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Efficacy and Safety of Ruxolitinib Cream for the Treatment of Atopic Dermatitis: Results From Two Phase 3, Randomized, Double-Blind Studies

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Presenting Author Disclosures

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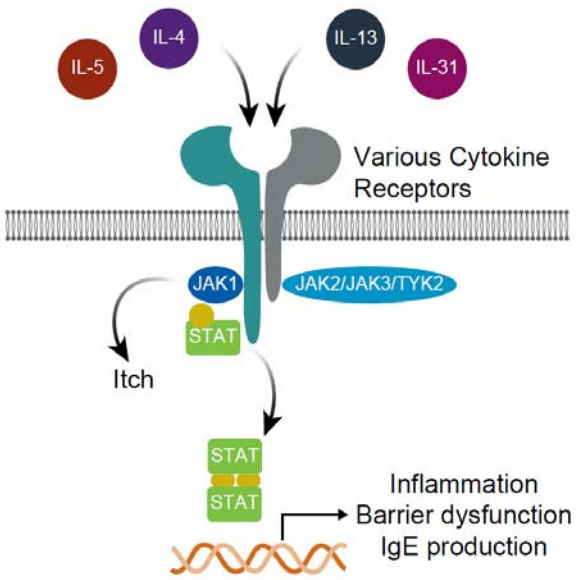
Atopic Dermatitis and JAK Signaling

- Atopic dermatitis (AD) is a chronic, inflammatory skin disease that greatly impacts patients' quality of life[1,2]
- JAKs modulate inflammatory cytokines involved in the pathogenesis of AD[3] and may also directly modulate itch[4]
- Ruxolitinib (RUX) is a potent, selective inhibitor of JAK1 and JAK2[5]
- In a phase 2 study (NCT03011892), RUX cream provided dose-dependent efficacy in patients with AD, with no notable adverse events[6]

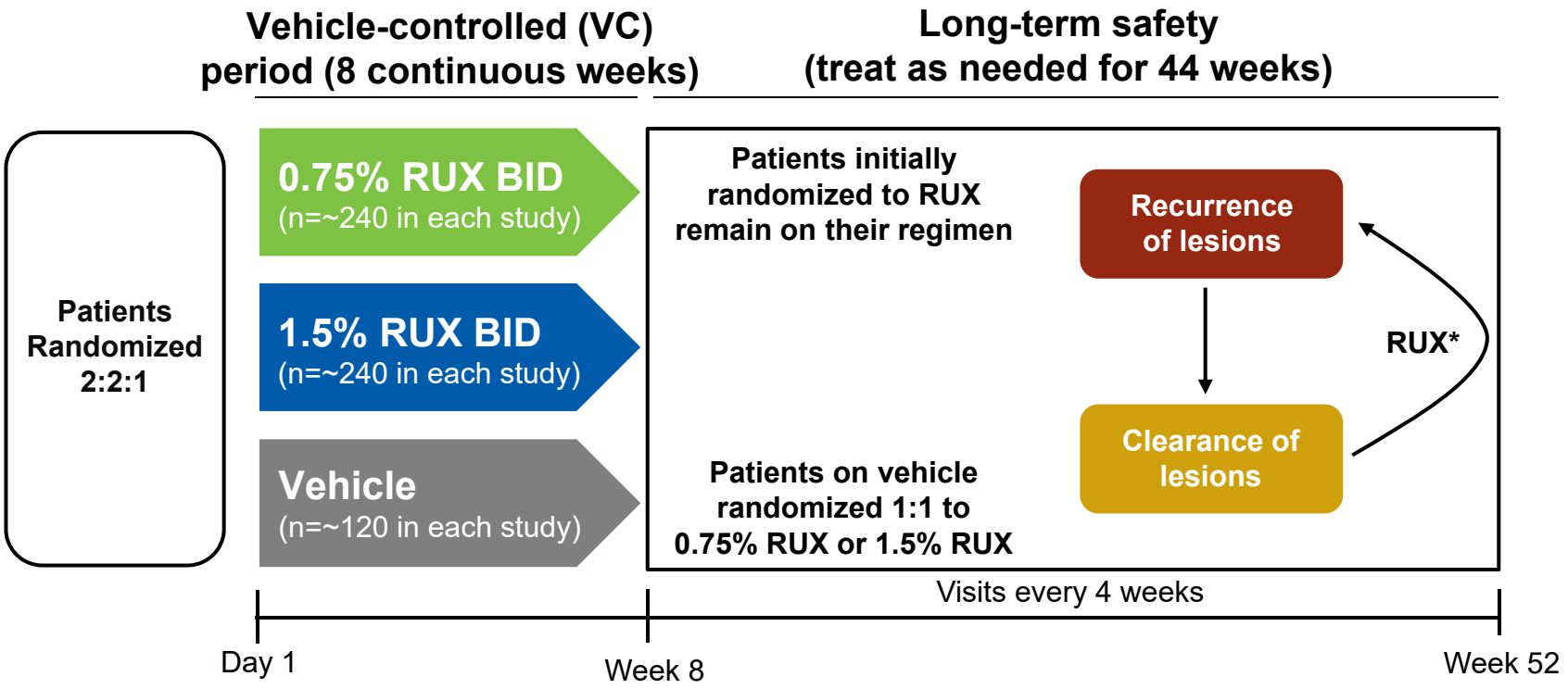
Objective: To report efficacy and safety of RUX cream in patients with AD in two phase 3 studies (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651])



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

1. Wei W, et al. *J Dermatol*. 2018;45(2):150-157; 2. Silverberg JI, et al. *Ann Allergy Asthma Immunol*. 2018;121(3):340-347; 3. Bao L, et al. *JAKSTAT*. 2013;2(3):e24137; 4. Oetjen LK, et al. *Cell*. 2017;171(1):217-228; 5. Quintas-Cardama A, et al. *Blood*. 2010;115(15):3109-3117; 6. Kim BS, et al. *J Allergy Clin Immunol*. 2020;145(2):572-582.

