

# Efficacy of Ruxolitinib Cream for the Treatment of Atopic Dermatitis by Anatomic Region: Pooled Analysis From Two Randomized Phase 3 Studies

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## Introduction

- Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by itching, dryness, and redness<sup>1</sup>
- Distribution pattern of disease may be affected by exposure to different triggering factors, and anatomic location of lesions may affect treatment options<sup>2</sup>
- Janus kinases (JAKs) play an important role in the pathogenesis of AD and the development of itch by mediating proinflammatory cytokines in skin and sensory neurons<sup>3,4</sup>
- Ruxolitinib cream is a topical formulation of ruxolitinib, a selective inhibitor of JAK1 and JAK2<sup>5,6</sup>
- In two phase 3 randomized studies of identical design (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651]), ruxolitinib cream demonstrated anti-inflammatory activity with antipruritic action vs vehicle and was well tolerated<sup>5</sup>

## Objective

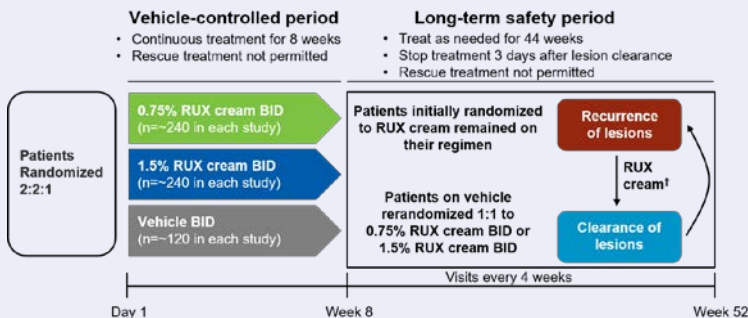
- To analyze the efficacy and safety of ruxolitinib cream by anatomic region and signs of AD using pooled data from the vehicle-controlled period of two phase 3 trials in adolescent and adult patients with AD

## Methods

### Patients and Study Design

- Eligible patients were aged ≥12 years with AD disease duration for ≥2 years and had an Investigator's Global Assessment score of 2 or 3 and 3%–20% affected body surface area (excluding scalp)
- Key exclusion criteria were unstable course of AD, other types of eczema, immunocompromised status, concomitant skin disorders that may interfere with evaluation of AD lesions, 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, and any serious illness or medical condition that could interfere with study conduct, interpretation of data, or patients' well-being
- TRuE-AD1 and TRuE-AD2 had identical study designs (Figure 1)
  - In both studies, patients were randomized (2:2:1) to either of 2 ruxolitinib cream strength regimens (0.75% twice daily [BID], 1.5% BID) or vehicle cream BID for 8 weeks of double-blind treatment
  - Patients on ruxolitinib cream subsequently continued treatment for 44 weeks (long-term safety period); patients initially randomized to vehicle were rerandomized 1:1 (blinded) to either ruxolitinib cream strength

Figure 1. Study Design



AD, atopic dermatitis; BID, twice daily; BSA, body surface area; RUX, ruxolitinib.  
† Patients self-evaluated recurrence of lesions between study visits and treated lesions with active AD (≤20% BSA). If lesions cleared between study visits, patients stopped treatment 3 days after lesion disappearance. If new lesions were extensive or appeared in new areas, patients contacted the investigator to determine if an unscheduled additional visit was needed.

### Assessments

- Efficacy endpoints included in this analysis were mean percentage reductions from baseline in Eczema Area and Severity Index (EASI) subscores by body region (head/neck, trunk, upper limbs, lower limbs) and signs of AD (induration/papulation/edema, erythema, excoriations, lichenification) at Weeks 2, 4, and 8

### Statistical Analyses

- All analyses were conducted using the pooled data from both studies
- Reductions from baseline in EASI scores and subscores were analyzed with a mixed-effect model with repeated measures

# Results

## Patients

- A total of 1249 patients (median age, 32 years) were randomized, and 1208 were included in the efficacy-evaluable population and in this analysis
- Distribution of baseline demographics and clinical characteristics was similar across treatment groups (**Table 1**)

