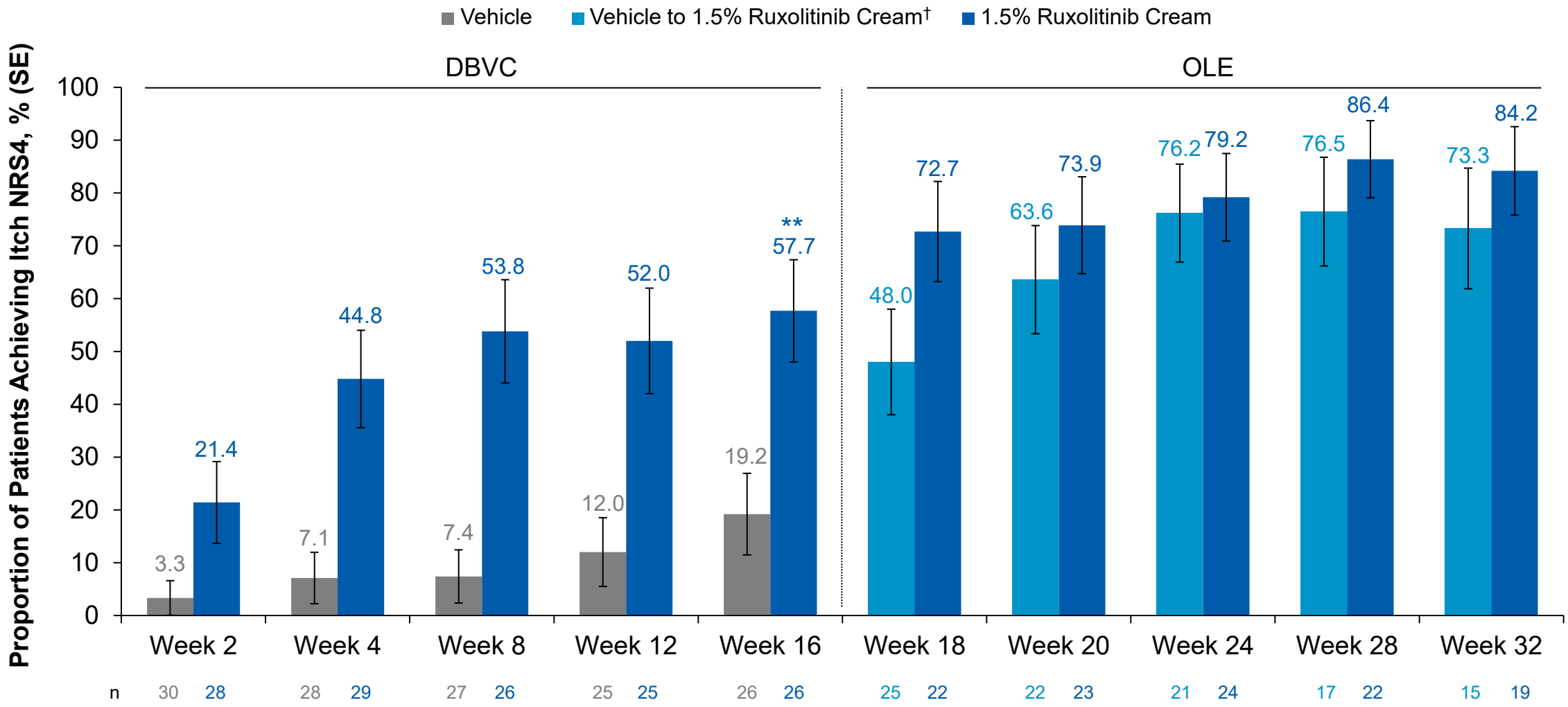


** *P*<0.01 vs vehicle (Cochran-Mantel-Haenszel test stratified by baseline IGA score [3 or 4]; only assessed at Week 16).

† Patients with missing post-baseline values were imputed as nonresponders.

