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Ruxolitinib Cream Demonstrates Maintenance of Disease and Symptom Control With As-Needed Use in Adults and Adolescents With Atopic Dermatitis: Pooled Analysis From the Long-Term Safety Periods of Two Phase 3 Studies

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Introduction

- Atopic dermatitis (AD) is a highly pruritic inflammatory skin disease[1]
- Quality of life in patients with AD can be significantly reduced by itch and sleep disturbances[2]
- Ruxolitinib cream is a topical formulation of ruxolitinib, a selective inhibitor of Janus kinase (JAK) 1 and JAK2 , approved for the treatment of AD in patients 12 years of age and older[3,4]
- 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 and substantial improvement in itch and sleep vs vehicle, and was well tolerated during the 8-week vehicle-controlled (VC) period in patients with AD[5,6]
  - During the 44-week long-term safety (LTS) period, ruxolitinib cream was well tolerated and demonstrated effective disease and symptom control (ie, itch and sleep disturbance) with as-needed use[6,7]

Objective

- To evaluate long-term maintenance of disease and symptom control in adolescent and adult patients with AD applying ruxolitinib cream as needed using pooled data from the LTS periods of two phase 3 studies

Methods

Patients and Study Design

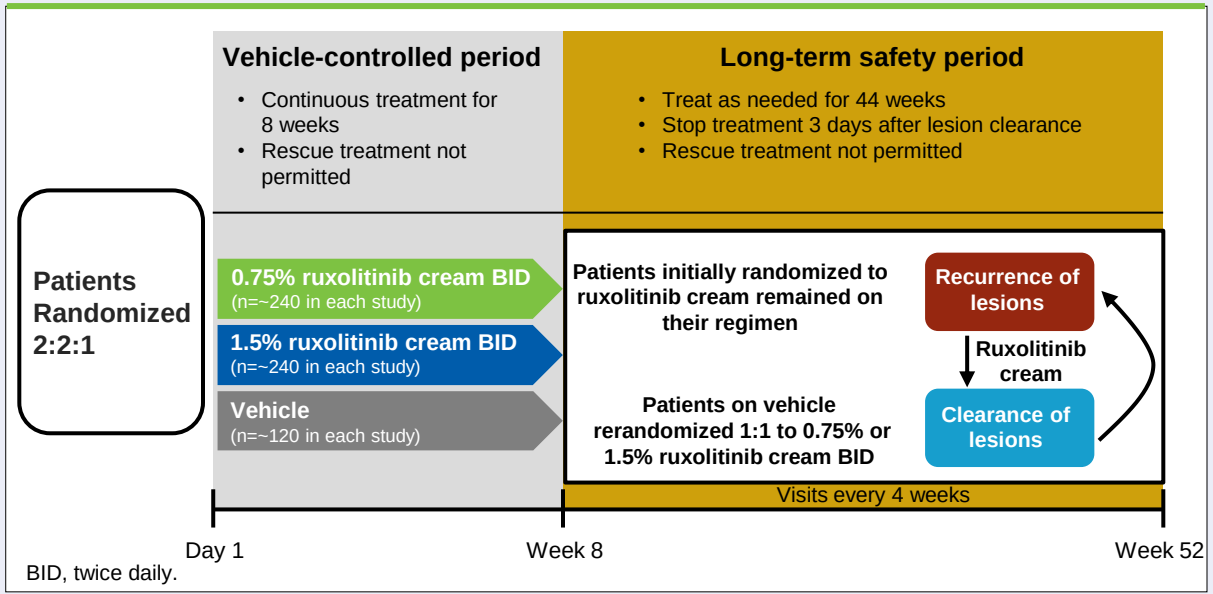
- Eligible patients were aged ≥12 years with AD for ≥2 years and had an Investigator's Global Assessment (IGA) score of 2 or 3 and 3%–20% affected body surface area, excluding scalp
- TRuE-AD1 and TRuE-AD2 had identical study designs (**Figure 1**)
  - In both studies, patients were randomized (2:2:1) 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 continuous treatment (VC period); patients were instructed to continue treating lesions even if they improved
  - Patients initially randomized to ruxolitinib cream subsequently remained on their regimen for the 44-week LTS period (as-needed treatment); patients initially randomized to vehicle were rerandomized 1:1 (blinded) to either ruxolitinib cream strength
    - During the LTS period, patients were instructed to treat skin areas with active AD only and to stop treatment 3 days after clearance of lesions; patients were to restart treatment with ruxolitinib cream at the first sign of recurrence
  - No concomitant or rescue treatments were permitted at any time during the study
  - Only patients who applied ruxolitinib cream since Day 1 were included in the analysis

