Long-Term Safety and Disease Control of Ruxolitinib Cream Among Adolescents With Atopic Dermatitis: Results From Two Phase 3 Studies

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Introduction

- Atopic dermatitis (AD) is a highly pruritic, chronic, inflammatory skin disease[1]
- AD often begins in childhood and can persist into adolescence and adulthood[2]
- Janus kinases (JAKs) act downstream of proinflammatory cytokines and itch mediators involved in the pathogenesis of AD[3,4]
- Ruxolitinib cream is a topical formulation of ruxolitinib, a selective inhibitor of JAK1 and JAK2[5]
- 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 in patients with AD[5]

Objective

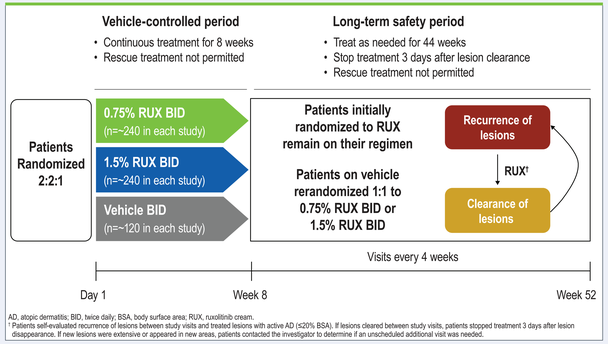
- To evaluate the long-term safety and disease control of ruxolitinib cream in adolescent patients with AD (aged 12–17 years)

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 (BSA), 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], 1.5% BID) or vehicle cream BID for 8 weeks of double-blind treatment (vehicle-controlled [VC] period); patients were instructed to continue treating lesions even if they improved
  - Patients on ruxolitinib cream subsequently continued treatment for 44 weeks (long-term safety [LTS] period); patients initially randomized to vehicle were rerandomized 1:1 (blinded) to either ruxolitinib cream regimen
    - 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

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 unscheduled additional visit was needed.

Assessments

- Disease control was assessed by the proportion of patients who achieved no or minimal skin lesions (IGA score of 0 or 1 [clear or almost clear skin]) and mean percentage of BSA affected by AD at each visit (every 4 weeks) during the LTS period
- Safety and tolerability assessments included the frequency of reported treatment-emergent adverse events (TEAEs), treatment-related adverse events, and TEAEs leading to treatment discontinuation
- Patients initially randomized to 0.75% or 1.5% ruxolitinib cream who remained on ruxolitinib cream during the LTS period were included in this analysis; patients initially on vehicle who received ruxolitinib cream during the LTS are not included in this analysis

Statistical Analyses

- Data were analyzed by descriptive statistics
- The safety analysis was conducted using pooled data from both studies
- Disease control data (IGA 0/1 and BSA) are reported as observed

Results

Patients

- Of the 1249 patients randomized in the VC period, 245 (19.6%) were between 12–17 years old
- Distribution of baseline demographics and clinical characteristics for the pooled adolescent population was similar across treatment groups (**Table 1**)

Table 1. Adolescent Patient Demographics and Baseline Clinical Characteristics (Pooled)