Study Design



BID, twice daily; BSA, body surface area.
* Patients will self-evaluate recurrence of lesions between study visits and will treat lesions with active AD (≤20% BSA). If lesions clear between study visits, patients will stop treatment 3 days after lesion disappearance. If new lesions are extensive or appear in new areas, patients will contact the investigator to determine if an additional visit is needed.

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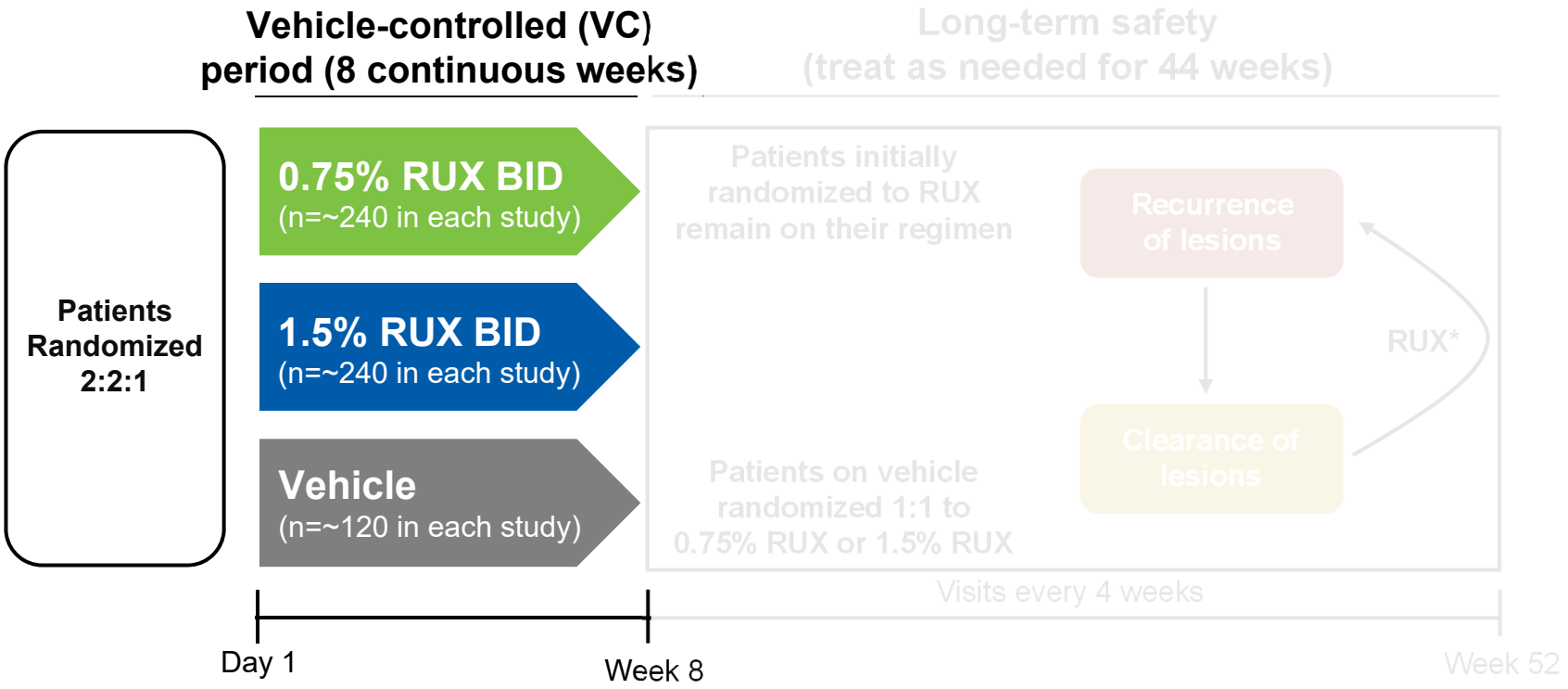

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Study Endpoints

- **Primary Endpoint**
  - Proportion of patients achieving IGA-TS (score of 0/1 with ≥2-grade improvement from baseline) at Week 8
- **Main Secondary Endpoints**
  - Proportion of patients achieving ≥75% improvement in EASI score vs baseline (EASI-75)
  - Proportion of patients with a ≥4-point improvement in itch NRS score from baseline to Week 8

EASI, Eczema Area and Severity Index; IGA-TS, Investigator's Global Assessment treatment success; NRS, numerical rating scale. .

