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Patient-Reported Outcomes of Ruxolitinib Cream for the Treatment of Atopic Dermatitis: Pooled Results From Two Phase 3 Studies

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Background

- Atopic dermatitis (AD) is a chronic inflammatory skin disease that often negatively impacts quality of life (QoL), with significant physical and psychological impairment compared with people without AD[1-3]
- Janus kinases (JAKs) act downstream of proinflammatory cytokines and itch mediators involved in the pathogenesis of AD[4,5]
- Ruxolitinib cream is a topical selective inhibitor of JAK1 and JAK2 in development for the treatment of AD[6]
- In two phase 3 AD studies of identical design (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651]), ruxolitinib cream demonstrated anti-inflammatory activity with rapid and sustained antipruritic action vs vehicle and was well tolerated[7]

Objective

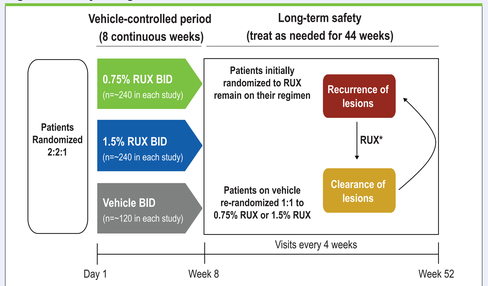
- To describe the efficacy of ruxolitinib cream on patient-reported outcomes (PROs) using pooled data from two phase 3 trials in adolescent and adult patients with AD

Methods

Study Design and Patients

- Eligible patients were aged ≥12 years with AD 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, 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) at the Week 8 study visit 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

- Change from baseline in the Patient-Oriented Eczema Measure (POEM) score and responses by POEM categories were assessed at baseline and Weeks 2, 4, and 8
  - The POEM consists of 7 questions that evaluate how many days the patient has been bothered by various aspects of the disease (itching, sleep disturbance, skin bleeding, weeping/oozing, cracking, flaking, dryness) during the past 7 days, with higher scores indicating more severe skin symptoms (range, 0 [clear] to 28 [very severe])[8]
- Change from baseline in Dermatology Life Quality Index (DLQI) score and Children's DLQI (CDLQI) score as well as responses by DLQI/CDLQI categories were assessed at baseline and Weeks 2, 4, and 8
  - The DLQI is a 10-item questionnaire used to assess various aspects of QoL in a variety of dermatologic conditions,[9] with higher scores indicating greater impairment (range, 0–30)
  - The CDLQI is a 10-item questionnaire for children and adolescents (aged 12–15 years in TRuE-AD1 and TRuE-AD2) evaluating symptoms and feelings, leisure, school, personal relationships, sleep, and treatment[10]
- Change from baseline in AD skin pain numerical rating scale score (NRS) was assessed at Weeks 2, 4, and 8
  - Patients were provided an electronic diary to be completed each evening and were instructed to report their worst level of skin pain during each 24-hour period from 0 (no pain) to 10 (worst imaginable pain)
- Responses by Patient Global Impression of Change (PGIC) categories were assessed at Weeks 2, 4, and 8
  - The PGIC is a self-reported 7-point scale used to measure a patient's perception about overall improvement (very much improved, much improved, minimally improved, no change, minimally worse, much worse, very much worse)[11]

Statistical Analyses

- All analyses were conducted using the pooled data from both studies. No imputation was applied; summary and analyses were based on as-observed data
- The efficacy population consisted of 1208 patients (vehicle, n=244; 0.75% ruxolitinib cream, n=483; 1.5% ruxolitinib cream, n=481)
- Statistical significance was assessed using analysis of covariance

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**)

Table 1. Patient Demographics and Baseline Clinical Characteristics

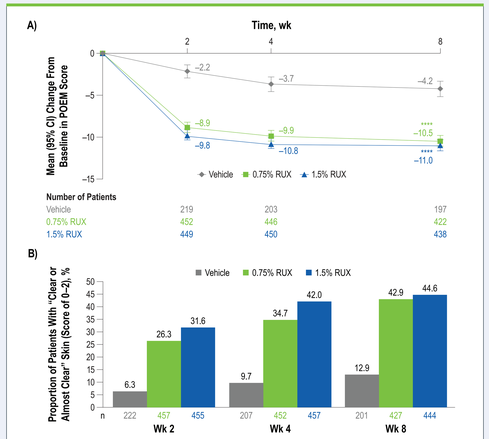
Characteristic	Vehicle (n=250)	0.75% RUX (n=500)	1.5% RUX (n=499)	Total (N=1249)
Age, median (range), y	34.0 (12–82)	33.0 (12–85)	31.0 (12–85)	32.0 (12–85)
Female, n (%)	159 (63.6)	304 (60.8)	308 (61.7)	771 (61.7)
Race, n (%)				
White	170 (68.0)	345 (69.0)	355 (71.1)	870 (69.7)
Black	61 (24.4)	118 (23.6)	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)
Ethnicity, n (%)*				
Hispanic or Latino	38 (15.2)	61 (12.2)	67 (13.4)	166 (13.3)
Not Hispanic or Latino	211 (84.4)	435 (87.0)	428 (85.8)	1074 (86.0)
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)
POEM score, mean (SD)†	15.0 (6.6)	15.5 (6.3)	15.5 (6.3)	NA
DLQI score, mean (SD)†	9.4 (6.4)	9.9 (6.5)	9.5 (6.5)	NA
CDLQI score, mean (SD)†	8.0 (5.8)	7.0 (6.2)	9.0 (6.3)	NA
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)