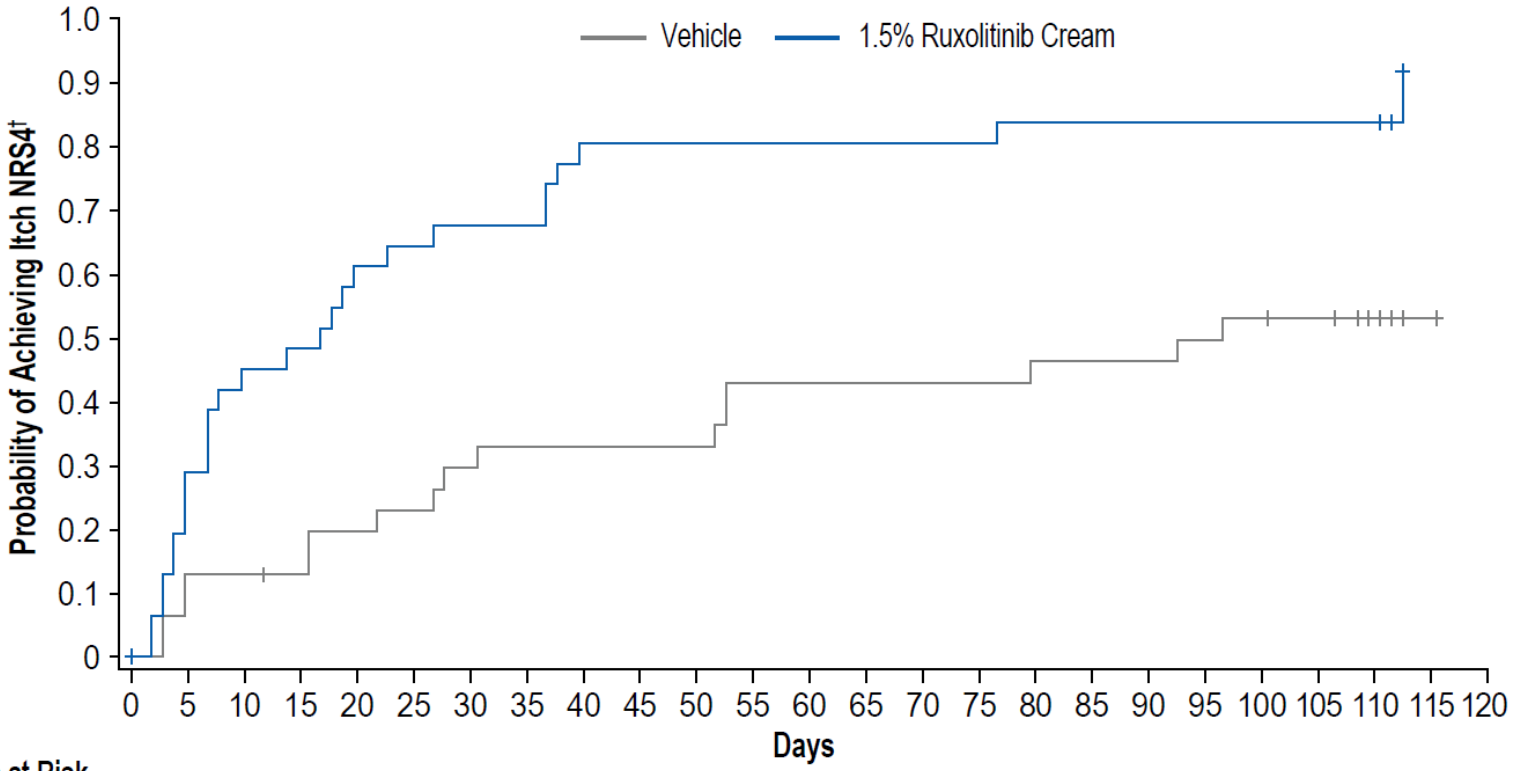
Achievement of Itch NRS4

DBVC Period and OLE (As Observed)



** *P*<0.01 vs vehicle (Cochran-Mantel-Haenszel test stratified by baseline IGA score [3 or 4]; only assessed at Week 16); † After Week 16, patients applied 1.5% ruxolitinib cream.