Eligibility Criteria

- **Key Inclusion Criteria**
  - Patients aged ≥12 years with AD ≥2 years
  - IGA score of 2 or 3
  - 3%–20% affected BSA
- **Key Exclusion Criteria**
  - Unstable course of AD
  - Other types of eczema
  - Immunocompromised status
  - Any serious illness/medical condition that could interfere with study conduct, interpretation of data, or patients' well-being
  - Use of AD systemic therapies during the washout period and during the study
  - Use of AD topical therapies (except bland emollients) during the washout period and during the study

Patient Demographics

- Distribution of baseline demographics was similar across treatment groups

	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 (range), y	31.5 (12–82)	34.0 (12–85)	30.0 (12–77)	37.5 (12–82)	33.0 (12–81)	32.0 (12–85)
12–17, n (%)	23 (18.3)	53 (21.0)	47 (18.6)	22 (17.7)	55 (22.2)	45 (18.3)
≥18, n (%)	103 (81.7)	199 (79.0)	206 (81.4)	102 (82.3)	193 (77.8)	201 (81.7)
Female, n (%)	79 (62.7)	154 (61.1)	158 (62.5)	80 (64.5)	150 (60.5)	150 (61.0)
Race, n (%)*						
White	85 (67.5)	171 (67.9)	175 (69.2)	84 (67.7)	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)	21 (8.3)	8 (6.5)	11 (4.4)	11 (4.5)
Region, n (%)						
North America	88 (69.8)	176 (69.8)	176 (69.6)	84 (67.7)	166 (66.9)	165 (67.1)
Europe	38 (30.2)	76 (30.2)	77 (30.4)	40 (32.3)	82 (33.1)	81 (32.9)

* Data missing from 1 patient in the 1.5% RUX group in TRuE-AD1.

Patient Clinical Characteristics

- Distribution of baseline clinical characteristics was similar across treatment groups

	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)
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
Itch NRS score ≥4, n (%)	78 (61.9)	156 (61.9)	161 (63.6)	81 (65.3)	168 (67.7)	154 (62.6)
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)
Facial involvement, n (%)	52 (41.3)	112 (44.4)	118 (46.6)	41 (33.1)	83 (33.5)	79 (32.1)

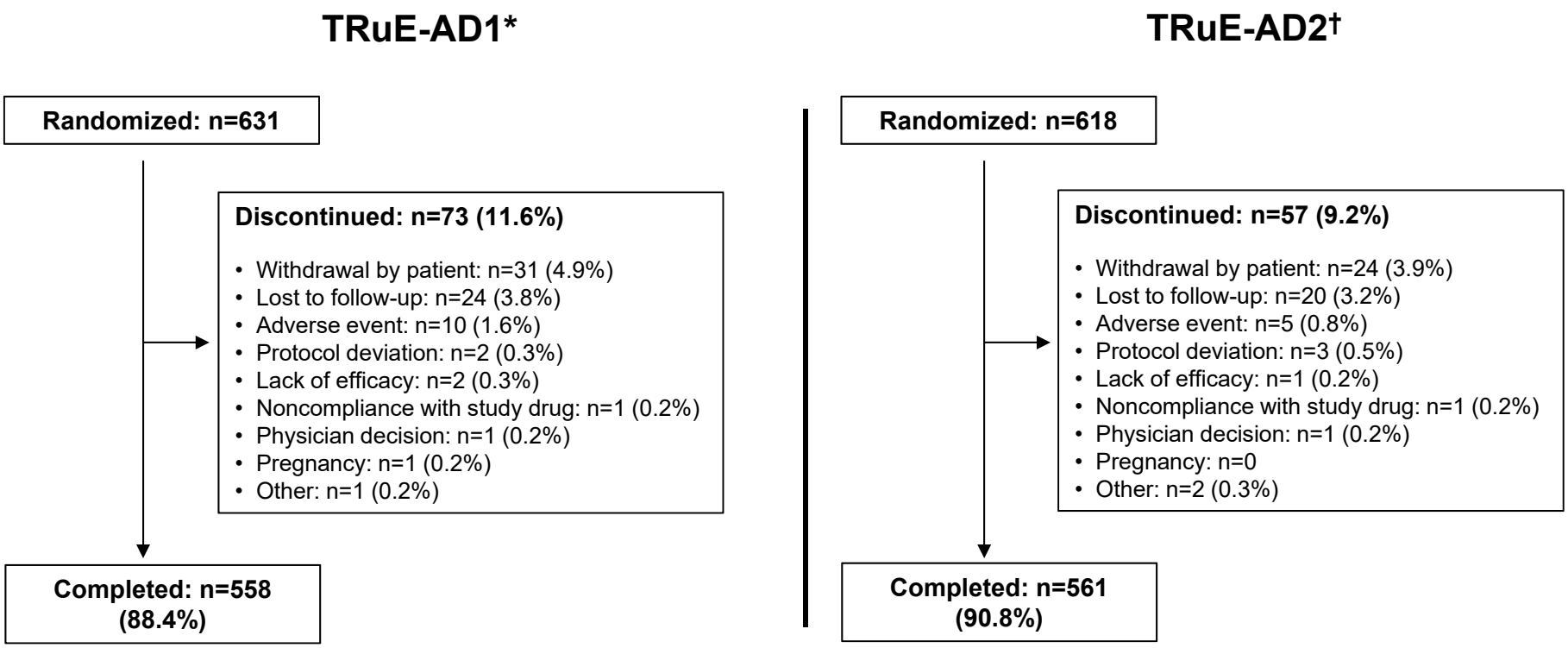
Safety

- RUX cream was well tolerated and not associated with clinically significant application site reactions
- All treatment-related TEAEs were mild or moderate in severity
- No TEAEs suggestive of a relationship to systemic exposure were observed

