

Long-Term Safety and Disease Control With Ruxolitinib Cream in Atopic Dermatitis: Results From Two Phase 3 Studies

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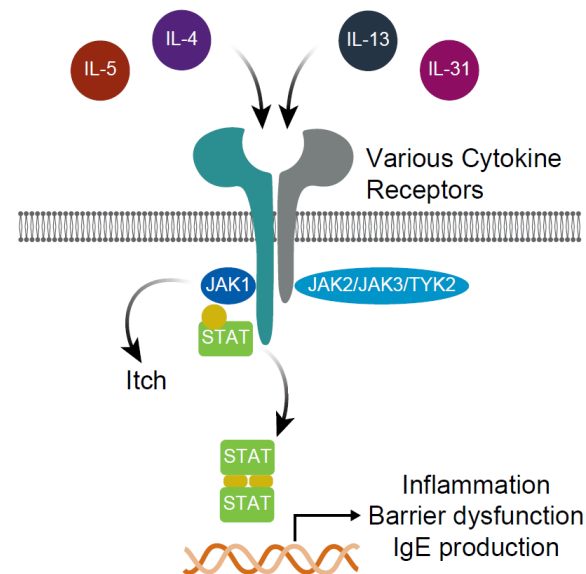
Presenting Author Disclosures

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Introduction

- Atopic dermatitis (AD) is a highly pruritic inflammatory skin disease¹
- The pathogenesis of AD involves JAKs acting downstream of proinflammatory cytokines and itch mediators^{2,3}
- In two phase 3 AD studies of identical design (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651]), ruxolitinib (RUX) cream demonstrated anti-inflammatory activity with rapid and sustained antipruritic action vs vehicle and was well tolerated⁴

Objective: To evaluate the long-term safety and disease control of RUX cream in patients with AD in TRuE-AD1 and TRuE-AD2



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IgE, immunoglobulin E; IL, interleukin; JAK, Janus kinase; STAT, signal transducer and activator of transcription; TYK2, tyrosine kinase 2.

1. Langan SM, et al. *Lancet*. 2020;396(10247):345-360. 2. Bao L, et al. *JAKSTAT*. 2013;2:e24137. 3. Oetjen LK, et al. *Cell*. 2017;171:217-228. 4. Papp K, et al. *J Am Acad Dermatol*. 2021;doi:10.1016/j.jaad.2021.1004.1085. [Epub ahead of print]. 5. Kim BS, et al. *J Allergy Clin Immunol*. 2020;145(2):572-582.

