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

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Disclosures

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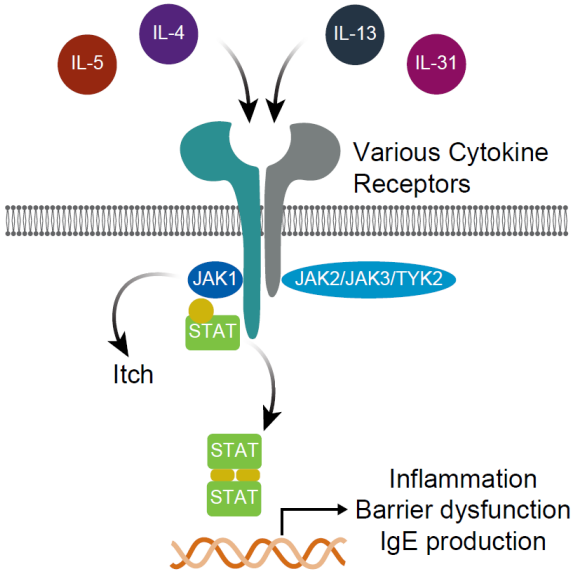
JAK-Targeted Therapy for Atopic Dermatitis

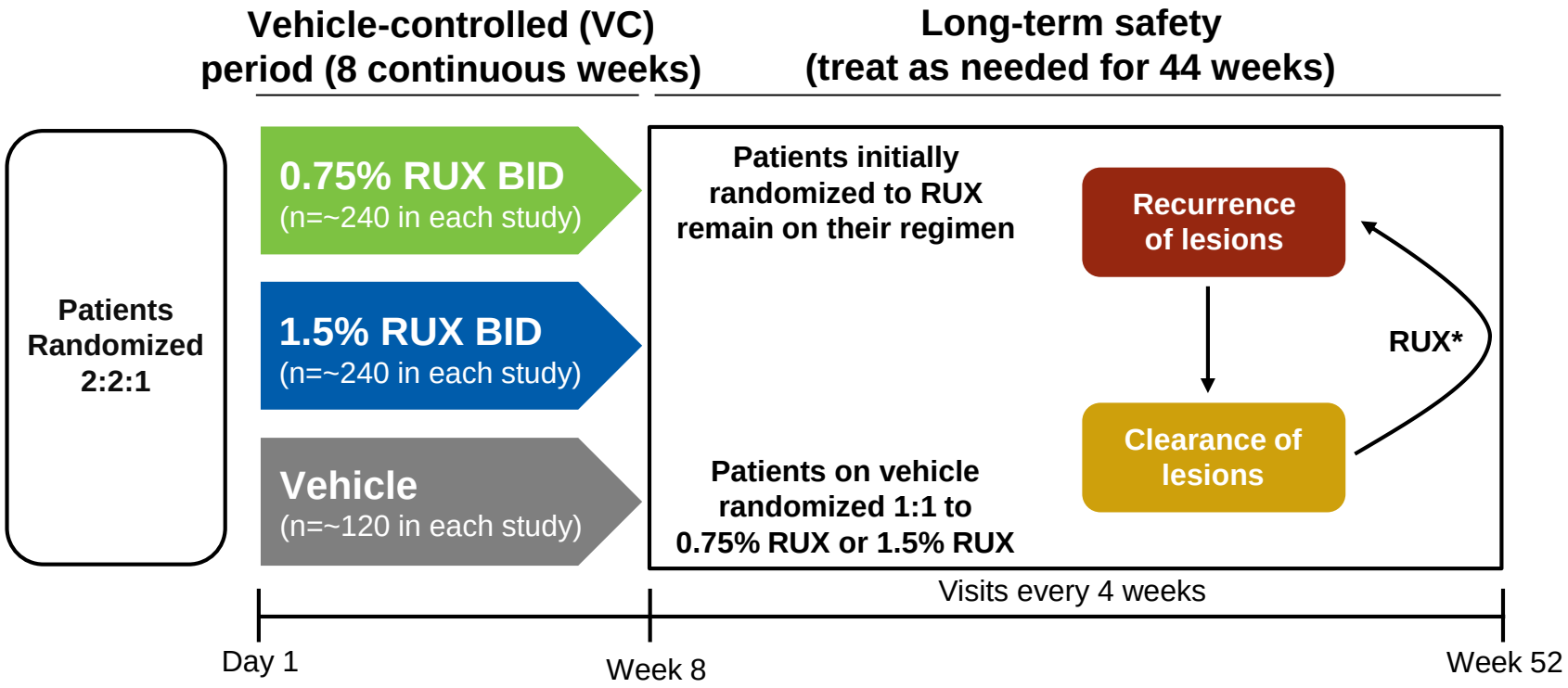
- Atopic dermatitis (AD) is a chronic, intensely pruritic, inflammatory skin dermatosis[1]
- Janus kinases (JAKs) act downstream of proinflammatory cytokines and itch mediators involved in AD pathogenesis[1,2]
- Ruxolitinib (RUX) cream is a topical selective inhibitor of JAK1 and JAK2[3]
- In a phase 2 study (NCT03011892), RUX cream provided high rates of strength-dependent efficacy in patients with AD and a safety profile similar to vehicle[4]
- **Objective:** to evaluate the efficacy and safety of RUX cream using pooled data from two phase 3 AD studies of identical design (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651]) in adolescent and adult patients with AD