Methods *(cont.)*

Assessments

- The percentage of patients who achieved IGA score of 0 or 1 (clear or almost clear skin) or score ≥2 (2, mild; 3, moderate; 4, severe) was assessed at baseline and each visit (every 4 weeks) during the LTS period
  - Mean percentage of visits with patients reporting IGA 0 or 1 was reported for patients with ≥1 visit in the LTS period, with an additional sensitivity analysis in patients with ≥2 visits in the LTS period

Figure 1. Study Design



BID, twice daily.

- Itch was assessed by the percentage of patients reporting 0, 1–2, or ≥3 days of itch per question 1 of the Patient-Oriented Eczema Measure (POEM Q1)[8] at Weeks 8, 12, 24, and 52
  - Patients reported the number of days of itchy skin due to eczema in the past week
- Sleep disturbance was assessed by the percentage of patients reporting 0, 1–2, or ≥3 nights of disturbed sleep per question 2 of the POEM (POEM Q2)[8] at Weeks 8, 12, 24, and 52
  - Patients reported the number of nights of disturbed sleep due to eczema in the past week
- Safety and tolerability assessments included frequency of treatment-emergent adverse events (AEs), treatment-related AEs, serious AEs, and AEs leading to treatment discontinuation

Statistical Analyses

- Data were summarized using descriptive statistics, reported as observed
- All patients who applied ≥1 dose of study drug were included in the safety analysis

Results

Patients

- Of 1249 randomized patients, 1072 (85.8%) continued into the LTS period; 837 (67.0%) who applied ruxolitinib cream since Day 1 were evaluated for disease and symptom control in the LTS period (0.75% ruxolitinib cream, n=409; 1.5% ruxolitinib cream, n=428)
  - A majority (≈75%) completed the LTS period, with 11 (1.3%) discontinuing due to AE and 15 (1.8%) discontinuing due to lack of efficacy
- Baseline demographics and clinical characteristics are summarized in **Table 1** and are similar to those in the overall study population

Results *(cont.)*

Table 1. Patient Demographics and Baseline Clinical Characteristics Among Patients Who Applied Ruxolitinib Cream Since Day 1 and Continued Into the LTS Period