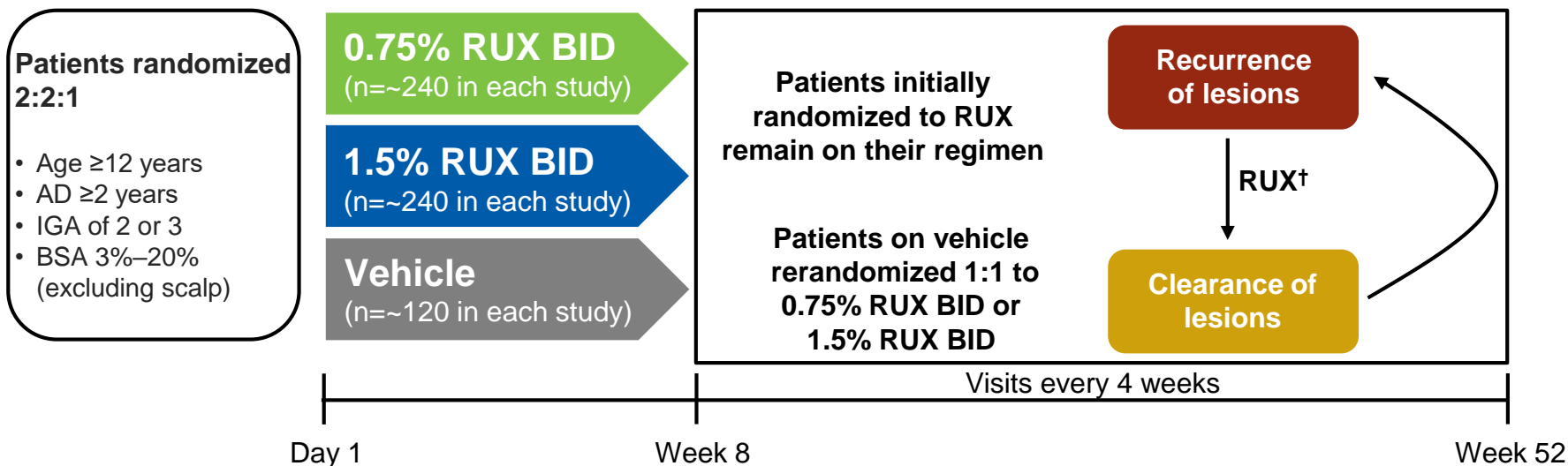
Study Design

Vehicle-controlled (VC) period

- Continuous treatment for 8 weeks
- Rescue treatment not permitted

Long-term safety (LTS) period

- Treatment discontinuation with IGA 0 at Week 8
- Treat as needed for 44 weeks
- Stop treatment 3 days after lesion clearance
- Rescue treatment not permitted



BID, twice daily; BSA, body surface area; IGA, Investigator's Global Assessment.

[†] Patients self-evaluated recurrence of lesions between study visits and treated lesions with active AD ($\leq 20\%$ BSA). If new lesions were extensive or appeared in new areas, patients contacted the investigator to determine if an unscheduled additional visit was needed.

Patient Demographics and Clinical Characteristics

	TRuE-AD1			TRuE-AD2		
	Vehicle (n=126)	0.75% RUX (n=252)	1.5% RUX (n=253)	Vehicle (n=124)	0.75% RUX (n=248)	1.5% RUX (n=246)
Age, median (IQR), y	31.5 (20–49)	34.0 (19–51)	30.0 (19–47)	37.5 (21.5–53.5)	33.0 (19–52)	32.0 (21–49)
Race, n (%)						
White	85 (67.5)	171 (67.9)	177 (77.0)	85 (68.5)	174 (70.2)	178 (72.4)
Black	29 (23.0)	55 (21.8)	56 (22.1)	32 (25.8)	63 (25.4)	57 (23.2)
Other	12 (9.5)	26 (10.3)	20 (7.9)	7 (5.6)	11 (4.4)	11 (4.5)
BSA, mean (SD), %	9.2 (5.1)	9.9 (5.4)	9.3 (5.2)	10.1 (5.8)	10.1 (5.3)	9.9 (5.4)
Baseline EASI, mean (SD)	7.4 (4.3)	8.2 (4.8)	7.9 (4.6)	8.2 (5.2)	8.1 (5.0)	7.8 (4.9)
Baseline IGA, n (%)						
2	31 (24.6)	61 (24.2)	60 (23.7)	33 (26.6)	64 (25.8)	63 (25.6)
3	95 (75.4)	191 (75.8)	193 (76.3)	91 (73.4)	184 (74.2)	183 (74.4)
Itch NRS score, mean (SD)	5.1 (2.5)	5.1 (2.3)	5.2 (2.5)	5.1 (2.4)	5.2 (2.5)	4.9 (2.5)
Facial involvement, n (%)*	52 (41.3)	112 (44.4)	118 (46.6)	41 (33.1)	83 (33.5)	79 (32.1)
Duration of disease, median (range), y	17.9 (1.9–79.1)	14.1 (1.0–68.8)	16.0 (0–69.2)	15.9 (0.8–70.7)	15.9 (0.1–68.6)	16.6 (0–68.8)