Time to Achievement of Itch NRS4



Patients at Risk

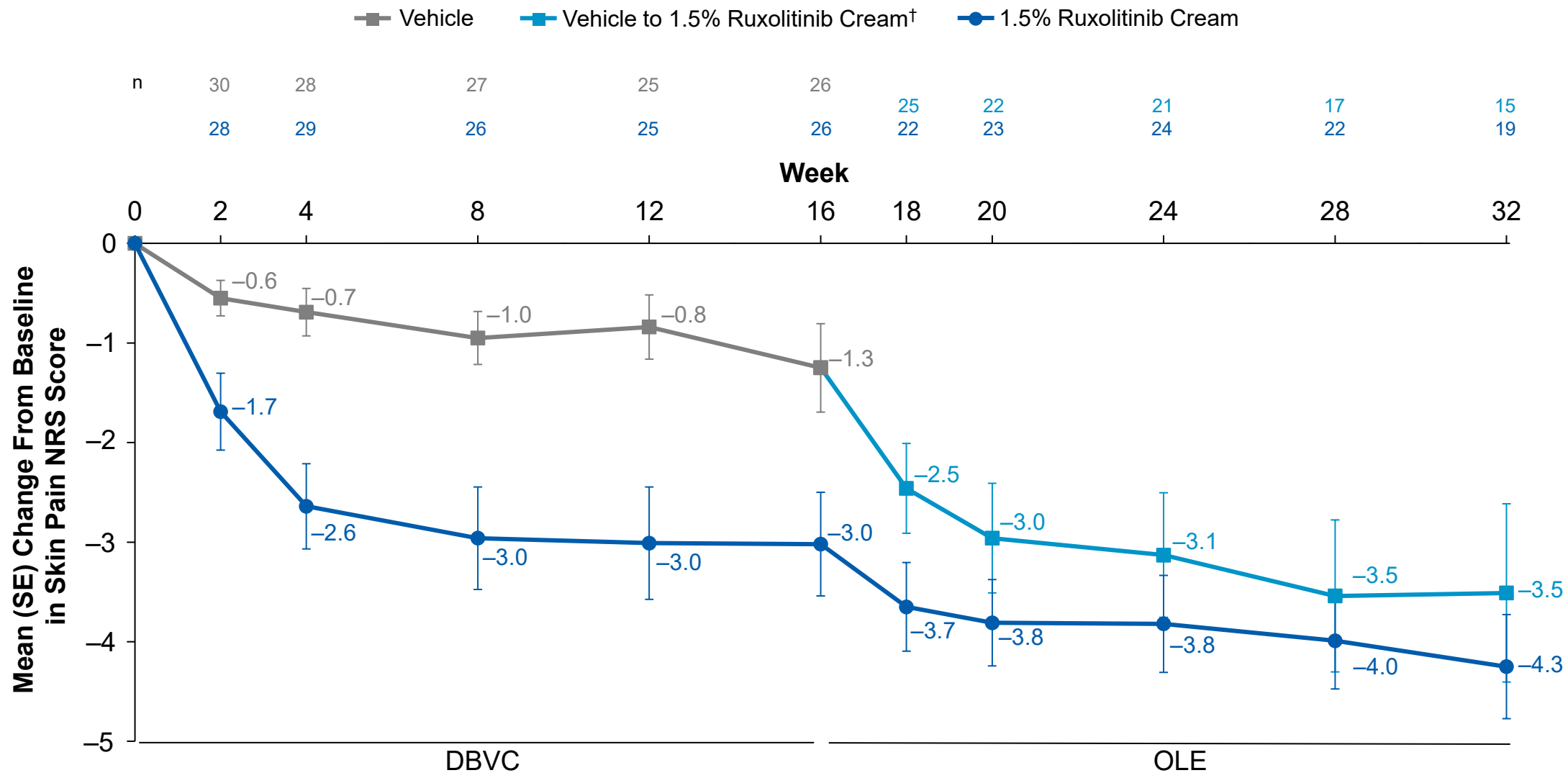
Vehicle	31	29	27	26	24	23	21	20	20	20	20	17	17	17	17	17	17	16	16	15	14	13	11	1	0
1.5% Ruxolitinib Cream	32	25	18	16	13	11	10	10	7	6	6	6	6	6	6	6	5	5	5	5	5	5	5	0	