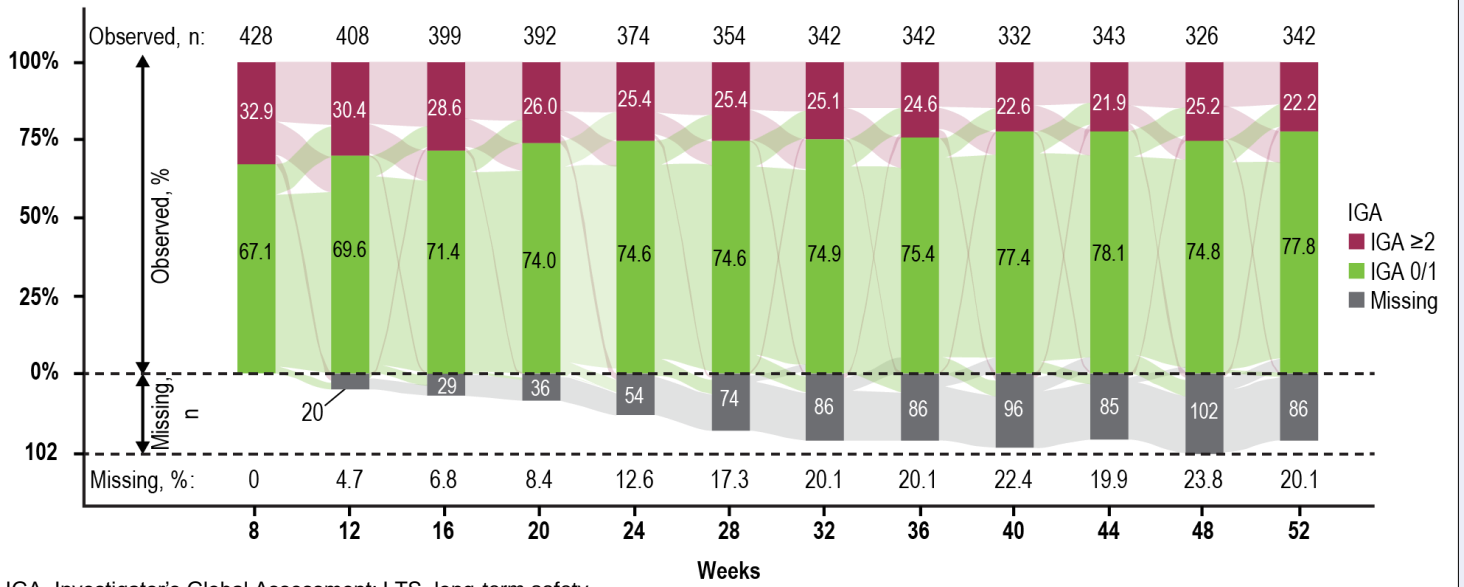
Characteristic	0.75% Ruxolitinib cream (n=409)	1.5% Ruxolitinib cream (n=428)
Age, median (range) y	36.0 (12–85)	31.0 (12–85)
12 – <18 y, n (%)	89 (21.8)	77 (18.0)
Female, n (%)	252 (61.6)	263 (61.4)
Race, n (%)		
White	291 (71.1)	302 (70.6)
Black	91 (22.2)	97 (22.7)
Asian	15 (3.7)	19 (4.4)
Other	12 (2.9)	10 (2.3)
BSA affected, mean (SD), %	9.9 (5.3)	9.6 (5.2)
EASI score, mean (SD)	8.2 (5.1)	8.0 (4.8)
IGA score, n (%)		
2	100 (24.4)	100 (23.4)
3	309 (75.6)	328 (76.6)
Itch NRS score, mean (SD)	5.1 (2.4)	5.2 (2.4)
Duration of disease, median (range), y	14.2 (0.1–68.6)	15.5 (0–69.2)
Facial involvement, n (%)*	172 (42.1)	181 (42.3)
Number of flares in last 12 mo, mean (SD)*	5.1 (7.0)	5.1 (7.2)

BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; LTS, long-term safety; NRS, numerical rating scale.
* Patient reported.

Maintenance of Disease Control in the LTS Period

- The mean (SD) cumulative number of days with no treatment due to lesion clearance was 116.5 (85.9) and 133.8 (89.8) days with 0.75% ruxolitinib cream and 1.5% ruxolitinib cream, respectively
  - The median (range) cumulative time with no treatment due to lesion clearance as a proportion of the LTS duration (approximately 44 weeks) was 38% (1%–99%) and 44% (1%–97%), with 0.75% ruxolitinib cream and 1.5% ruxolitinib cream, respectively
- Based on observed data, the percentage of patients who applied 0.75/1.5% ruxolitinib cream and achieved IGA 0/1 was 61.8%/67.1% at Week 8 and 76.8%/77.8% at Week 52
- With each consecutive visit, the majority of patients in either treatment group maintained IGA 0/1 (**Figure 2**)
  - 80%–90% of patients maintained or improved their response between subsequent visits

Figure 2. Change in IGA Scores with As-Needed Treatment with 1.5% Ruxolitinib Cream During the LTS Period



IGA, Investigator's Global Assessment; LTS, long-term safety.
All patients were IGA 2/3 at baseline.