	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)
Patients with TEAE, n (%)	44 (34.9)	74 (29.4)	73 (28.9)	40 (32.3)	73 (29.4)	58 (23.6)
Treatment-related TEAE, n (%)	16 (12.7)	15 (6.0)	14 (5.5)	12 (9.7)	8 (3.2)	11 (4.5)
Most common treatment-related TEAEs, n (%)						
Application site burning	2 (1.6)	0	2 (0.8)	8 (6.5)	2 (0.8)	2 (0.8)
Application site pruritus	2 (1.6)	2 (0.8)	0	4 (3.2)	2 (0.8)	0
Pruritus	2 (1.6)	2 (0.8)	1 (0.4)	0	0	0
Discontinuation due to a TEAE, n (%)	5 (4.0)	3 (1.2)	3 (1.2)	3 (2.4)	1 (0.4)	0
Serious TEAE, n (%)*	2 (1.6)	1 (0.4)	2 (0.8)	0	3 (1.2)	1 (0.4)

TEAE, treatment-emergent adverse event.
* No serious TEAEs were related to RUX treatment.

Patient Disposition During the VC Period

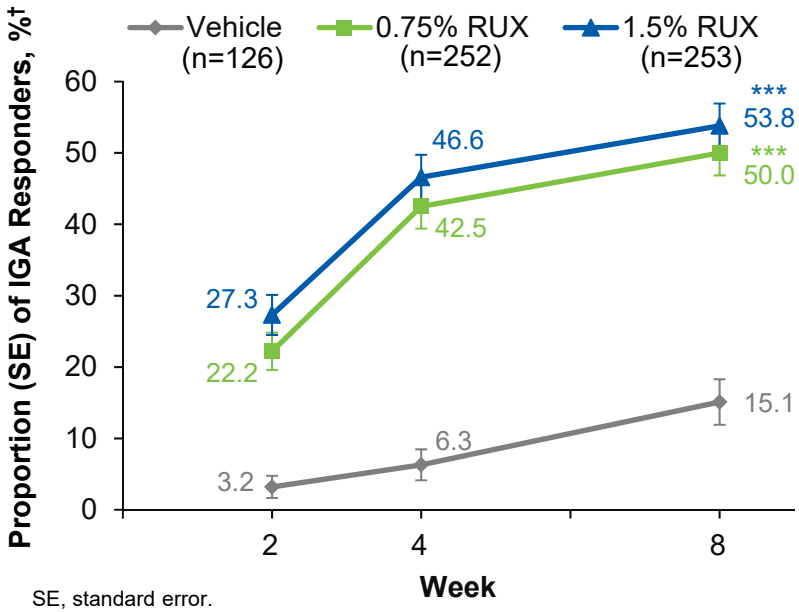


* All randomized patients were included in the efficacy analysis. † Efficacy population consisted of 577 patients (vehicle, n=118; 0.75% RUX, n=231; 1.5% RUX, n=228).

Proportion of Patients With IGA-TS

- Significantly more patients treated with RUX cream regimens vs vehicle demonstrated IGA-TS (primary endpoint); responses were time and dose dependent

TRuE-AD1



SE, standard error.
*** *P*<0.0001.
† Defined as patients achieving an IGA score of 0 or 1 with an improvement of ≥2 points from baseline.

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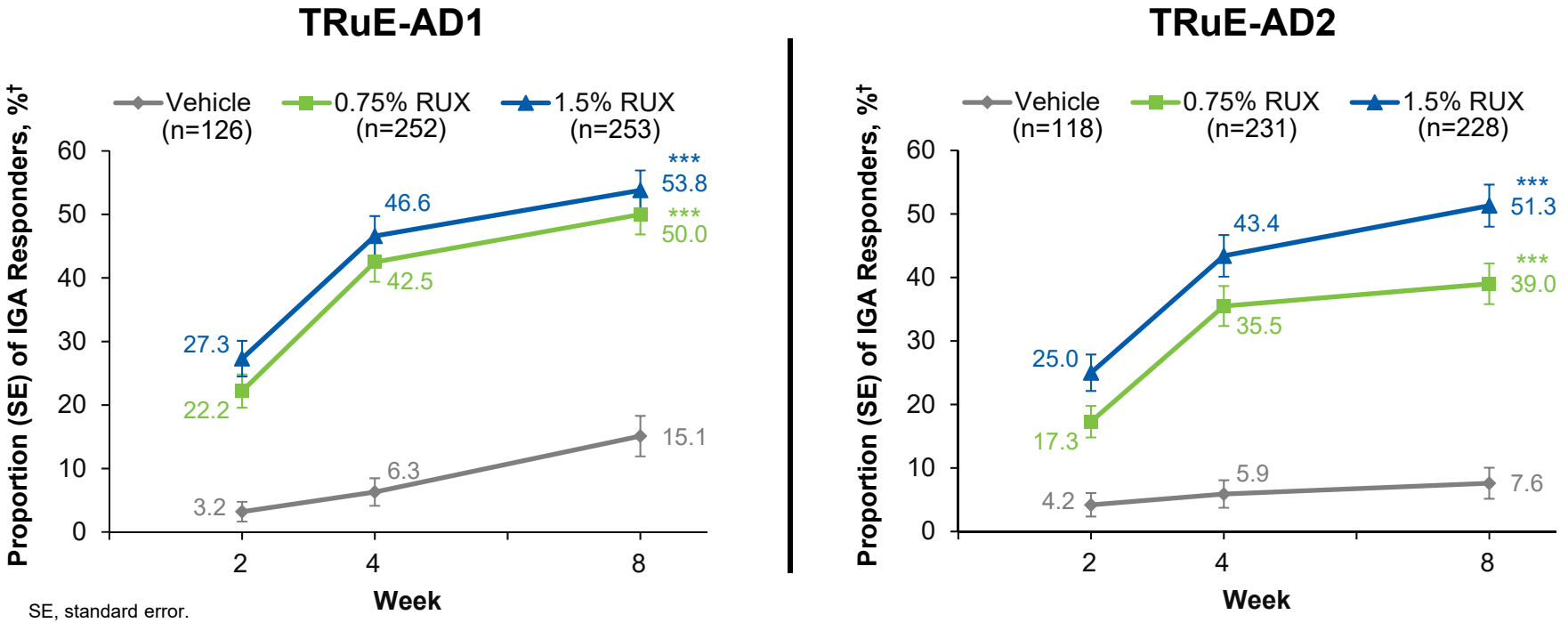
- Significantly more patients treated with RUX cream regimens vs vehicle demonstrated IGA-TS (primary endpoint); responses were time and dose dependent