	Vehicle	1.5% Ruxolitinib Cream
Time to Itch NRS4, median (95% CI), d	97.0 (31–NE)	17.0 (7–27)
Hazard ratio (95% CI)	ref	2.85 (1.51–5.38)
P value	ref	0.0008

NE, not estimable.
† Assessed using a Cox regression model.

Skin Pain NRS

DBVC Period and OLE (As Observed)



† After Week 16, patients applied 1.5% ruxolitinib cream.

Safety

n (%)	DBVC		OLE	
	Vehicle Cream (n=32)	1.5% Ruxolitinib Cream (n=31)	Vehicle to 1.5% Ruxolitinib Cream (n=29)	1.5% Ruxolitinib Cream (n=30)
Patients with TEAE	9 (28.1)	15 (48.4)	11 (37.9)	8 (26.7)
Patients with treatment-related TEAE	0	3 (9.7)†	0	0
Patients with grade ≥3 TEAE	0	0	1 (3.4)‡	0
Patients with serious TEAE	0	0	0	0
Patients with TEAE leading to interruption of study drug	1 (3.1)	0	0	0
Patients with TEAE leading to discontinuation of study drug	0	0	0	0

TEAE, treatment-emergent adverse event.
† Application site folliculitis, COVID-19, and insomnia (n=1 each).
‡ Increased blood creatine phosphokinase owing to increased physical activity; this TEAE was assessed by the investigator as not related to study drug and resolved with no action taken with study drug.

Most Common TEAEs†

DBVC

n (%)	Vehicle Cream (n=32)	1.5% Ruxolitinib Cream (n=31)
Nasopharyngitis	1 (3.1)	3 (9.7)
Hypertension	1 (3.1)	2 (6.5)
Contusion	0	2 (6.5)
Fall	0	2 (6.5)
Hypothyroidism	2 (6.3)	0
Upper respiratory tract infection	0	2 (6.5)

OLE

n (%)	1.5% Ruxolitinib Cream (n=59)
Sinusitis	3 (5.1)
Blood cholesterol increased	2 (3.4)
Blood creatine phosphokinase increased‡	2 (3.4)
COVID-19	2 (3.4)
Nasopharyngitis	2 (3.4)
Urinary tract infection	2 (3.4)

† Reported in >1 patient in any treatment group.
‡ 2 patients who crossed over from vehicle to 1.5% ruxolitinib cream had elevated blood creatine phosphokinase (grade 2 [specific value unavailable] and grade 3 [1369 U/L]) judged as occurring owing to increased physical activity (not treatment-related); both cases resolved with no action taken with the study drug.

Conclusions

- Ruxolitinib cream BID resulted in significant improvements in cutaneous LP disease severity versus vehicle control at Week 16 (IGA-TS primary endpoint met)
  - Clinical signs and symptoms (ie, itch, skin pain) were improved
  - Responses (IGA-TS, Itch NRS4, Skin Pain NRS) were achieved at earlier time points in patients randomized to ruxolitinib cream during the DBVC period
- Cutaneous LP symptoms and signs further improved during 16 weeks of additional open-label, as-needed BID application of ruxolitinib cream
- Ruxolitinib cream was generally well tolerated in patients with cutaneous LP and consistent with the known safety profile[1,2]
- Ruxolitinib cream represents a promising potential treatment for cutaneous LP

1. Papp K, et al. *J Am Acad Dermatol.* 2023;88(5):1008-1016. 2. Rosmarin D, et al. *N Engl J Med.* 2022;387(16):1445-1455.

Thank You For Your Attention

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To download Incyte content presented at EADV 2024, scan code.

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