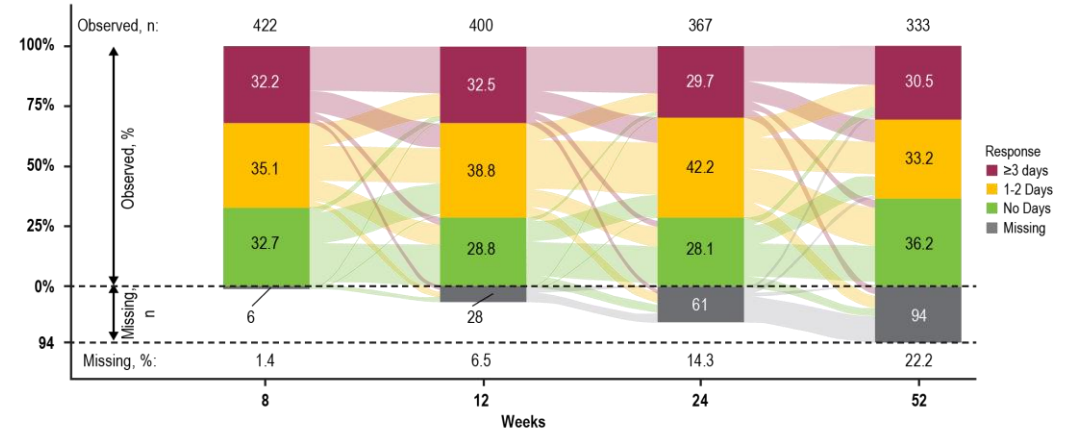
Results *(cont.)*

- Patients applying 0.75%/1.5% ruxolitinib cream achieved IGA 0/1 for a mean (95% CI) of 68.3% (65.0%, 71.6%; n=396)/73.6% (70.6%, 76.7%; n=414) of all visits, respectively, among those with ≥1 visit in the LTS period, and 69.1% (65.9%, 72.4%; n=384)/73.5% (70.4%, 76.5%; n=400) among those with ≥2 visits in the LTS period

Maintenance of Symptom Control in the LTS Period

- Based on observed data, itch for 0 days in the past week was reported in 27.7%/32.7% of patients applying 0.75%/1.5% ruxolitinib cream at Week 8 and in 28.0%/36.2% at Week 52
  - Itch for 1–2 days in the past week was reported in 33.2%/35.1% at Week 8 and in 37.9%/33.2% at Week 52

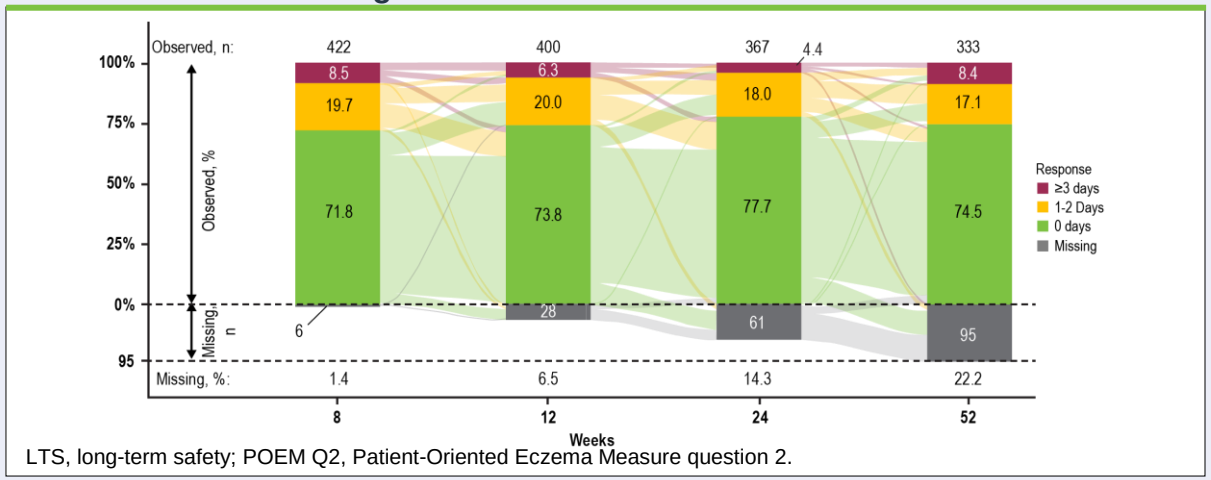
Figure 3. Change in POEM Q1 Scores with As-Needed Treatment with 1.5% Ruxolitinib Cream During the LTS Period



LTS, long-term safety; POEM Q1, Patient-Oriented Eczema Measure question 1.