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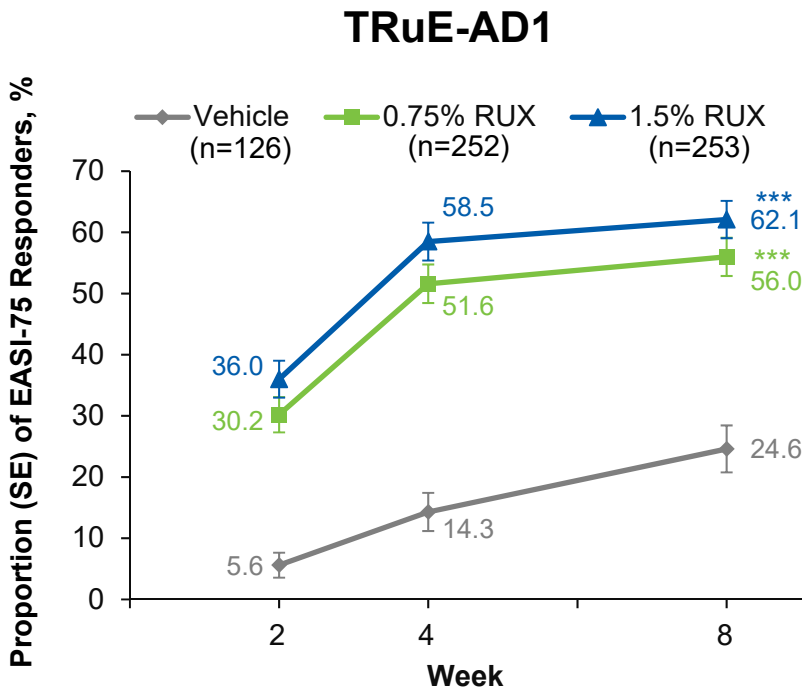
Proportion of Patients Achieving EASI-75

- Significantly more patients treated with RUX cream achieved EASI-75 vs vehicle; responses were time and dose dependent



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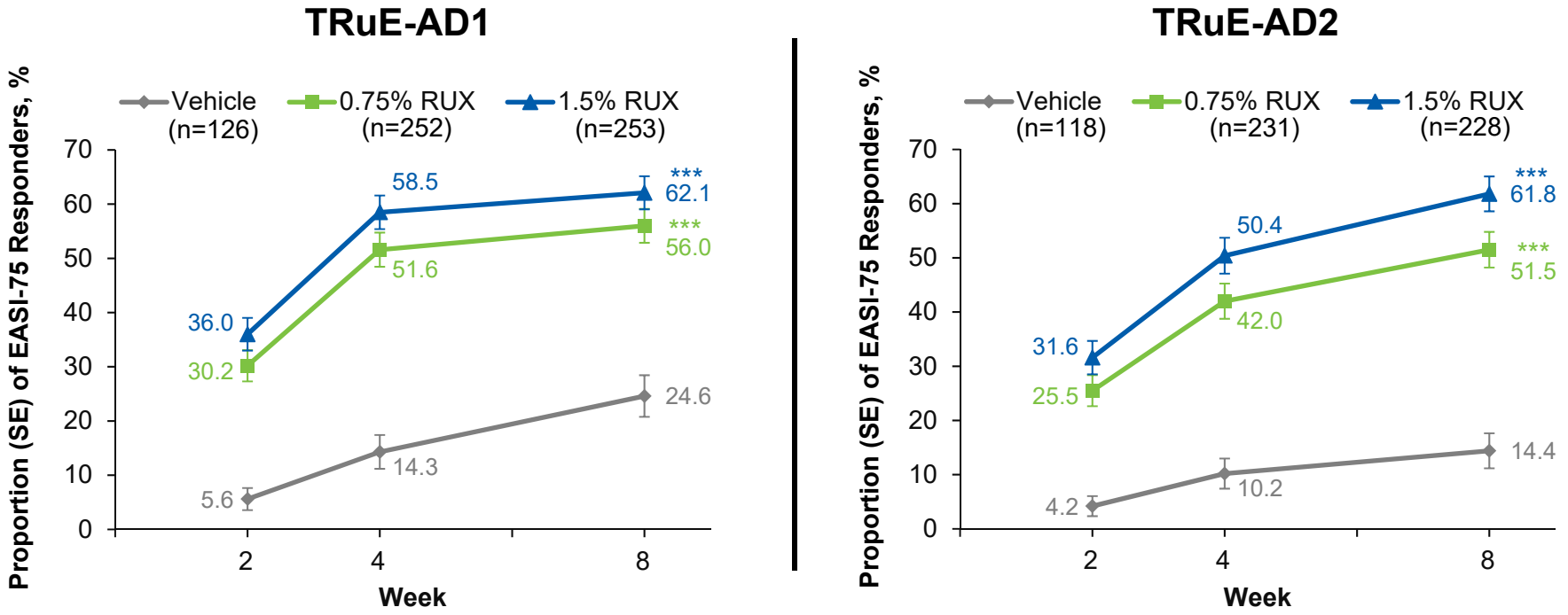