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

1. Bao L, et al. *JAKSTAT*. 2013;2(3):e24137; 2. Oetjen LK, et al. *Cell*. 2017;171(1):217-228; 3. Quintas-Cardama A, et al. *Blood*. 2010;115(15):3109-3117; 4. 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.

Study Endpoints

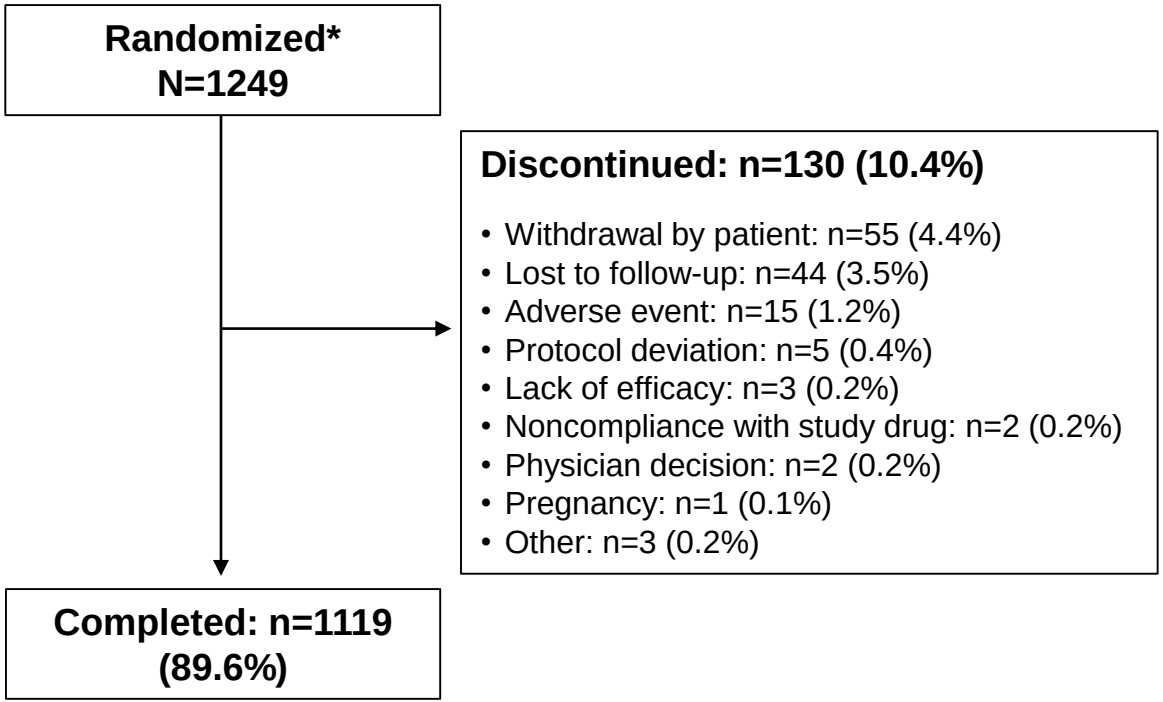
- **Primary Endpoint**
  - Proportion of patients achieving IGA-TS (score of 0 or 1 with ≥2-grade improvement from baseline) at Week 8
- **Key Secondary Endpoints**
  - Proportion of patients achieving ≥75% improvement in EASI score (EASI-75) at Week 8 vs baseline
  - Proportion of patients with a ≥4-point improvement in itch NRS score at Week 8 vs baseline
  - Proportion of patients with a ≥6-point improvement in the PROMIS Short Form – Sleep Disturbance (8b) 24-hour recall score at Week 8
- **Additional Secondary Endpoint**
  - Mean percentage change from baseline in SCORAD score