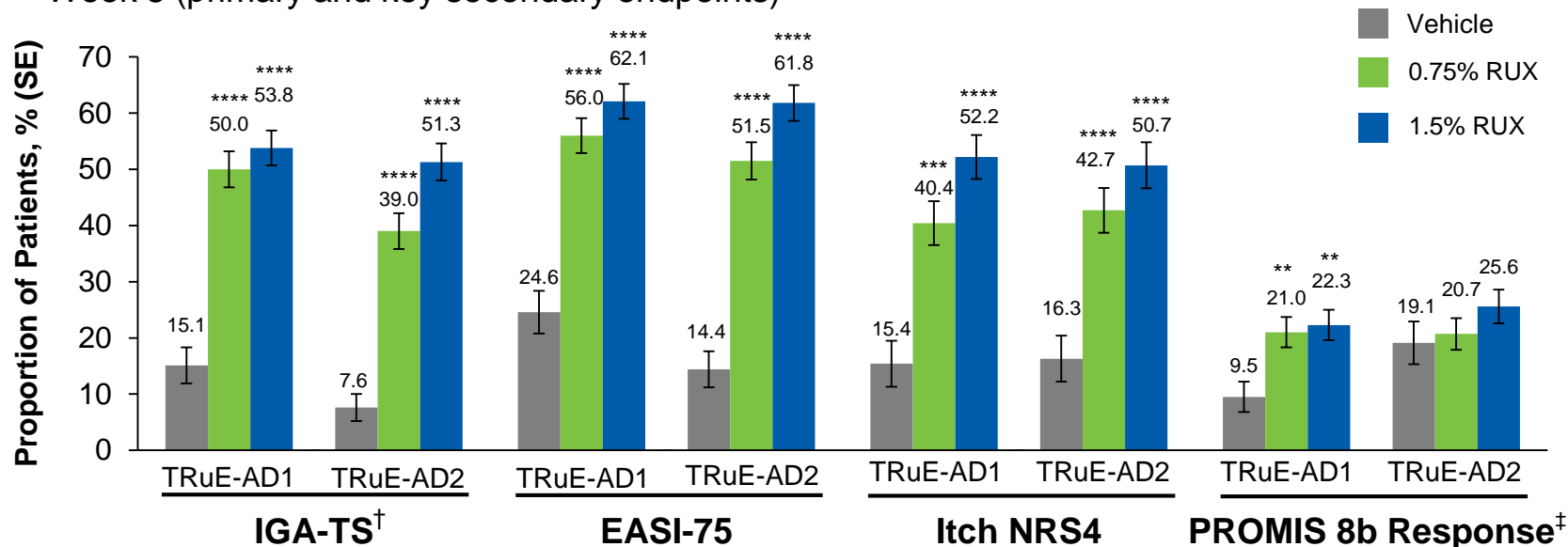
EASI, Eczema Area and Severity Index; IQR, interquartile range; NRS, numerical rating scale.

* Patient reported.

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Efficacy Measures at Week 8 of the VC Period

- Significantly more patients who applied 0.75% and 1.5% RUX cream vs vehicle achieved IGA-TS, EASI-75, itch NRS4, and clinically meaningful improvement in PROMIS 8b (TRuE-AD1 only) at Week 8 (primary and key secondary endpoints)



EASI-75, $\geq 75\%$ improvement from baseline in EASI score; IGA-TS, IGA-treatment success; NRS4, ≥ 4 -point improvement in itch NRS score from baseline; PROMIS, Patient-Reported Outcomes Measurement Information System.

** $P < 0.01$ vs vehicle; *** $P < 0.001$ vs vehicle; **** $P < 0.0001$ vs vehicle.

[†] IGA score of 0 or 1 and ≥ 2 -point improvement from baseline. [‡] ≥ 6 -point improvement in PROMIS Short Form sleep disturbance score 8(b).

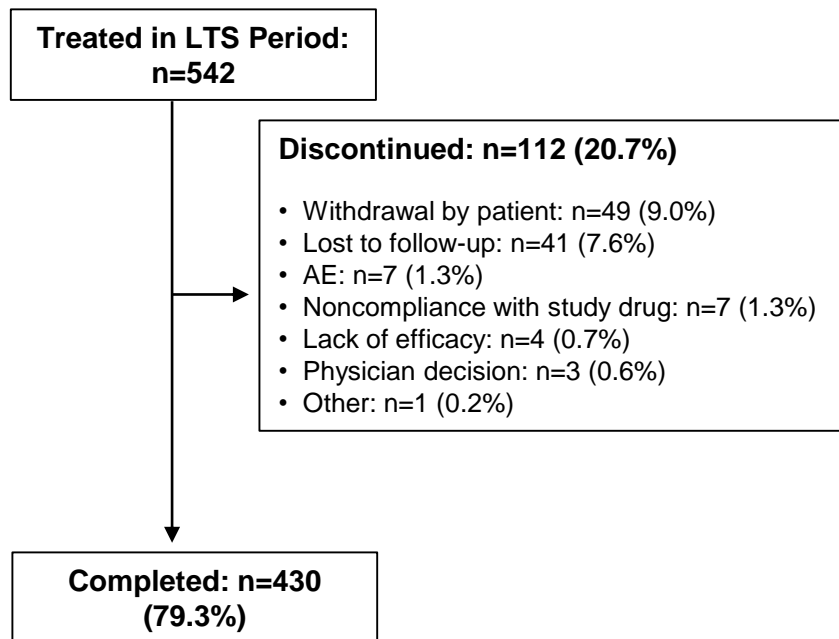
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LTS Assessments