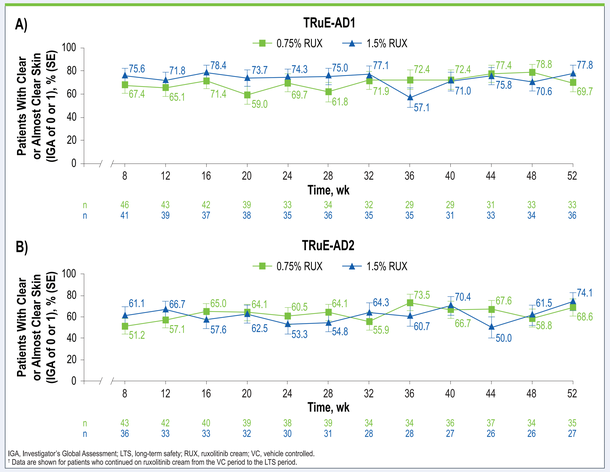
Characteristic	Vehicle (n=45)	0.75% RUX (n=108)	1.5% RUX (n=92)	Total (N=245)
Age, median (range), y	14.0 (12–17)	15.0 (12–17)	15.0 (12–17)	15.0 (12–17)
Female, n (%)	23 (51.1)	60 (55.6)	59 (64.1)	142 (58.0)
Race, n (%)				
White	33 (73.3)	75 (69.4)	72 (78.3)	180 (73.5)
Black	11 (24.4)	27 (25.0)	13 (14.1)	51 (20.8)
Asian	1 (2.2)	0	3 (3.3)	4 (1.6)
Other	0	6 (5.6)	4 (4.3)	10 (4.1)
Region, n (%)				
North America	31 (68.9)	76 (70.4)	64 (69.6)	171 (69.8)
Europe	14 (31.1)	32 (29.6)	28 (30.4)	74 (30.2)
BSA, mean (SD), %	10.8 (5.3)	10.8 (5.5)	10.4 (6.0)	10.6 (5.6)
EASI, mean (SD)	8.2 (5.0)	8.4 (4.6)	8.0 (5.2)	8.2 (4.9)
≤7, n (%)	23 (51.1)	48 (44.4)	45 (48.9)	116 (47.3)
>7, n (%)	22 (48.9)	60 (55.6)	47 (51.1)	129 (52.7)
IGA, n (%)				
2	13 (28.9)	25 (23.1)	23 (25.0)	61 (24.9)
3	32 (71.1)	83 (76.9)	69 (75.0)	184 (75.1)
Itch NRS score, mean (SD)	4.5 (2.4)	4.5 (2.3)	4.3 (2.4)	4.4 (2.4)
≥4, n (%)	24 (53.3)	60 (55.6)	50 (54.3)	134 (54.7)
Duration of disease, median (range), y	11.4 (2.9–16.9)	12.0 (0.1–18.1)	13.0 (2.4–17.9)	12.2 (0.1–18.1)
Facial involvement, n (%)*	19 (42.2)	45 (41.7)	41 (44.6)	105 (42.9)
Number of flares in last 12 mo, mean (SD)*	6.7 (6.8)	5.7 (8.1)	6.2 (6.9)	6.1 (7.4)

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

Disease Control

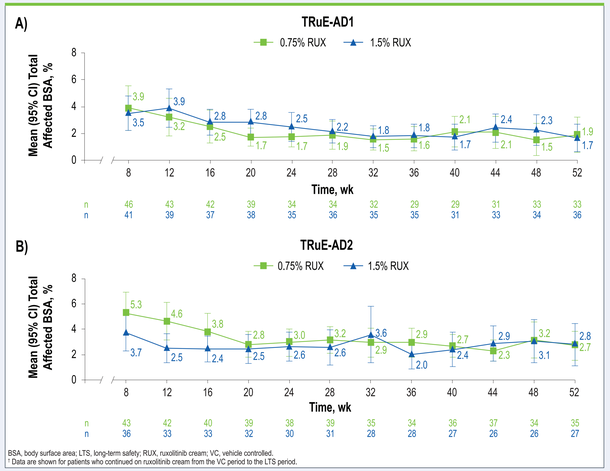
- The evaluable population for disease control consisted of 166 patients who remained on ruxolitinib cream from the VC period to the LTS period (TRuE-AD1: 0.75% ruxolitinib cream, n=46; 1.5% ruxolitinib cream, n=41; TRuE-AD2: 0.75% ruxolitinib cream, n=43; 1.5% ruxolitinib cream, n=36)
- The proportion of patients with clear or almost clear skin (IGA 0/1) was sustained or further increased during the LTS period with as-needed use of ruxolitinib cream (**Figure 2**)
- Mean affected BSA during the LTS period was low and generally below 3%, attesting to a mild/limited extent of disease (**Figure 3**)

Figure 2. Proportion of Patients† With Clear or Almost Clear Skin (IGA 0/1) in the LTS Period in (A) TRuE-AD1 and (B) TRuE-AD2



IGA, Investigator's Global Assessment; LTS, long-term safety; RUX, ruxolitinib cream; VC, vehicle controlled.
† Data are shown for patients who continued on ruxolitinib cream from the VC period to the LTS period.

Figure 3. Affected BSA in the LTS Period† in (A) TRuE-AD1 and (B) TRuE-AD2



BSA, body surface area; LTS, long-term safety; RUX, ruxolitinib cream; VC, vehicle controlled.
† Data are shown for patients who continued on ruxolitinib cream from the VC period to the LTS period.