BSA, body surface area; CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NA, not available; NRS, numerical rating scale; POEM, Patient-Oriented Eczema Measure; RUX, ruxolitinib cream.
* Data missing from 9 patients (vehicle, n=1; 0.75% RUX, n=4; 1.5% RUX, n=4).
† Data from the efficacy-evaluable population.
‡ Patient reported.

Patient-Reported Outcomes

- Patients on ruxolitinib cream reported significant mean change from baseline (ie, improvement) at Week 8 in POEM (–10.5 and –11.0 for 0.75% and 1.5% ruxolitinib creams, respectively) vs vehicle (–4.2; both *P*<0.0001; **Figure 2A**)
- At Weeks 2, 4, and 8, more patients who applied ruxolitinib cream reported "clear or almost clear" skin vs patients who applied vehicle (**Figure 2B**)

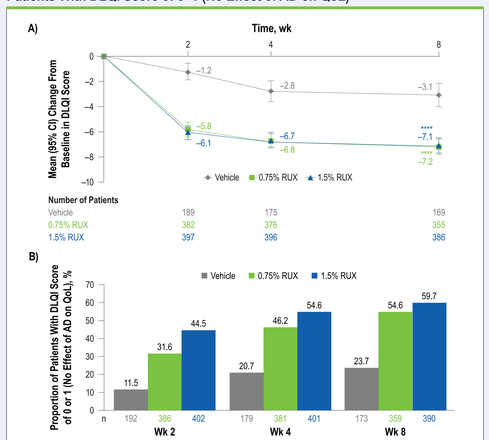
Figure 2. (A) Change From Baseline in POEM and (B) Proportion of Patients With "Clear or Almost Clear" Skin in POEM



POEM, Patient-Oriented Eczema Measure; RUX, ruxolitinib cream.
**** *P*<0.0001 vs vehicle.

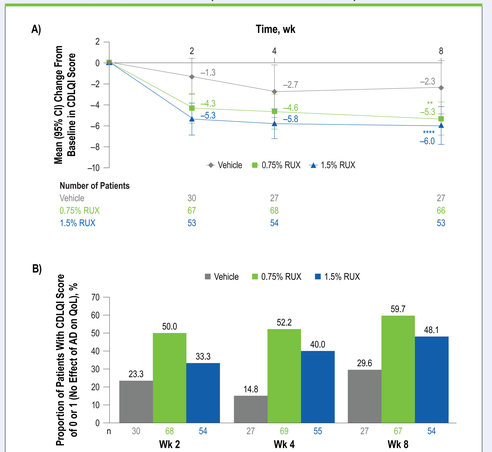
- Patients on ruxolitinib cream reported significant mean change from baseline at Week 8 in DLQI (–7.2 and –7.1 for 0.75% and 1.5% ruxolitinib creams, respectively; vehicle, –3.1; both *P*<0.0001; **Figure 3A**) and CDLQI (–5.3 and –6.0 for 0.75% and 1.5% ruxolitinib creams, respectively; vehicle, –2.3; both *P*<0.01; **Figure 4A**)
- At Weeks 2, 4, and 8, more patients who applied ruxolitinib cream reported no QoL effect from their AD vs patients who applied vehicle (**Figures 3B** and **4B**)

Figure 3. (A) Change From Baseline in DLQI and (B) Proportion of Adult Patients With DLQI Score of 0–1 (No Effect of AD on QoL)



AD, atopic dermatitis; DLQI, Dermatology Life Quality Index; QoL, quality of life; RUX, ruxolitinib cream.
**** *P*<0.0001 vs vehicle.

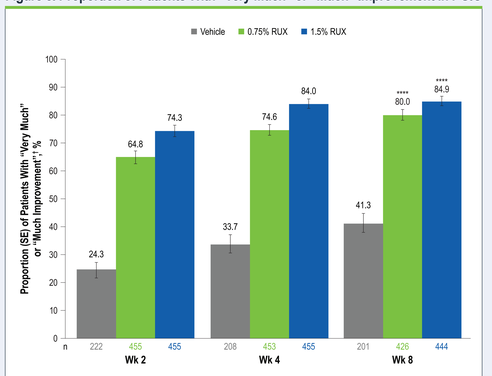
Figure 4. (A) Change From Baseline in CDLQI and (B) Proportion of Adolescent Patients With CDLQI Score of 0–1 (No Effect of AD on QoL)



AD, atopic dermatitis; CDLQI, Children's Dermatology Life Quality Index; QoL, quality of life; RUX, ruxolitinib cream.
** *P*<0.01 vs vehicle.
**** *P*<0.0001 vs vehicle.