## Efficacy

- Significant improvements with either strength of ruxolitinib cream vs vehicle were noted as early as 2 weeks in the head/neck (**Figure 2A**), trunk (**Figure 2B**), upper limbs (**Figure 2C**), and lower limbs (**Figure 2D**)

**Table 1. Demographics and Baseline Clinical Characteristics**

Characteristic	Vehicle (n=244)	0.75% RUX Cream (n=483)	1.5% RUX Cream (n=481)	Total (N=1208)
Age, median (range), y	34 (12–82)	34 (12–85)	31 (12–85)	32 (12–85)
Female, n (%)	154 (63.1)	292 (60.5)	293 (60.9)	739 (61.2)
Race, n (%)				
White	164 (67.2)	330 (68.3)	337 (70.1)	831 (68.8)
Black	61 (25.0)	118 (24.4)	113 (23.5)	292 (24.2)
Asian	10 (4.1)	16 (3.3)	20 (4.2)	46 (3.8)
Other*	9 (3.7)	19 (3.9)	11 (2.3)	39 (3.2)
Region, n (%)				
North America	172 (70.5)	342 (70.8)	341 (70.9)	855 (70.8)
Europe	72 (29.5)	141 (29.2)	140 (29.1)	353 (29.2)
BSA, mean (SD), %	9.5 (5.4)	9.7 (5.2)	9.4 (5.2)	9.6 (5.2)
EASI, mean (SD)	7.8 (4.8)	8.1 (4.9)	7.8 (4.8)	7.9 (4.9)
IGA, n (%)				
2	64 (26.2)	125 (25.9)	123 (25.6)	312 (25.8)
3	180 (73.8)	358 (74.1)	358 (74.4)	896 (74.2)
Itch NRS score, mean (SD)	5.2 (2.5)	5.1 (2.4)	5.1 (2.5)	5.1 (2.4)
Duration of disease, median (range), y	16.5 (0.8–79.1)	14.8 (0.1–68.8)	15.9 (0–69.2)	15.3 (0–79.1)
Facial involvement, n (%)†	93 (38.1)	190 (39.3)	193 (40.1)	476 (39.4)
Number of flares in last 12 mo, mean (SD)†	7.3 (26.0)	5.1 (6.7)	5.8 (17.9)	5.8 (16.8)

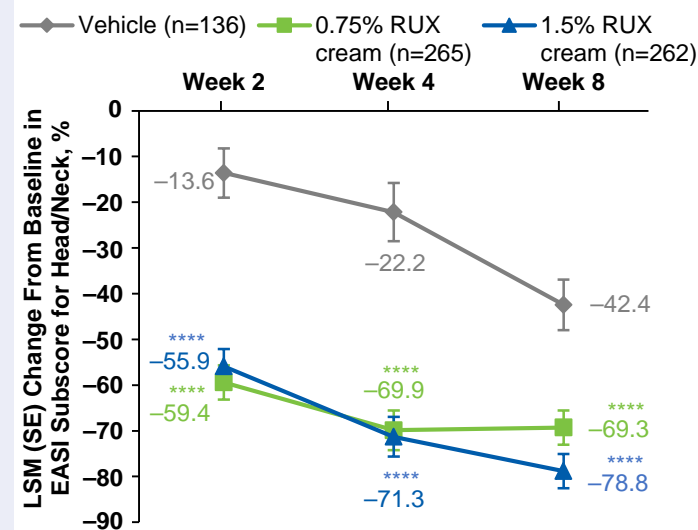
BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NRS, numerical rating scale; RUX, ruxolitinib.

\* Includes American Indian/Alaska native, native Hawaiian/Pacific Islander, and "other."