EASI, Eczema Area and Severity Index; IGA-TS, Investigator's Global Assessment–treatment success; NRS, numerical rating scale; PROMIS, Patient-Reported Outcomes Measurement Information System; SCORAD, Scoring Atopic Dermatitis.

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 patient's well-being
  - Use of AD systemic therapies during the washout period or during the study
  - Use of AD topical therapies (except bland emollients) during the washout period or during the study

Patient Disposition During the VC Period



* All randomized patients were included in the safety analysis. The efficacy population consisted of 1208 patients (vehicle, n=244; 0.75% RUX, n=483; 1.5% RUX, n=481).

Patient Demographics

- Distribution of baseline demographics was similar across treatment groups

Demographic Characteristic	Vehicle (n=250)	0.75% RUX (n=500)	1.5% RUX (n=499)	Total (N=1249)
Age, median (range), y	34.0 (12–82)	33.0 (12–85)	31.0 (12–85)	32.0 (12–85)
12–17, n (%)	45 (18.0)	108 (21.6)	92 (18.4)	245 (19.6)
≥18, n (%)	205 (82.0)	392 (78.4)	407 (81.6)	1004 (80.4)
Female, n (%)	159 (63.6)	304 (60.8)	308 (61.7)	771 (61.7)
Race, n (%)*				
White	169 (67.6)	345 (69.0)	353 (70.7)	867 (69.4)
Black	61 (24.4)	118 (23.6)	113 (22.6)	292 (23.4)
Other	20 (8.0)	37 (7.4)	32 (6.4)	89 (7.1)
Region, n (%)				
North America	172 (68.8)	342 (68.4)	341 (68.3)	855 (68.5)
Europe	78 (31.2)	158 (31.6)	158 (31.7)	394 (31.5)

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

Patient Clinical Characteristics

- Distribution of baseline clinical characteristics was similar across treatment groups

Clinical Characteristic	Vehicle (n=250)	0.75% RUX (n=500)	1.5% RUX (n=499)	Total (N=1249)
BSA, mean ± SD, %	9.6±5.5	10.0±5.3	9.6±5.3	9.8±5.4
Baseline EASI, mean ± SD	7.8±4.8	8.1±4.9	7.8±4.8	8.0±4.8
≤7, n (%)	127 (50.8)	249 (49.8)	244 (48.9)	620 (49.6)
>7, n (%)	123 (49.2)	251 (50.2)	255 (51.1)	629 (50.4)
Baseline IGA, n (%)				
2	64 (25.6)	125 (25.0)	123 (24.6)	312 (25.0)
3	186 (74.4)	375 (75.0)	376 (75.4)	937 (75.0)
Itch NRS score, mean ± SD*	5.1±2.4	5.2±2.4	5.1±2.5	5.1±2.4
Itch NRS score ≥4, n (%)*	159 (63.6)	324 (64.8)	315 (63.1)	798 (63.9)
Duration of disease, median (range), y	16.5 (0.8–79.1)	15.1 (0.1–68.8)	16.1 (0–69.2)	15.8 (0–79.1)
Facial involvement, n (%)	93 (37.2)	195 (39.0)	197 (39.5)	485 (38.8)
Number of flares in last 12 mo, mean ± SD	7.3±25.7	5.2±6.7	6.0±17.6	5.9±6.5

* Data missing from 69 patients (vehicle, n=15; 0.75% RUX, n=33; 1.5% RUX, n=21).