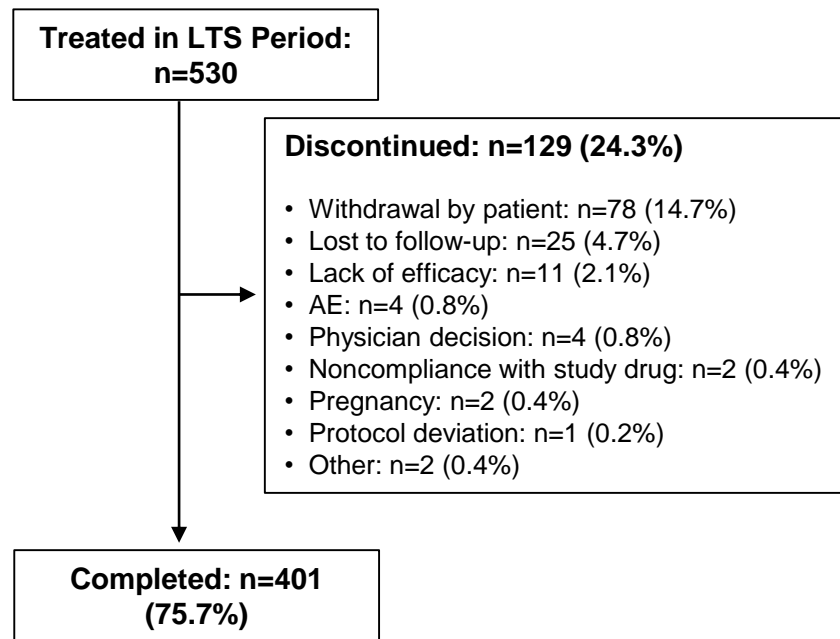
- Safety and tolerability were assessed by frequency and severity of adverse events (AEs)
- Disease control
 - Proportion of patients with clear or almost clear skin (IGA score of 0 or 1)
 - Extent of lesions (affected BSA)

Patient Disposition During the LTS Period

TRuE-AD1



TRuE-AD2



Time Off Treatment and Time to Retreatment: LTS Period

	TRuE-AD1*		TRuE-AD2*	
	0.75% RUX	1.5% RUX	0.75% RUX	1.5% RUX
Cumulative time off treatment due to lesion clearance, d	n=148	n=161	n=113	n=126
Mean (SD)	110.2 (90.0)	124.0 (81.7)	128.2 (83.1)	149.2 (100.0)
Median (range)	91.0 (2–307)	116.0 (2–286)	126.0 (3–308)	145.5 (2–312)

- Time to retreatment was assessed in patients who achieved clearance of their lesions (IGA 0) at the end of the VC period; patients self-evaluated recurrence of AD and treated areas of the skin with active AD

	TRuE-AD1		TRuE-AD2	
	0.75% RUX	1.5% RUX	0.75% RUX	1.5% RUX
Patients with IGA 0 at Week 8, n	26	36	22	30
Patients who applied RUX in the LTS, n (%)	26 (100)	36 (100)	17 (77.3)	27 (90.0)
Median time to first retreatment event, d	6.5	11.0	21.0	18.5

* Among patients who were initially randomized to RUX cream and remained on their regimen during the LTS.

Summary of Pooled Safety in the LTS Period

- The safety profile of RUX cream was consistent with the VC period, with no safety signals observed over 52 weeks
- RUX cream was well tolerated and the frequency of application site reactions was low
- No clinically meaningful changes or trends in hematologic parameters were noted over the 52-week period
- No adverse events suggestive of a relationship to systemic exposure were observed

n (%)	Vehicle to 0.75% RUX (n=101)	Vehicle to 1.5% RUX (n=99)	0.75% RUX (n=426)	1.5% RUX (n=446)
Patients with TEAE	54 (53.5)	57 (57.6)	256 (60.1)	240 (53.8)
Patients with treatment-related AE	2 (2.0)	6 (6.1)	20 (4.7)	13 (2.9)
Patients who discontinued due to a TEAE	0	0	9 (2.1)	0
Patients with serious TEAE	5 (5.0)	1 (1.0)	10 (2.3)	6 (1.3)

Most Common TEAEs for the 52-Week Study (Pooled)*

TEAE, n (%)	0.75% RUX (n=601) [†]	1.5% RUX (n=598) [†]
Upper respiratory tract infection	50 (8.3)	60 (10.0)
Nasopharyngitis	46 (7.7)	58 (9.7)
Headache	19 (3.2)	24 (4.0)
Bronchitis	16 (2.7)	20 (3.3)
Rhinitis	19 (3.2)	12 (2.0)
Atopic dermatitis	17 (2.8)	12 (2.0)
Influenza	8 (1.3)	18 (3.0)
Hypertension	16 (2.7)	11 (1.8)
Asthma	13 (2.2)	12 (2.0)
Sinusitis	17 (2.8)	8 (1.3)
Conjunctivitis	14 (2.3)	4 (0.7)

* TEAE >2.0% in either RUX cream group.