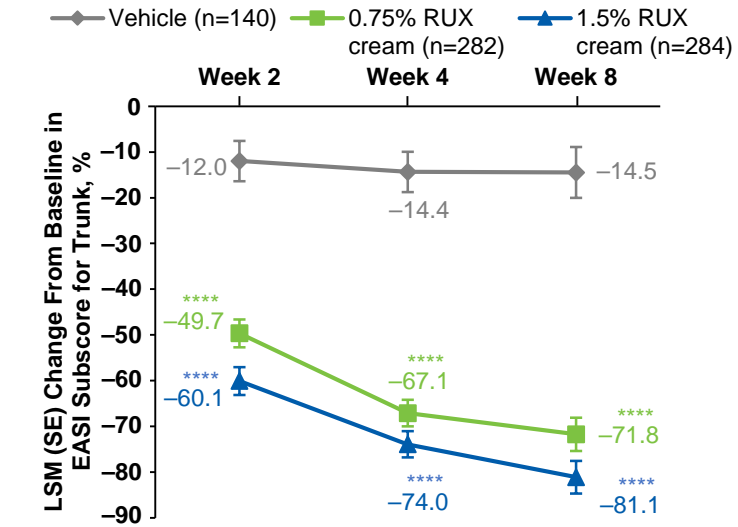
† Patient reported.

**Figure 2. Least Squares Mean Percentage Change From Baseline in Total EASI Anatomic Region Subscores for (A) Head/Neck, (B) Trunk, (C) Upper Limbs, and (D) Lower Limbs in Patients Applying 0.75% or 1.5% Ruxolitinib Cream vs Vehicle**

