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# Efficacy of Ruxolitinib Cream in Adults and Adolescents With Atopic Comorbidities

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## Background

- Patients with atopic dermatitis (AD), a highly pruritic inflammatory skin disease, may also experience comorbidities, including the atopic march[1,2]
- Development of atopic comorbidities, such as food allergy, asthma, and allergic rhinitis, indicate a type II immune bias[3]
- In two phase 3 AD studies of identical design (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651]), ruxolitinib cream, a Janus kinase (JAK) 1/JAK2 inhibitor, demonstrated anti-inflammatory activity with rapid and sustained antipruritic action vs vehicle and was well tolerated[4]

## Objective

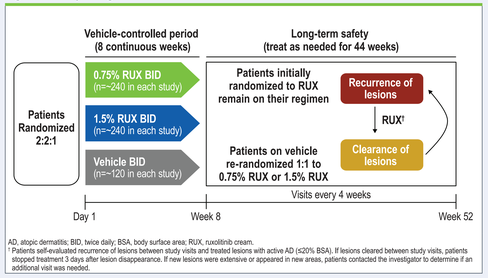
- To describe efficacy outcomes in patients with or without atopic comorbidities from a pooled analysis of two phase 3 studies

## Methods

### *Study Design and Patients*

- Eligible patients were aged ≥12 years with AD for ≥2 years and had an Investigator's Global Assessment (IGA) 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, 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 1 of 2 ruxolitinib cream strength regimens (0.75% twice daily [BID] or 1.5% BID) or vehicle cream BID for 8 weeks of double-blind treatment
  - Patients on ruxolitinib cream subsequently continued treatment for 44 weeks; patients initially randomized to vehicle were re-randomized 1:1 (blinded) to either ruxolitinib cream regimen

**Figure 1. Study Design**




AD, atopic dermatitis; BID, twice daily; BSA, body surface area; RUX, ruxolitinib cream.
† 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 additional visit was needed.

### *Assessments*

- In this analysis, atopic comorbidities included respiratory or eye disorders (allergic conjunctivitis, allergic rhinitis, asthma, bronchospasm, dyspnea exertional, exercise-induced asthma, perennial rhinitis), milk allergy, other allergies (allergy to animals, allergy to plants, mite allergy [house dust], multiple allergies, seasonal allergy), food intolerance, and cow's milk intolerance/lactose intolerance
- Efficacy by subpopulations of patients with or without atopic comorbidities at Weeks 2, 4, and 8 was assessed by the proportion of patients achieving IGA-treatment success (IGA-TS; IGA of 0/1 and ≥2-grade improvement vs baseline); ≥50%, ≥75%, and ≥90% improvement in Eczema Area and Severity Index (EASI-50, -75, and -90, respectively) vs baseline; and a ≥4-point improvement in itch numerical rating scale score (NRS4)
- Mean change from baseline in daily itch NRS score was also assessed in patients with and without atopic comorbidities

### *Statistical Analyses*

- All analyses were conducted using the pooled data from both studies
- All endpoints were summarized descriptively

## Results

### *Patients*

- A total of 1249 patients (median age, 32 years) were randomized
- Distribution of baseline demographics and clinical characteristics was similar across treatment groups (**Table 1**)
- Of 1208 efficacy-evaluable patients (vehicle, n=244; 0.75% ruxolitinib cream, n=483; 1.5% ruxolitinib cream, n=481), 51.1% of patients had atopic comorbidities at baseline