[†] Includes patients who received ≥1 dose of RUX cream in the VC and/or LTS period.

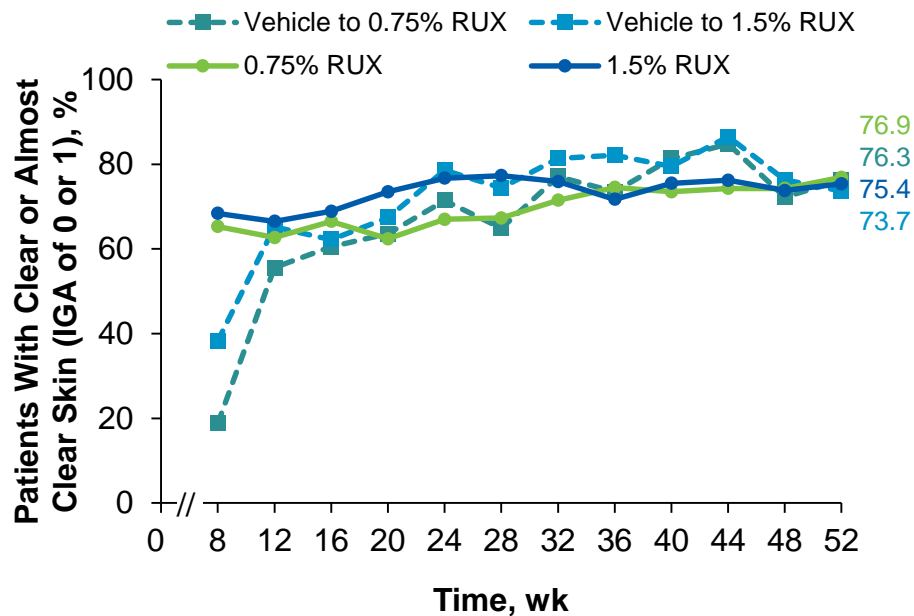
Exposure-Adjusted TEAEs

- Exposure-adjusted TEAEs and application site reactions were lower for patients who applied RUX cream vs vehicle

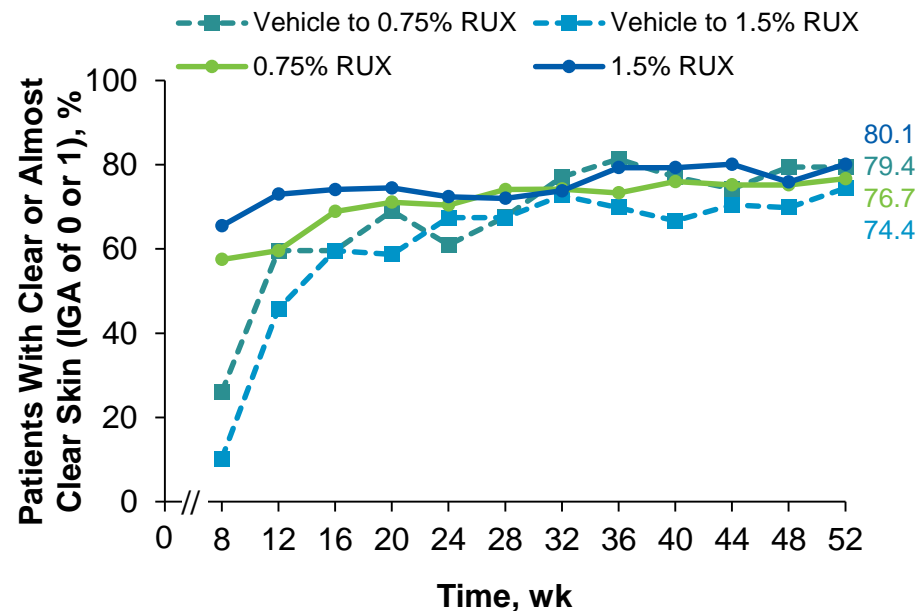
n (exposure-adjusted IR per 100 PY)	TRuE-AD1			TRuE-AD2		
	Vehicle (n=126)	0.75% RUX (n=300)	1.5% RUX (n=300)	Vehicle (n=124)	0.75% RUX (n=301)	1.5% RUX (n=298)
Any TEAE	44 (251.4)	171 (75.2)	172 (72.9)	39 (223.0)	197 (91.9)	173 (75.2)
Any application site reaction	8 (45.7)	8 (3.5)	5 (2.1)	11 (62.9)	10 (4.7)	5 (2.2)