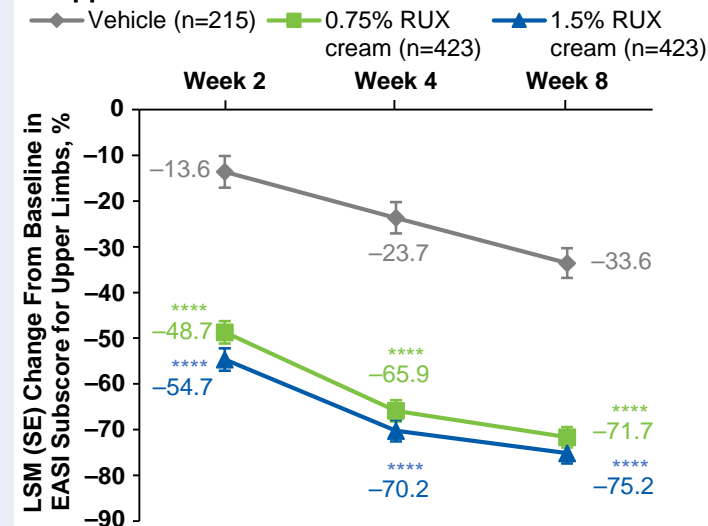
### A. Head/Neck



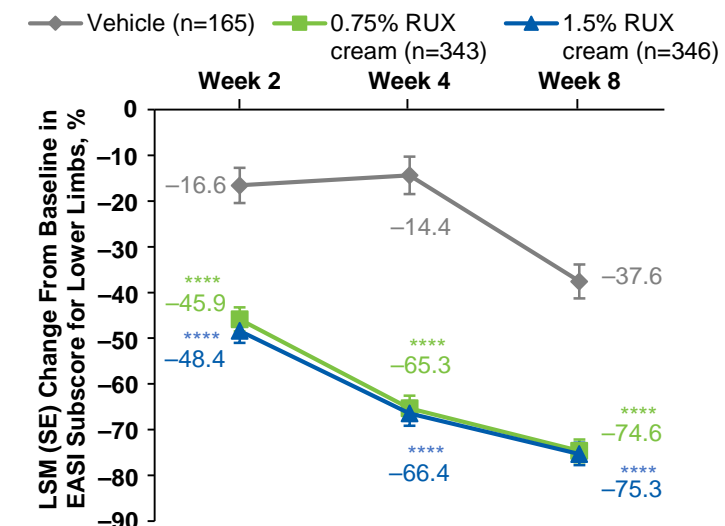
### B. Trunk



### C. Upper Limbs



### D. Lower Limbs



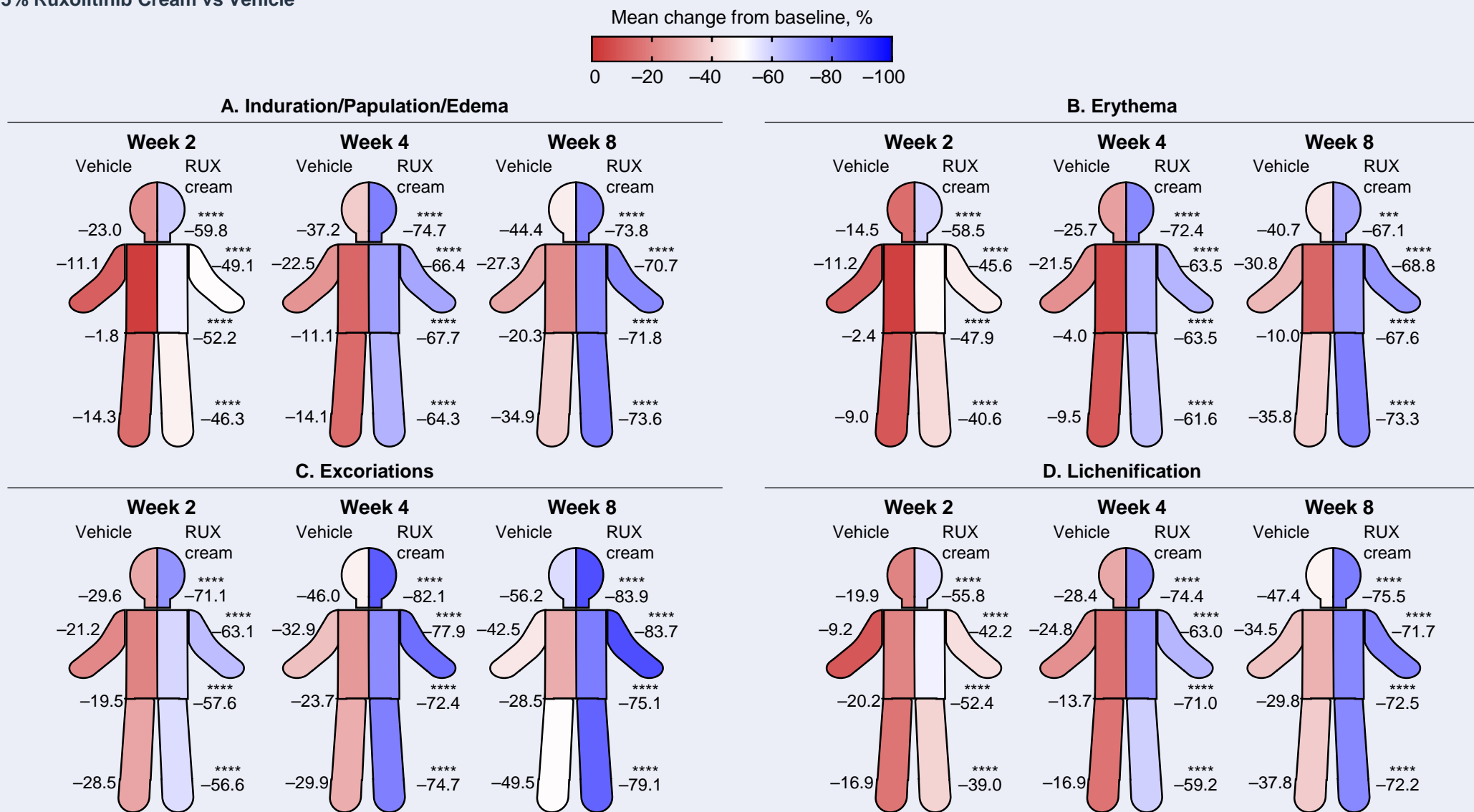
EASI, Eczema Area and Severity Index; LSM, least squares mean; RUX, ruxolitinib.

\*\*\*\*  $P < 0.0001$  vs vehicle.