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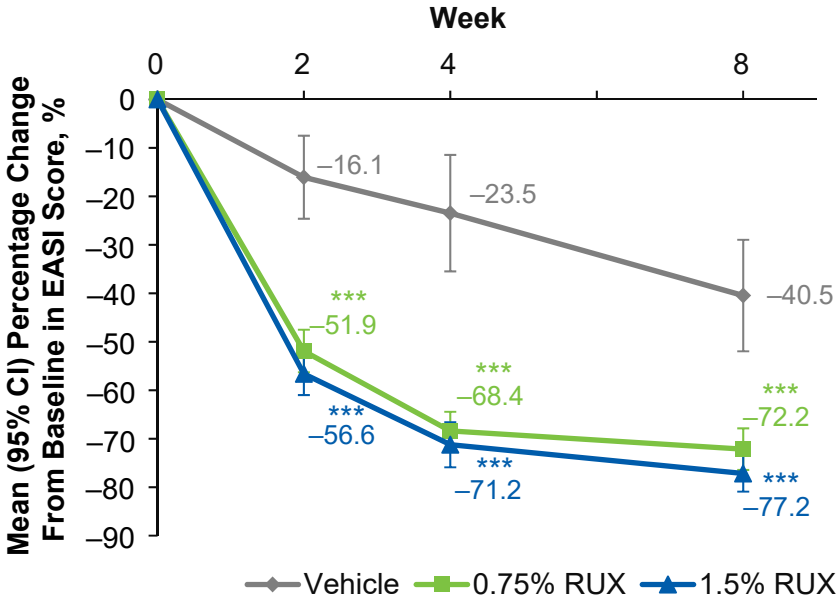
EASI Percentage Change From Baseline

- Both strengths of RUX cream showed greater improvement in mean percentage change in EASI scores vs vehicle; statistical significance was observed at Week 2 and later

TRuE-AD1



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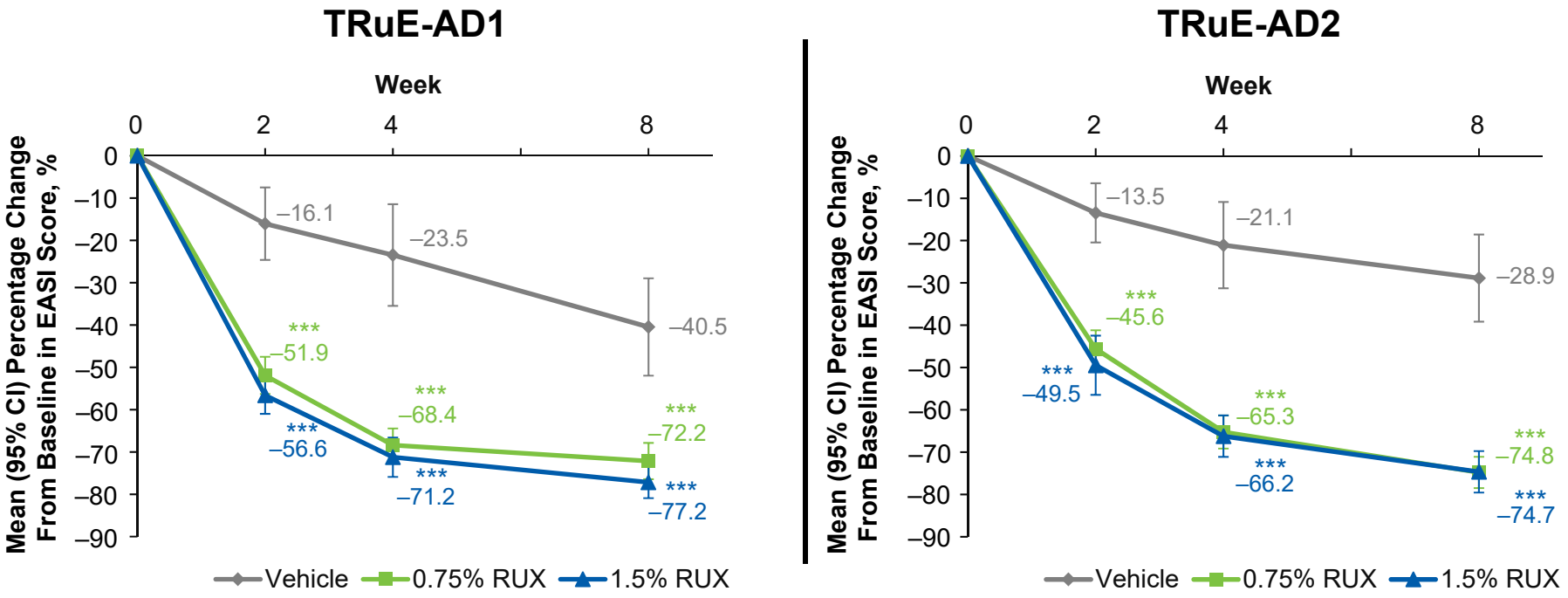