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

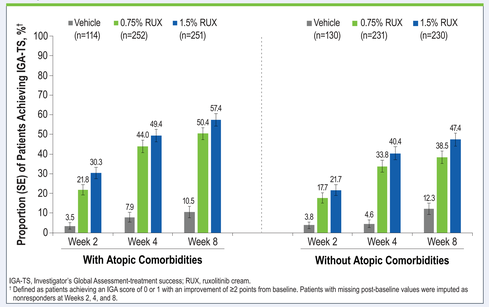
| Characteristic | Vehicle (n=250) | 0.75% RUX (n=500) | 1.5% RUX (n=499) | Total (N=1249) |
|---|---|---|---|---|
| Age, median (range), y | 34.0 (12–82) | 33.0 (12–85) | 31.0 (12–85) | 32.0 (12–85) |
| Female, n (%) | 159 (63.6) | 304 (60.8) | 308 (61.7) | 771 (61.7) |
| Race, n (%) | | | | |
| White | 170 (68.0) | 345 (69.0) | 355 (71.1) | 870 (69.7) |
| Black | 61 (24.4) | 118 (23.6) | 113 (22.6) | 292 (23.4) |
| Asian | 10 (4.0) | 16 (3.2) | 20 (4.0) | 46 (3.7) |
| Other | 9 (3.6) | 21 (4.2) | 11 (2.2) | 41 (3.3) |
| 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) |
| BSA, mean (SD), % | 9.6 (5.5) | 10.0 (5.3) | 9.6 (5.3) | 9.8 (5.4) |
| EASI, mean (SD) | 7.8 (4.8) | 8.1 (4.9) | 7.8 (4.8) | 8.0 (4.8) |
| 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) |
| ≥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 (16.5) |
| Milk allergy, n (%) | 5 (2.0) | 1 (0.2) | 5 (1.0) | 11 (0.9) |
| Food intolerance, n (%) | 0 | 2 (0.4) | 3 (0.6) | 5 (0.4) |
| Lactose intolerance, n (%) | 2 (0.8) | 5 (1.0) | 8 (1.6) | 15 (1.2) |
| Cow's milk intolerance, n (%) | 0 | 1 (0.2) | 1 (0.2) | 2 (0.2) |
| Respiratory/eye disorders, n (%) | | | | |
| Asthma | 61 (24.4) | 127 (25.4) | 136 (27.3) | 324 (25.9) |
| Allergic rhinitis | 25 (10.0) | 53 (10.6) | 45 (9.0) | 123 (9.8) |
| Allergic conjunctivitis | 7 (2.8) | 11 (2.2) | 12 (2.4) | 30 (2.4) |
| Perennial rhinitis | 4 (1.6) | 4 (0.8) | 11 (2.2) | 19 (1.5) |
| Bronchospasm | 0 | 0 | 3 (0.6) | 3 (0.2) |
| Exercise-induced asthma | 1 (0.4) | 0 | 1 (0.2) | 2 (0.2) |
| Dyspnea exertional | 0 | 1 (0.2) | 0 | 1 (0.1) |
| Other allergies, n (%) | | | | |
| Seasonal allergy | 69 (27.6) | 135 (27.0) | 135 (27.1) | 339 (27.1) |
| Mite allergy (house dust) | 25 (10.0) | 46 (9.2) | 55 (11.0) | 126 (10.1) |
| Allergy to animal | 25 (10.0) | 48 (9.6) | 40 (8.0) | 113 (9.0) |
| Allergy to plants | 9 (3.6) | 9 (1.8) | 12 (2.4) | 30 (2.4) |
| Multiple allergies | 4 (1.6) | 15 (3.0) | 6 (1.2) | 25 (2.0) |

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

### *Efficacy*

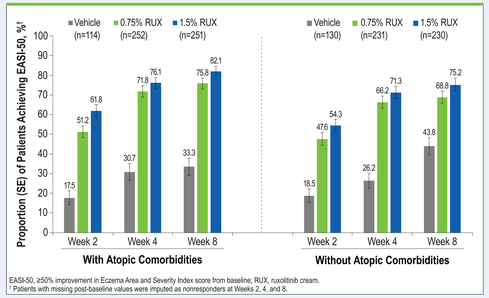
- Substantially more patients with atopic comorbidities who applied either strength of ruxolitinib cream achieved IGA-TS (**Figure 2**), EASI-50 (**Figure 3**), EASI-75 (**Figure 4**), EASI-90 (**Figure 5**), and itch NRS4 (**Figure 6**) vs vehicle at Week 8
  - Similar results were observed among patients without comorbidities, although patients with atopic comorbidities appeared to have greater efficacy responses to ruxolitinib cream

**Figure 2. Proportion of Patients Achieving IGA-TS by the Presence or Absence of Atopic Comorbidities**



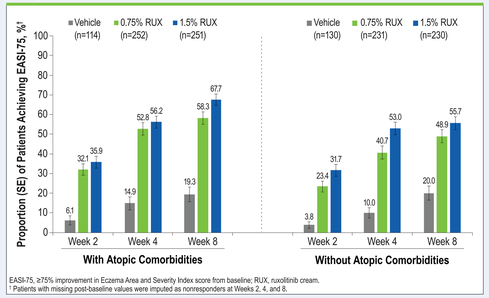

IGA-TS, Investigator's Global Assessment-treatment success; RUX, ruxolitinib cream.
† Defined as patients achieving an IGA score of 0 or 1 with an improvement of ≥2 points from baseline. Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