- The majority of patients maintained or demonstrated improvements in symptom control of itch (ie, reporting itch for 0 or 1–2 days in the past week) between consecutive assessments (**Figure 3**)
- Based on observed data, sleep disturbance for 0 days in the past week was reported in 64.9%/71.8% of patients applying 0.75%/1.5% ruxolitinib cream at Week 8 and in 74.5%/74.5% at Week 52
  - Sleep disturbance for 1–2 days in the past week was reported in 23.2%/19.7% at Week 8 and in 15.9%/17.1% at Week 52
- The majority of patients maintained or demonstrated improvements in sleep (ie, reporting sleep disturbance for 0 or 1–2 days in the past week) between consecutive assessments (**Figure 4**)

Figure 4. Change in POEM Q2 Scores with As-Needed Treatment with 1.5% Ruxolitinib Cream During the LTS Period



LTS, long-term safety; POEM Q2, Patient-Oriented Eczema Measure question 2.

Safety

- Ruxolitinib cream was well tolerated during the 52-week study, confirming 8-week VC data[7]

Conclusions

- **Ruxolitinib cream demonstrated maintenance of disease and symptom control with as-needed use over a 44-week period in adults and adolescents with AD**

Disclosures

AB has served as a speaker (received honoraria) for AbbVie, Bristol Myers Squibb, Eli Lilly and Company, Pfizer, Regeneron, and Sanofi; served as a scientific advisor (received honoraria) for AbbVie, Abcentra, Aclaris, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Dermavant, EcoR1, Eli Lilly and Company, Escient, Evelo, Evommune, Forte, Galderma, HighlightII Pharma, Incyte Corporation, InnoventBio, Janssen, Landos, Leo, Merck, Novartis, Pfizer, Rani, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, TLL Pharmaceutical, TrialSpark, UCB Pharma, Union, Vibliome, and Xencor; and has acted as a clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Concert, Dermavant, Eli Lilly and Company, Evelo, Evommune, Galderma, Incyte, Janssen, Leo, Merck, Novartis, Pfizer, Regeneron, Sun Pharma, and UCB Pharma. LK has served as an investigator, consultant, or speaker for AbbVie, Amgen, Anaptys, Arcutis, Dermavant, Eli Lilly, Glenmark, Incyte, Kamedis, LEO Pharma, L'Oreal, Menlo Therapeutics, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and Taro. 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, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and Valeant. PL reports research grants/funding from AOBiome, Regeneron/Sanofi Genzyme, and AbbVie; is on the speakers bureau for Regeneron/Sanofi Genzyme, Pfizer, Incyte, Hyphens Pharma, LEO, Eli Lilly, Galderma, and L'Oreal; reports consulting/advisory boards for Almirall, ASLAN Pharmaceuticals, Bristol Myers, Dermavant, Regeneron/Sanofi Genzyme, Merck, Pfizer, LEO Pharmaceuticals, AbbVie, Eli Lilly, Micreos (stock options), L'Oreal, Pierre-Fabre, Johnson & Johnson, Unilever, Menlo Therapeutics, Theraplex, IntraDerm, Exeltis, AOBiome, Realm Therapeutics, Altus Labs (stock options), Galderma, Arbonne, Amyris, Bodewell, and Burt's Bees; has a patent pending for a Theraplex product with royalties paid; and is a Board member of the National Eczema Association. DS, HK, HR, DP, and JG are employees and shareholders of Incyte. LFE has served as an investigator, consultant, speaker, or data safety monitoring board member for Amgen, AbbVie, Almirall, Arcutis, Arena, Aslan, Castle, Dermavant, Eli Lilly, Forte Biosciences, Galderma, Incyte, Janssen, LEO Pharma, Novartis, Ortho, Otsuka, Pfizer, Regeneron, and Sanofi Genzyme.

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