Safety

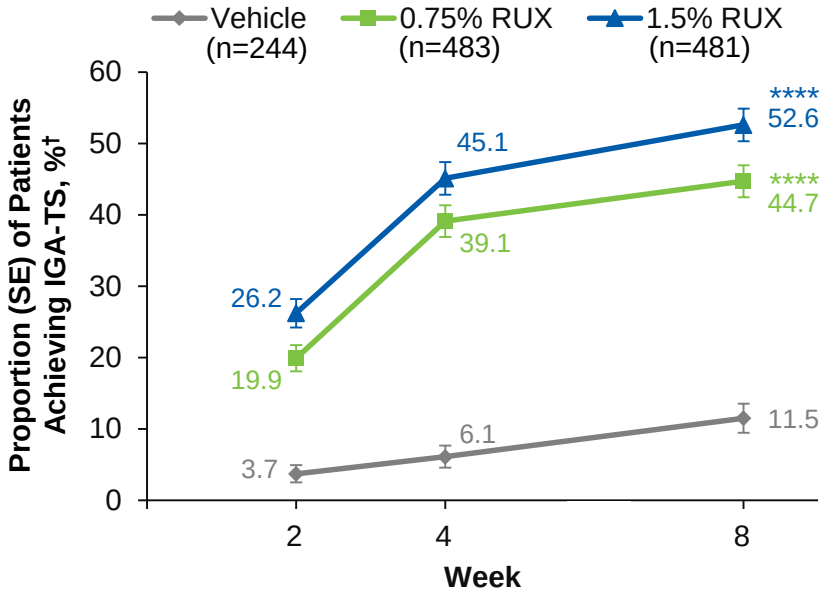
- RUX cream was well tolerated and not associated with clinically significant application site reactions
- No serious AEs related to RUX cream were reported
- No TEAEs suggestive of a relationship to bioavailability were observed
  - RUX plasma levels were consistently low, with near-flat mean value curves throughout treatment

	Vehicle (n=250)	0.75% RUX (n=500)	1.5% RUX (n=499)
Patients with TEAE, n (%)	84 (33.6)	147 (29.4)	131 (26.3)
Treatment-related TEAE, n (%)	28 (11.2)	23 (4.6)	25 (5.0)
Most common treatment-related TEAEs, n (%)*			
Application site burning	10 (4.0)	2 (0.4)	4 (0.8)
Application site pruritus	6 (2.4)	4 (0.8)	0 (0.0)
Discontinuation due to a TEAE, n (%)	8 (3.2)	4 (0.8)	3 (0.6)
Serious TEAE, n (%)†	2 (0.8)	4 (0.8)	3 (0.6)

AE, adverse event; TEAE, treatment-emergent adverse event.
* Occurring in >0.5% of the total patient population.
† No serious TEAEs were related to RUX treatment.

Proportion of Patients Achieving IGA-TS (Primary Endpoint)

