Long-Term Safety and Disease Control With Ruxolitinib Cream Among Patients With Atopic Dermatitis Based on Previous Medication History: Pooled Results From Two Phase 3 Studies

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Introduction

- Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by itching, dryness, and redness[1]
- Treatments for AD include topical corticosteroids (TCS), topical calcineurin inhibitors (TCI), and systemic immunomodulatory agents[1]
- Some topical treatments may be insufficient because of inadequate efficacy, delayed onset of efficacy, duration-of-use limitations, anatomic use restrictions, poor tolerability, and/or adverse reactions[1,2]
  - TCS are associated with decreased skin thickness and elasticity (eg, striae); they are also not recommended for long-term application or use in sensitive areas
  - TCI are associated with local reactions, such as stinging and burning
- Ruxolitinib cream is a topical formulation of ruxolitinib, a selective inhibitor of Janus kinase (JAK) 1 and JAK2[3]
- 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[3]

Objective

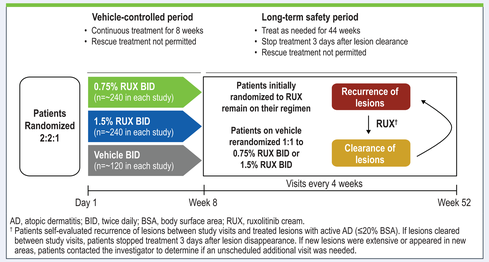
- To evaluate the long-term safety and disease control of ruxolitinib cream based on types of previous medication using pooled data from two phase 3 trials in patients with AD

Methods

Study Design and Patients

- Eligible patients were aged ≥12 years with AD for ≥2 years and had an Investigator's Global Assessment (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
  - The washout period for prior therapies was 1 week for topical AD treatments, 4 weeks for systemic corticosteroids or other immunomodulating agents, and 12 weeks or 5 half-lives for biologics
- 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-blinded continuous 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 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 adverse events (AEs) leading to treatment discontinuation

Statistical Analysis

- All analyses were conducted using the pooled data from both studies
  - The disease control analysis included patients who remained on their initial ruxolitinib cream strength regimen from the VC period through the LTS period; data are reported as observed
  - The safety analysis included patients who received ruxolitinib cream in any period (VC or LTS)
- Data were summarized using descriptive statistics

Results

Patients

- A total of 1249 patients (median age, 32 years) were randomized in the VC period, and 1072 continued in the LTS period (vehicle to ruxolitinib cream, n=200 [101 to 0.75% and 99 to 1.5%]; 0.75% ruxolitinib cream, n=426; 1.5% ruxolitinib cream, n=446)
- Distribution of baseline demographics and clinical characteristics was similar across treatment groups (**Table 1**)

Table 1. Patient Demographics and Baseline Clinical Characteristics

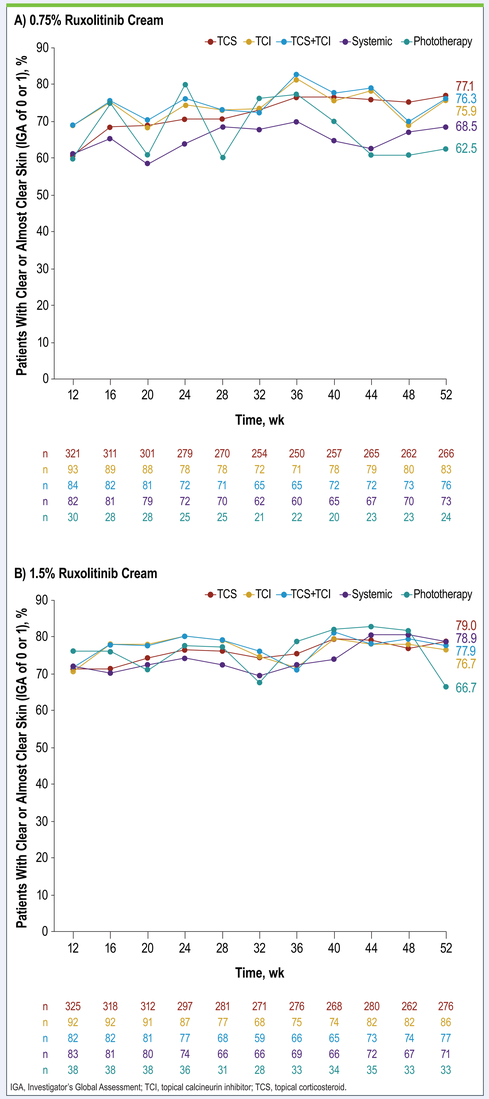
Characteristic	Vehicle (n=250)	0.75% RUX (n=500)	1.5% RUX (n=499)	Total (N=1249)
Age, median (range), y	34.0 (12–82)	33.0 (12–85)	31.0 (12–85)	32.0 (12–85)
Female, n (%)	159 (63.6)	304 (60.8)	308 (61.7)	771 (61.7)
Race, n (%)				
White	170 (68.0)	345 (69.0)	355 (71.1)	870 (69.7)
Black	61 (24.4)	118 (23.6)	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)
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)