Proportion of Patients With Clear or Almost Clear Skin (IGA 0/1)

TRuE-AD1

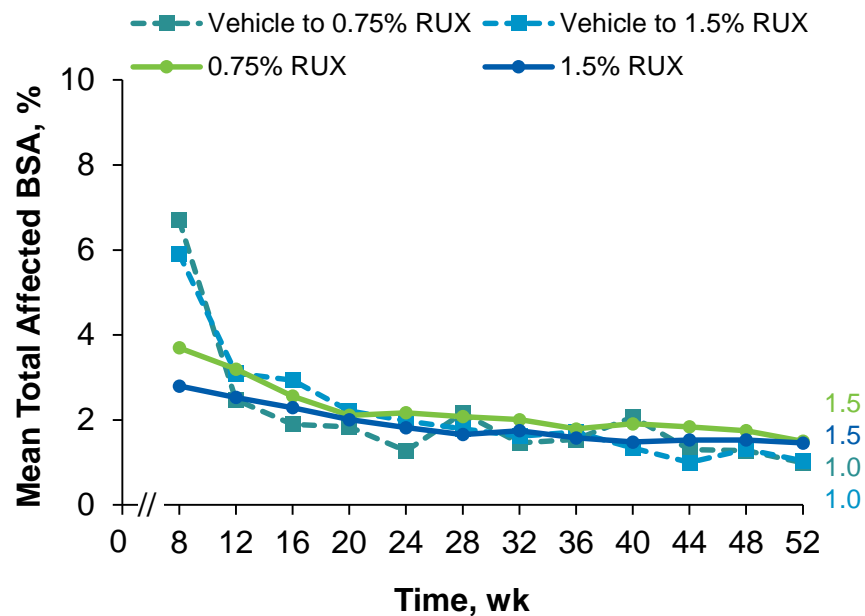


TRuE-AD2

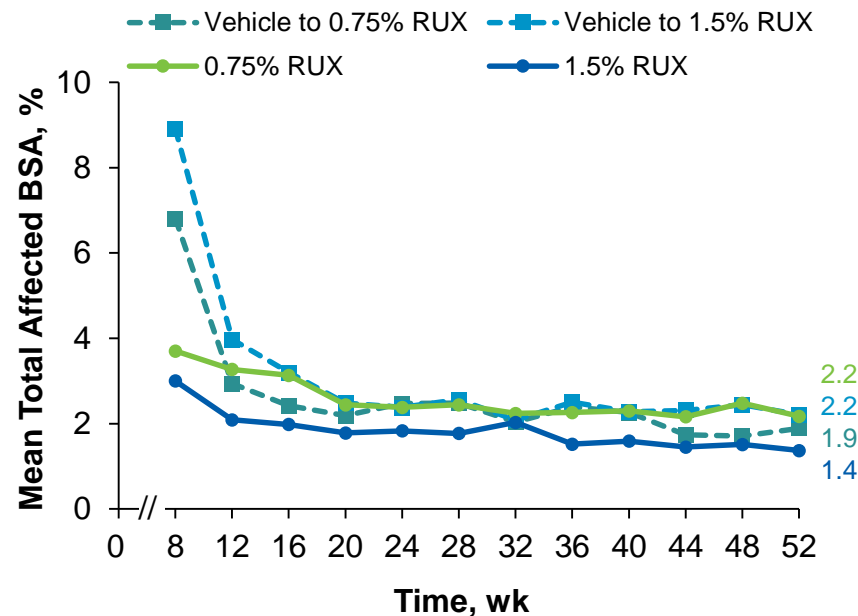


Affected BSA

TRuE-AD1



TRuE-AD2



Conclusions

- Over 75% of patients who entered the long-term safety period completed the study
- Ruxolitinib cream was well tolerated over 52 weeks, with no safety signals
 - Incidence of application site reactions was low
 - No clinically meaningful changes or trends in hematologic parameters were observed
- Patients achieved disease control with ruxolitinib cream monotherapy use as needed during the long-term safety period
 - A high proportion of patients maintained clear or almost clear skin using ruxolitinib cream as needed
 - Mean affected BSA was low throughout the long-term safety period
 - Patients who previously applied vehicle exhibited disease control through achievement of clear or almost clear skin and reductions in affected BSA