Safety

- The safety profile of ruxolitinib cream in the LTS period was consistent with the VC period
- Ruxolitinib cream was well tolerated (**Table 2**)
- Application site reactions (ie, erythema, pain, or pruritus) were reported in 6 patients (4.6%) and 1 patient (1.1%) who applied 0.75% and 1.5% ruxolitinib cream, respectively

Table 2. Adverse Events in the Full 52-Week Period (Pooled)*

n, %	0.75% RUX (n=108)	1.5% RUX (n=92)
Patients with TEAE	64 (59.3)	43 (46.7)
Most common TEAEs†		
Upper respiratory tract infection	10 (9.3)	15 (16.3)
Nasopharyngitis	8 (7.4)	7 (7.6)
Influenza	4 (3.7)	5 (5.4)
Pharyngitis	3 (2.8)	5 (5.4)
Patients with treatment-related AE	7 (6.5)	3 (3.3)
Patients who discontinued due to a TEAE	3 (2.8)	0
Patients with serious TEAE	0	0

AE, adverse event; LTS, long-term safety; RUX, ruxolitinib cream; TEAE, treatment-emergent AE; VC, vehicle controlled.
* Data are shown for patients who continued on ruxolitinib cream from the VC period to the LTS period.
† Occurring in >5% of patients in either group.

Conclusions

- **Adolescent patients achieved disease control with ruxolitinib cream monotherapy use as needed during the LTS period, comparable to previously reported findings in the overall patient population (adolescents and adults)[6]**
  - **A high proportion of patients maintained clear or almost clear skin using ruxolitinib cream as needed**
  - **Mean affected BSA was low throughout the LTS period**
- **Ruxolitinib cream was well tolerated over 52 weeks, with a consistent safety profile throughout the study period**
  - **The incidence of application site reactions was low**

Disclosures

LFE has served as an investigator, consultant, speaker, or data safety monitoring board member for AbbVie, Almirall, Arcutis, Asana, Dermavant, Eli Lilly, Forte Biosciences, Galderma, Ichnos/Glenmark, Incyte Corporation, Janssen, LEO Pharma, Novartis, Ortho Dermatologics, Otsuka, Pfizer, Regeneron, and Sanofi Genzyme. 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. 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, Gilead, GlaxoSmithKline, Incyte Corporation, InflaRx, Janssen, Kyowa Hakko Kirin, LEO Pharma, 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. JCS has served as an advisor for AbbVie, LEO Pharma, Menlo Therapeutics, Novartis, Pierre Fabre, and Trevi; has received speaker honoraria from AbbVie, Eli Lilly, Janssen-Cilag, LEO Pharma, Novartis, Sanofi Genzyme, and Sun Pharma; and has received clinical trial funding from AbbVie, Almirall, Amgen, Galapagos, Holm, Incyte Corporation, InflaRX, Janssen-Cilag, Menlo Therapeutics, Merck, Novartis, Pfizer, Regeneron, Trevi, and UCB. LK has served as an investigator, consultant, or speaker for AbbVie, Amgen, Anaptys, Arcutis, Dermavant, Eli Lilly, Glenmark, Incyte Corporation, Kamedis, LEO Pharma, L'Oreal, Menlo Therapeutics, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and Taro. DT has served as an investigator for AbbVie, Amgen, Arcutis, Astellas, Astion, Avillion, Boehringer Ingelheim, Celgene, Dermira, Dow Pharmaceuticals, DS BioPharma, Eli Lilly, F. Hoffmann-La Roche Ltd, Galderma, GlaxoSmithKline, Incyte Corporation, Isotechnika, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, and UCB Biopharma. SBF has received honoraria, clinical research grants, or fees as a consultant, speaker, advisory board member, and/or investigator for AbbVie, Aclaris Therapeutics, Asana BioSciences, AstraZeneca, Athenex, Celgene Corporation, Cutanea Life Sciences, Eli Lilly, Incyte Corporation, Innovaderm Research, Novartis, Pfizer, Promius Pharma, Regeneron, UCB, Valeant Pharmaceuticals North America, and XBiotech. MEK was an employee and shareholder of Incyte Corporation at the time of development of the original presentation. MEV and HR are employees and shareholders of Incyte Corporation. ASP has served as an investigator, consultant, or data safety monitoring board member for AbbVie, Abeona, Alcimed, Almirall, Amagma, AnaptysBio, Arena, Azitra, Bausch, BiomX, Boehringer Ingelheim, Castle Biosciences, Catawba, Dermira, Eli Lilly, Exicure, Forte, Galderma, Incyte Corporation, Janssen, Kamari, KrystalBio, LEO Pharma, Lifemax, NAOS, Novan, Novartis, Pfizer, Phoenix, Pierre Fabre, Regeneron, Sanofi Genzyme, Seanergy, Trifecta, and UCB.

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