- Significantly more patients who applied ruxolitinib cream reported "very much" or "much" improvement in their PGIC at Week 8 (80.0% and 84.9% for 0.75% and 1.5% ruxolitinib creams, respectively) vs vehicle (41.3%; both *P*<0.0001; **Figure 5**)

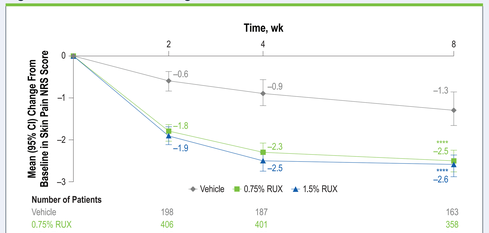
Figure 5. Proportion of Patients With "Very Much" or "Much" Improvement in PGIC



PGIC, Patient Global Impression of Change; RUX, ruxolitinib cream.
**** *P*<0.0001 vs vehicle.
† PGIC score of 1 or 2.

- Significantly greater reductions in skin pain NRS score were observed within 12 hours of the first application of ruxolitinib cream (–0.34 and –0.28 for 0.75% and 1.5% ruxolitinib creams, respectively) vs vehicle (–0.04; both *P*<0.05), with further reductions at Week 8 (**Figure 6**)

Figure 6. Skin Pain NRS Change From Baseline



NRS, numerical rating scale; RUX, ruxolitinib cream.
**** *P*<0.0001 vs vehicle.

Safety

- Ruxolitinib cream was well tolerated with an adverse event (AE) profile similar to vehicle[7]; no serious AEs were related to ruxolitinib cream

Conclusions

- **Significant improvement in multiple PROs was achieved with both strengths of ruxolitinib cream in adolescents and adults with AD**
- **Application of ruxolitinib cream resulted in more "clear skin," less skin pain, and less QoL impairment compared with vehicle**

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. MA has served as a consultant, researcher, and/or has received research grants from AbbVie, ALK-Abelló, Almirall, Amgen, Bayer, Beiersdorf, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Centocor, Dermira, Eli Lilly, Galderma, Genzyme, GlaxoSmithKline, Hexal, Janssen, LEO Pharma, Medac, Menlo, MSD, Mylan B.V., Novartis, Pfizer, Regeneron, Sandoz, Sanofi, Stallergenes, Trevi, and XenoPort. DT has served as an investigator and/or consultant/advisor for AbbVie, Almirall, Amgen, Asana Biosciences, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Galderma, Janssen-Cilag, Kyowa Kirin, LEO Pharma, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Target-Solution, and UCB and has received grants from AbbVie, Celgene, LEO Pharma, and Novartis. LM is an investigator for AbbVie, Eli Lilly, Galderma, Incyte Corporation, LEO Pharma, Pfizer, and Sanofi and is a consultant with honorarium for AbbVie, Eli Lilly, Galderma, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, and Sanofi. JIS has received honoraria for advisory board, speaker, and consultant services from AbbVie, Asana, Bluefin, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Glenmark, Incyte Corporation, Kiniksa, LEO Pharma, Menlo, Novartis, Pfizer, Realm, Regeneron, and Sanofi and research grants for investigator services from GlaxoSmithKline and Galderma. AWA has served as a research investigator and/or scientific advisor to AbbVie, Bristol Myers Squibb, Dermavant, Dermira, Incyte Corporation, Janssen, LEO Pharma, Lilly, Modmed, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB. ZCCF has served as a consultant for the Asthma and Allergy Foundation of America and the National Eczema Association, AbbVie, Incyte Corporation, and Pfizer; has received research grants from LEO Pharma, Menlo Therapeutics, Regeneron, Sanofi, Tioga, and Vanda for work related to atopic dermatitis; and has received honoraria for continuing medical education work in atopic dermatitis sponsored by education grants from Regeneron/Sanofi. MEK, MEV, and KS are employees and shareholders of Incyte Corporation. KP has received honoraria or clinical research grants as a consultant, speaker, scientific officer, advisory board member, and/or steering committee member for AbbVie, Akros, Amgen, Anacor, Arcutis, Astellas, Bausch Health/Valeant, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite, Celgene, Coherus, Dermira, Dow Pharmaceuticals, Eli Lilly, Galderma, Genentech, Gilead, GlaxoSmithKline, Incyte Corporation, InflaRx, Janssen, Kyowa Hakko Kirin, Leo, MedImmune, Meiji Seika Pharma, Merck (MSD), Merck Serono, Mitsubishi Pharma, Moberg Pharma, Novartis, Pfizer, PRCL Research, Regeneron, Roche, Sanofi-Aventis/Genzyme, Sun Pharmaceuticals, Takeda, and UCB.

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