## Results

- Within each anatomic region, EASI subscores for each AD sign were also significantly improved among patients who applied 0.75% ruxolitinib cream vs vehicle as early as Week 2 (**Figure 3**)

**Figure 3. Least Squares Mean Improvements in EASI Anatomic Region Subscores for (A) Induration/Papulation/Edema, (B) Erythema, (C) Excoriations, and (D) Lichenification in Patients Applying 0.75% Ruxolitinib Cream vs Vehicle**



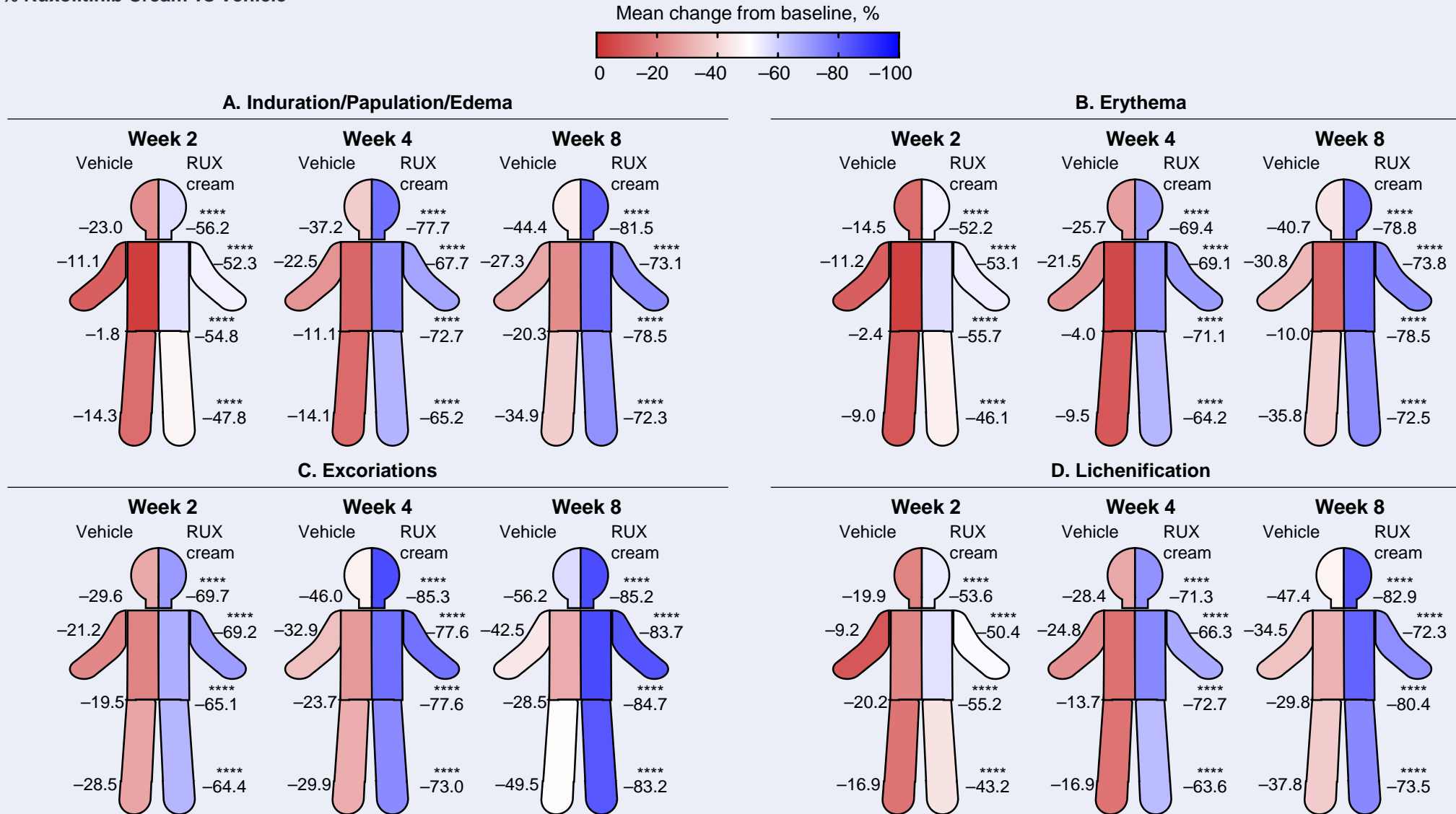
EASI, Eczema Area and Severity Index; RUX, ruxolitinib.  
Data are shown for head/neck, trunk, upper limbs, and lower limbs regions.