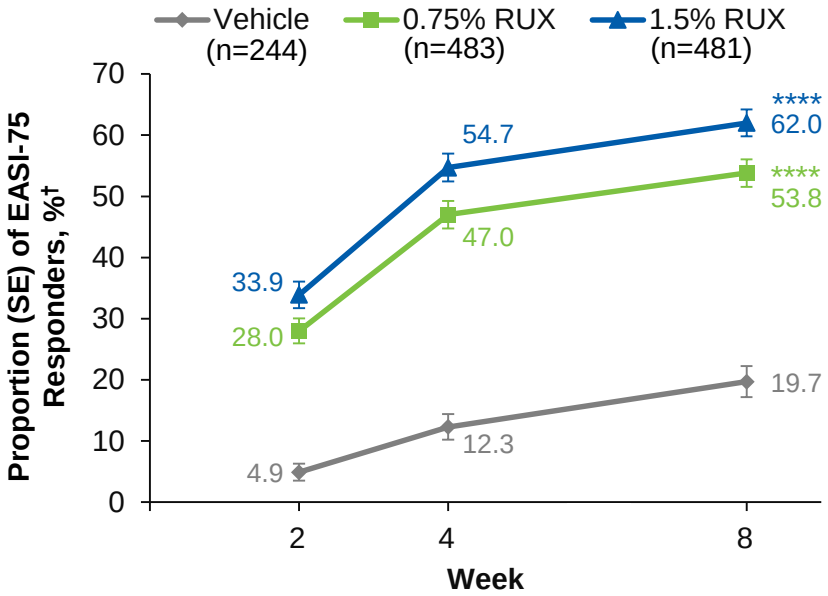
- Significantly more patients achieved IGA-TS at Week 8 with 0.75% and 1.5% RUX cream vs vehicle (44.7% and 52.6% vs 11.5%, respectively; both *P*<0.0001)



SE, standard error.
**** *P*<0.0001 vs vehicle at Week 8.
† Defined as patients achieving an IGA score of 0 or 1 with an improvement of ≥2 points from baseline. Patients with missing postbaseline values were imputed as nonresponders at Weeks 2, 4, and 8.

Proportion of Patients Achieving EASI-75

- Significantly more patients achieved EASI-75 at Week 8 with 0.75% and 1.5% RUX cream vs vehicle (53.8% and 62.0% vs 19.7%, respectively; both *P*<0.0001)

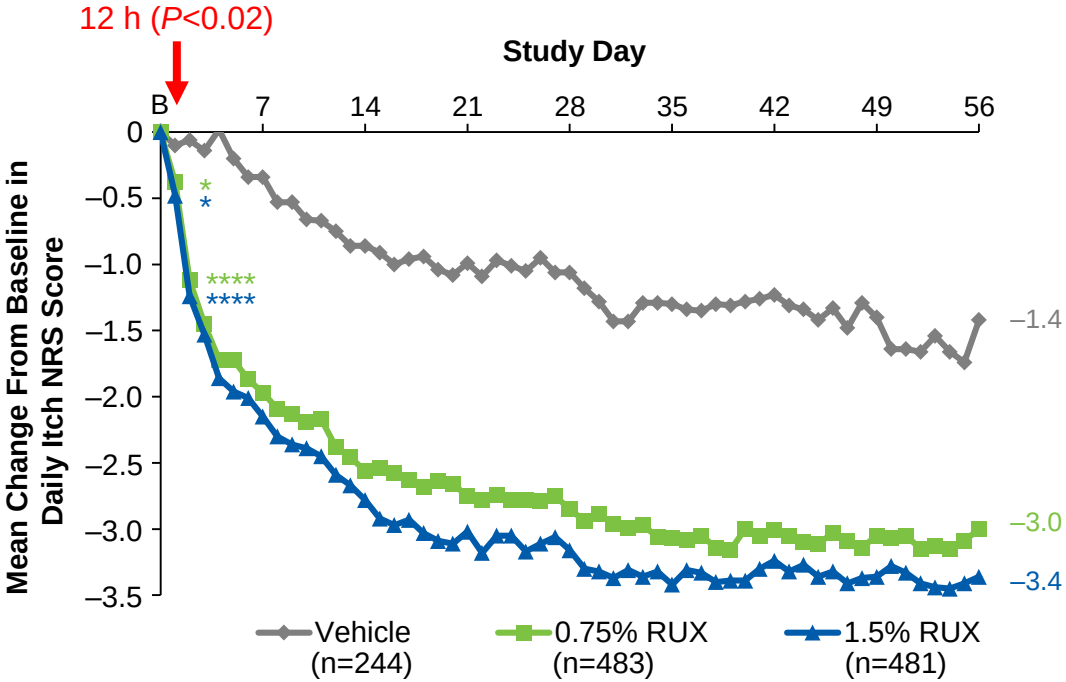


**** *P*<0.0001 vs vehicle at Week 8.

† Patients with missing postbaseline values were imputed as nonresponders at Weeks 2, 4, and 8.