**Figure 3. Proportion of Patients Achieving EASI-50 by the Presence or Absence of Atopic Comorbidities**



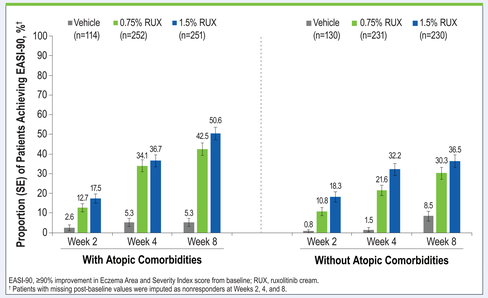

EASI-50, ≥50% improvement in Eczema Area and Severity Index score from baseline; RUX, ruxolitinib cream.
† Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

**Figure 4. Proportion of Patients Achieving EASI-75 by the Presence or Absence of Atopic Comorbidities**



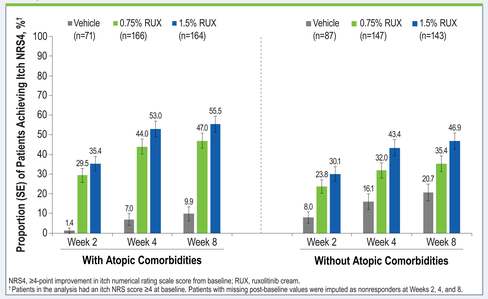

EASI-75, ≥75% improvement in Eczema Area and Severity Index score from baseline; RUX, ruxolitinib cream.
† Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

**Figure 5. Proportion of Patients Achieving EASI-90 by the Presence or Absence of Atopic Comorbidities**




EASI-90, ≥90% improvement in Eczema Area and Severity Index score from baseline; RUX, ruxolitinib cream.
† Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

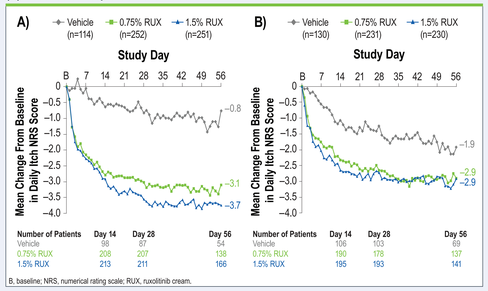
**Figure 6. Proportion of Patients Achieving Itch NRS4 by the Presence or Absence of Atopic Comorbidities**




NRS4, ≥4-point improvement in itch numerical rating scale score from baseline; RUX, ruxolitinib cream.
† Patients in the analysis had an itch NRS score ≥4 at baseline. Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

- Among patients with or without atopic comorbidities who applied ruxolitinib cream, considerably greater itch reduction was observed within 12 hours of the first application vs vehicle; further itch reductions were reported at later time points and were sustained through Week 8 (**Figure 7**)

**Figure 7. Change From Baseline in Daily Itch NRS Score by the (A) Presence or (B) Absence of Atopic Comorbidities**




B, baseline; NRS, numerical rating scale; RUX, ruxolitinib cream.

### *Safety*

- Ruxolitinib cream was well tolerated with an adverse event (AE) profile similar to vehicle[4]; no serious AEs were related to ruxolitinib cream

## Conclusions

- **Treatment with ruxolitinib cream resulted in markedly improved AD signs and symptoms regardless of atopic comorbidities**
  - **Although not statistically tested, all efficacy endpoints were achieved by a greater proportion of patients with atopic comorbidities than without atopic comorbidities**
  - **Patients with a type II immune bias (ie, those with atopic comorbidities) may respond differently than patients with less type II involvement**
- **Considerably greater itch reduction with ruxolitinib cream vs vehicle was observed within 12 hours among patients with or without atopic comorbidities**

### 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 Bio, Galderma, Incyte Corporation, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and Valeant. ML is an investigator for AbbVie, Arcutis, AstraZeneca, Bausch Health, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly, Incyte Corporation, Janssen, Kiniksa Pharmaceuticals, LEO Pharma, Pfizer, RAPT Therapeutics, Reistone Biopharma, Regeneron, and UCB Biopharma. KKB has served as an investigator for Incyte Corporation, NIH ADRN, and Regeneron. MEK, MEV, and KS are employees and shareholders of Incyte Corporation. DT has served as an investigator for AbbVie, Avillion, Amgen, Arcutis, Astellas, Astion, Boehringer Ingelheim, Celgene, Dermira, DS BioPharma, Dow Pharmaceuticals, Eli Lilly, F. Hoffmann-La Roche Ltd, Galderma, GlaxoSmithKline, Incyte Corporation, Isotechnika, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, and UCB Biopharma.

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