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

## Results

- Within each anatomic region, EASI subscores for each AD sign were also significantly improved among patients who applied 1.5% ruxolitinib cream vs vehicle as early as Week 2 (**Figure 4**)

**Figure 4. Least Squares Mean Improvements in EASI Anatomic Region Subscores for (A) Induration/Papulation/Edema, (B) Erythema, (C) Excoriations, and (D) Lichenification in Patients Applying 1.5% Ruxolitinib Cream vs Vehicle**



EASI, Eczema Area and Severity Index; RUX, ruxolitinib.  
Data are shown for head/neck, trunk, upper limbs, and lower limbs regions.  
\*\*\*\*  $P < 0.0001$  vs vehicle.

## Results

### Safety

- Ruxolitinib cream was well tolerated with a favorable safety profile in adolescents and adults, with a low incidence of application site reactions<sup>5</sup>
- During the vehicle-controlled period, treatment-emergent adverse events (TEAEs) were reported by 145/500 (29.0%), 132/499 (26.5%), and 83/250 (33.2%) patients in the 0.75% ruxolitinib cream, 1.5% ruxolitinib cream, and vehicle groups, respectively<sup>5</sup>
  - The most common TEAEs in the ruxolitinib cream groups (0.75% and 1.5%) were nasopharyngitis (3.0% and 2.6%; vehicle, 0.8%) and upper respiratory tract infection (1.4% and 2.4%; vehicle, 2.0%)
- Regardless of lesion location, ruxolitinib cream was well tolerated<sup>5</sup>

### Disclosures

ELS is an investigator for AbbVie, Eli Lilly, Galderma, Kyowa Hakko Kirin, LEO Pharma, Merck, Pfizer, and Regeneron and is a consultant with honorarium for AbbVie, Eli Lilly, Forte, Galderma, Incyte Corporation, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and Valeant. RB has served as an advisory board member, consultant, speaker and/or investigator and received honoraria and/or grants from AbbVie, Arcutis, Arena Pharma, Aristeia, Asana BioSciences, Bellus Health, Bluefin Biomedicine, Boehringer Ingelheim, CARA, Dermavant, Eli Lilly, EMD Serono, Evidera, Galderma, GlaxoSmithKline, Incyte Corporation, Inmagene Bio, Kiniksa, Kyowa Kirin, LEO Pharma, Novan, Pfizer, Ralexar, RAPT Therapeutics, Regeneron, Respivant, Sanofi-Genzyme, Sienna, Target RWE, and Vyne Therapeutics and is an employee and shareholder of Innovaderm Research. LFSG has served as an investigator, advisor, and/or speaker for AbbVie, Arcutis, Bristol Myers Squibb, Dermavant, Eli Lilly, Incyte Corporation, Ortho Derm, Pfizer, Regeneron, and Sanofi. ZCCF has served as a consultant for the Asthma and Allergy Foundation of America, the National Eczema Association, AbbVie, Beiersdorf, Incyte Corporation, and Pfizer; has received research grants from Eli Lilly, LEO Pharma, Regeneron, Sanofi, Tioga, and Vanda for work related to atopic dermatitis and Menlo Therapeutics for work related to prurigo nodularis; and has received honoraria for continuing medical education work in atopic dermatitis sponsored by education grants from Pfizer and Regeneron/Sanofi. MEV is an employee and shareholder of Incyte Corporation. JIS has received honoraria for advisory board, speaker, and consultant services from AbbVie, Asana BioSciences, Bluefin, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Glenmark, Incyte Corporation, Kiniksa, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Realm, Regeneron, and Sanofi; and research grants for investigator services from Galderma and GlaxoSmithKline.

## Conclusions

- **Significant improvements in induration/papulation/edema, erythema, excoriations, and lichenification across anatomic regions were observed with 0.75% and 1.5% ruxolitinib cream vs vehicle as early as Week 2 and continued to improve through Week 8**
- **Ruxolitinib cream was well tolerated regardless of lesion location<sup>5</sup>**

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