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

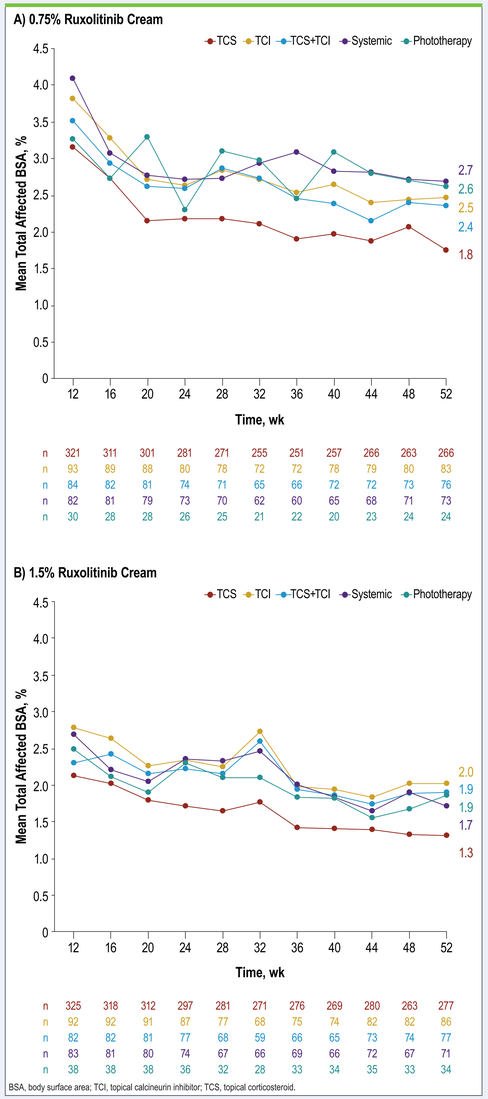
- At each visit in the LTS, most patients in the 0.75% or 1.5% ruxolitinib cream groups had an IGA score of 0/1 (clear or almost clear), regardless of the type of previous medication (**Figure 2**)
- Regardless of type of previous medication, mean affected BSA was low (generally <3%) during the LTS among patients who applied 0.75% or 1.5% ruxolitinib cream (**Figure 3**)

Figure 2. Patients Achieving IGA 0/1 Stratified by the Type of Previous Medication Among Patients Who Applied (A) 0.75% or (B) 1.5% Ruxolitinib Cream



IGA, Investigator's Global Assessment; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid.

Figure 3. Mean Affected BSA Stratified by the Type of Previous Medication Among Patients Who Applied (A) 0.75% or (B) 1.5% Ruxolitinib Cream



BSA, body surface area; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid.

Safety

- Ruxolitinib cream was well tolerated across all subgroups of previous treatment; the frequency of application site reactions was low (**Table 2**)
- In the overall population, the most common TEAEs through Week 52 were upper respiratory tract infection, nasopharyngitis, and headache
  - No AEs suggestive of a relationship to systemic exposure were observed

Table 2. Adverse Events According to the Type of Previous Medication Among Patients Who Applied Ruxolitinib Cream in the Phase 3 Studies (VC or LTS Periods)

Parameter	TCS	TCI	TCS+TCI	Systemic Therapies	Phototherapy
Patients, n					
0.75% RUX	461	134	121	106	42
1.5% RUX	461	121	109	110	48
TEAEs, n (%)					
0.75% RUX	286 (62.0)	97 (72.4)	87 (71.9)	80 (75.5)	30 (71.4)
1.5% RUX	270 (58.6)	85 (70.2)	80 (73.4)	76 (69.1)	38 (79.2)
Application site reactions, n (%)					
0.75% RUX	15 (3.3)	5 (3.7)	4 (3.3)	3 (2.8)	2 (4.8)
1.5% RUX	9 (2.0)	4 (3.3)	4 (3.7)	4 (3.6)	2 (4.2)
TRAEs, n (%)					
0.75% RUX	36 (7.8)	18 (13.4)	15 (12.4)	13 (12.3)	8 (19.0)
1.5% RUX	35 (7.6)	19 (15.7)	19 (17.4)	15 (13.6)	7 (14.6)
TEAEs resulting in discontinuation, n (%)					
0.75% RUX	8 (1.7)	1 (0.7)	1 (0.8)	3 (2.8)	1 (2.4)
1.5% RUX	4 (0.9)	1 (0.8)	1 (0.9)	1 (0.9)	0
Serious TEAEs, n (%)					
0.75% RUX	15 (3.3)	3 (2.2)	3 (2.5)	6 (5.7)	1 (2.4)
1.5% RUX	10 (2.2)	2 (1.7)	2 (1.8)	1 (0.9)	1 (2.1)

LTS, long-term safety; RUX, ruxolitinib cream; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; VC, vehicle controlled.

Conclusions

- **Ruxolitinib cream, used as maintenance therapy, demonstrated effective long-term disease control, regardless of the type of previous therapy**
- **Ruxolitinib cream was well tolerated over a period up to 52 weeks, regardless of the type of previous therapy**

Disclosures

AB has served as a scientific advisor and/or clinical study investigator for AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Aslan, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Evommune, Forte, Galderma, Incyte Corporation, Janssen, Landos, LEO Pharma, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma. 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. MEV and KS are employees and shareholders of Incyte Corporation. MEK was an employee and shareholder of Incyte Corporation at the time of development of the original presentation. 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 Therapeutics, Novartis, Pfizer, Realm, Regeneron, and Sanofi and research grants for investigator services from Galderma and GlaxoSmithKline.

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