Change From Baseline in Daily Itch NRS Score

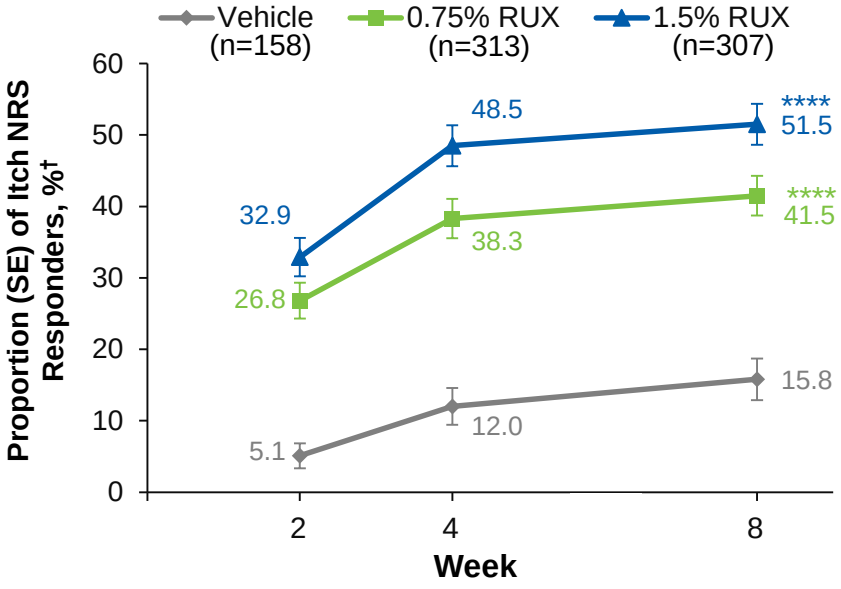
- Significantly greater itch reduction was observed within 12 hours of first 0.75% and 1.5% RUX cream application vs vehicle (mean change from baseline, –0.4 and –0.5 vs –0.1, respectively; both *P*<0.02)

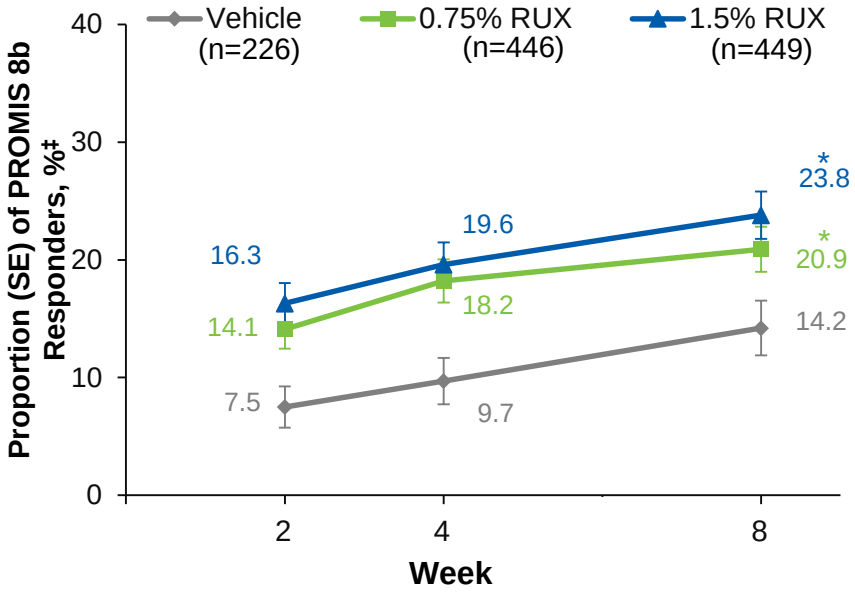


B, baseline.
* *P*<0.02 vs vehicle.
**** *P*<0.0001 vs vehicle.