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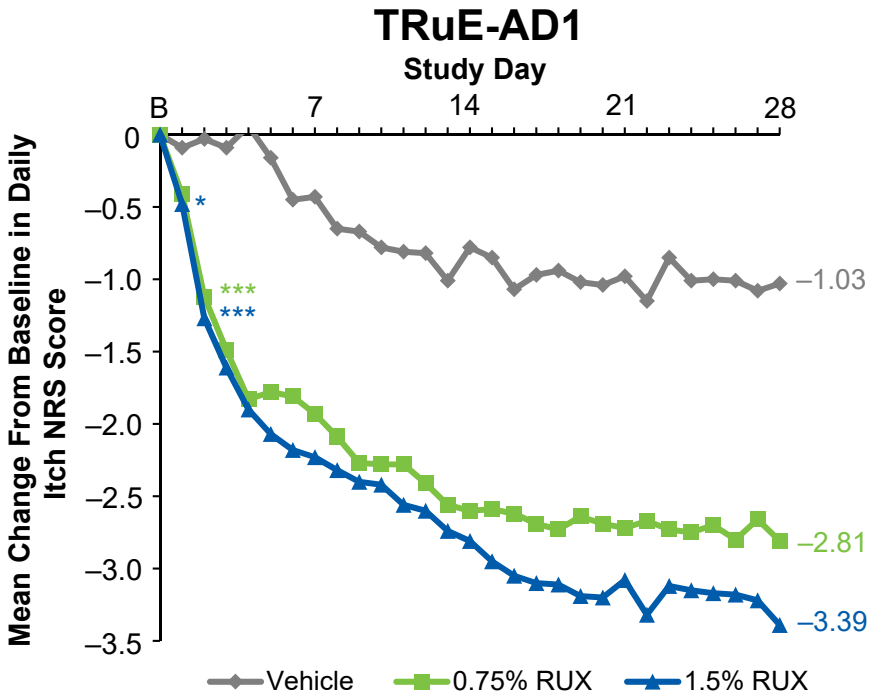
Change From Baseline in Daily Itch NRS Score

- Significantly greater itch reductions in itch NRS scores were observed within 12 hours of the first application of RUX cream (1.5%; *P*<0.05) vs vehicle



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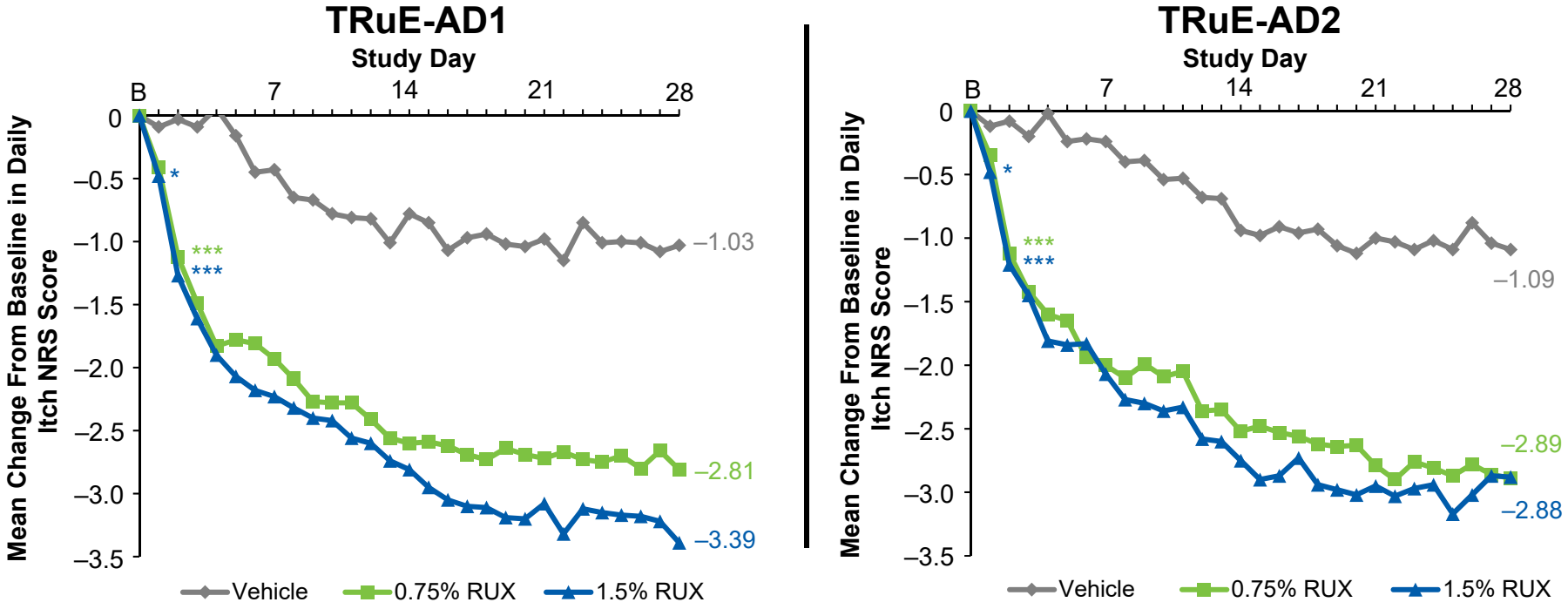

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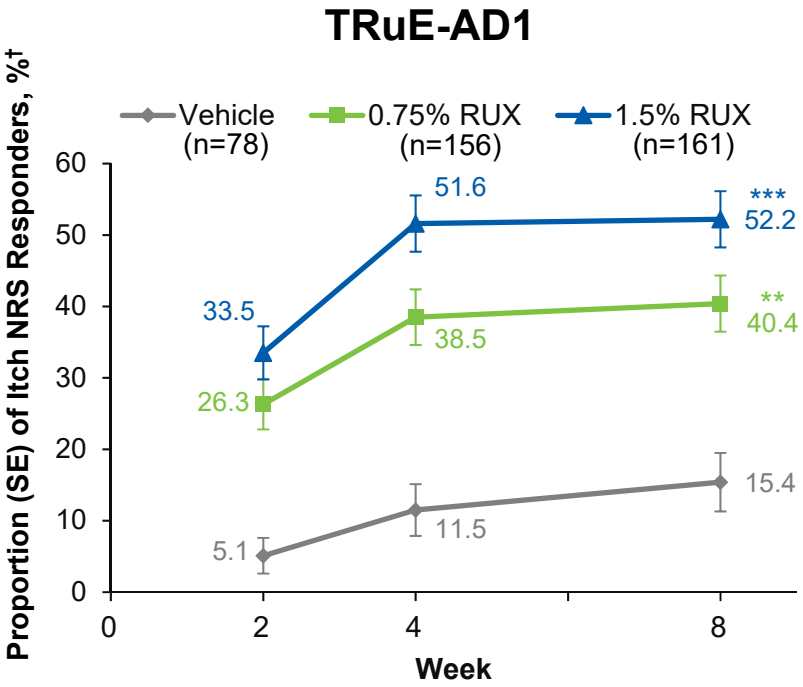
≥4-Point Improvement in Itch NRS

- Significantly more patients treated with RUX cream demonstrated clinically meaningful reduction in itch (≥4-point improvement in itch NRS) vs vehicle



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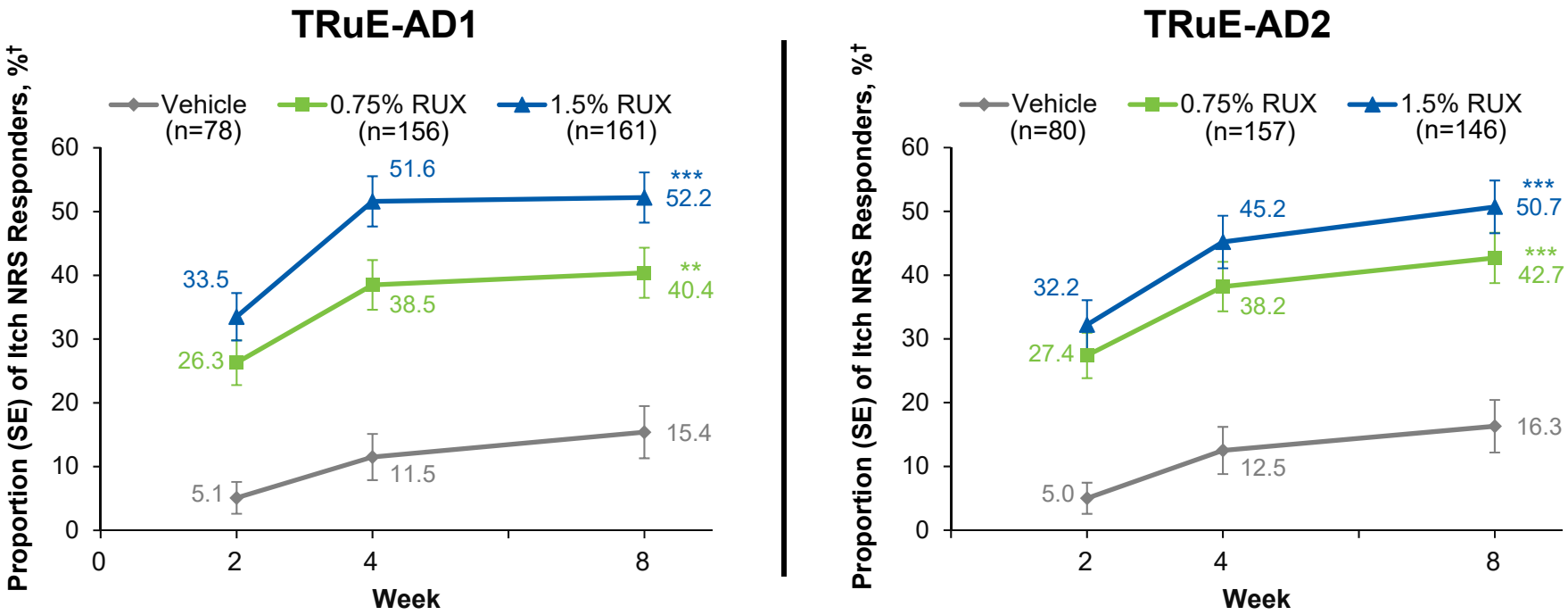

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Conclusions

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- Ruxolitinib cream demonstrated a dual mode of action: antipruritic and anti-inflammatory
- No notable safety findings (either local or systemic) were associated with treatment, including on sensitive skin areas
- **The successful outcomes of TRuE-AD1 and TRuE-AD2 support the potential of ruxolitinib cream as an effective and well-tolerated topical treatment for patients with AD**