Clinically Meaningful Improvement in Itch NRS and PROMIS Sleep Disturbance Score (8b)

- Significantly more patients demonstrated clinically meaningful improvement in itch (≥4-point improvement in itch NRS) and sleep disturbance (≥6-point improvement in PROMIS sleep disturbance [8b]) with RUX cream vs vehicle





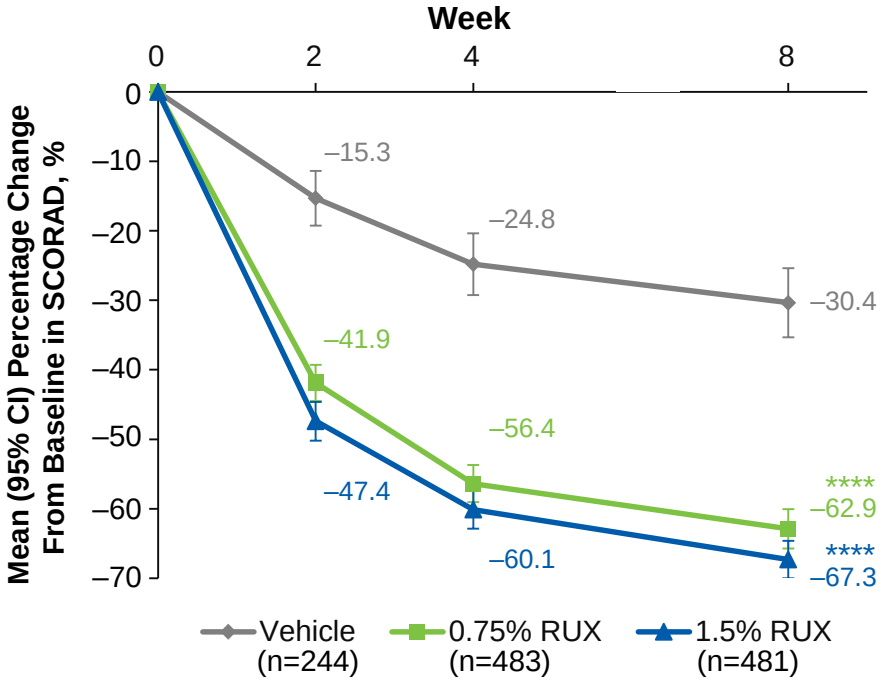
* *P*<0.05 vs vehicle at Week 8. **** *P*<0.0001 vs vehicle at Week 8.

† Patients in the analysis had an NRS score ≥4 at baseline. Patients with missing postbaseline values were imputed as nonresponders at Weeks 2, 4, and 8.

‡ Defined as a ≥6-point improvement from baseline in the PROMIS sleep disturbance score 8(b). Patients with missing postbaseline values were imputed as nonresponders at Weeks 2, 4, and 8.

Percentage Change From Baseline in SCORAD

- Significant change from baseline in SCORAD was achieved at Week 8 with 0.75% and 1.5% RUX cream regimens vs vehicle (62.9% and 67.3% vs 30.4%, respectively; both *P*<0.0001)



**** *P*<0.0001 vs vehicle at Week 8.

Conclusions

- Application of RUX cream brought about rapid (within 12 hours of initiation of therapy), substantial, and sustained reduction in itch
- RUX cream demonstrated superior efficacy vs vehicle for achieving IGA-TS, EASI-75, a ≥4-point reduction in itch NRS score, a ≥6-point improvement in PROMIS 8b, and change from baseline in SCORAD
- RUX cream demonstrated a dual mode of action: antipruritic and anti-inflammatory
- The AE profile was similar to vehicle; the rate of application site reactions was low
- These results demonstrate the potential of RUX cream as an effective and well-tolerated topical treatment for AD