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Effects of Ruxolitinib Cream in Patients With Atopic Dermatitis With Head and/or Neck Involvement

Presented at the
Society for Investigative Dermatology 2021 Virtual Meeting
May 3–8, 2021

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Background

- Atopic dermatitis (AD) is a highly pruritic inflammatory skin disease that often involves the head and/or neck (HN)[1,2]
- There is a need for well-tolerated treatments that can be used long term on body regions that are prone to irritation/burning and to side effects from topical steroid use, such as the face[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

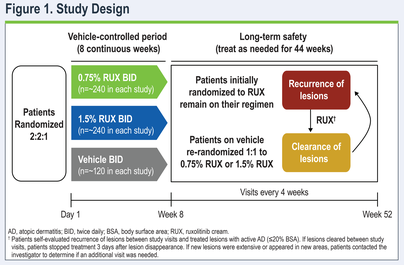
- To describe the effect of ruxolitinib cream on HN lesions in adolescent and adult patients with AD using pooled data from two phase 3 trials

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

- Pooled efficacy at Week 8 was assessed by achievement of the following endpoints in patients with HN involvement at baseline and the overall population:
  - IGA-treatment success (IGA-TS; IGA of 0/1 and ≥2-grade improvement from baseline)
  - ≥50%, ≥75%, and ≥90% improvement in Eczema Area and Severity Index vs baseline (EASI-50, EASI-75, and EASI-90 [overall and HN region])
  - ≥4-point improvement in itch numerical rating scale score vs baseline (NRS4)
- Percentage change from baseline in EASI score (overall and HN region) was also assessed
- Safety and application site tolerability were also assessed

Statistical Analyses

- All analyses were conducted using the pooled data from both studies
- EASI percentage change from baseline was analyzed by mixed-effect model with repeated measures with statistical significance determined at Weeks 2, 4, and 8
- All other efficacy endpoints were analyzed by logistic regression with statistical significance determined at Week 8
- The efficacy population consisted of 1208 patients (vehicle, n=244; 0.75% ruxolitinib cream, n=483; 1.5% ruxolitinib cream, n=481)

Results

Patients

- Of 1249 randomized patients, 696 (55.7%) had HN involvement at baseline
- Distribution of baseline demographics and clinical characteristics was similar across treatment groups (**Table 1**)

Table 1. Patient Demographics and Baseline Clinical Characteristics

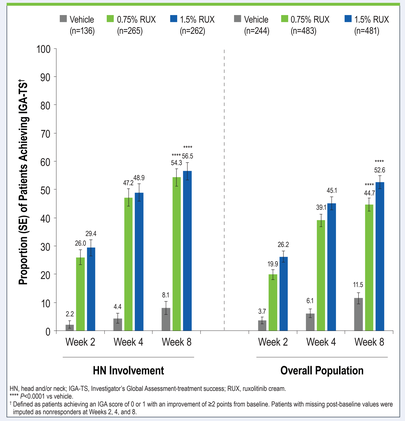
Characteristic	Vehicle (n=250)	0.75% RUX (n=500)	1.5% RUX (n=499)	Total (N=1249)
Age, median (range), y	34.0 (12–82)	33.0 (12–85)	31.0 (12–85)	32.0 (12–85)
Female, n (%)	159 (63.6)	304 (60.8)	308 (61.7)	771 (61.7)
Race, n (%)				
White	170 (68.0)	345 (69.0)	355 (71.1)	870 (69.7)
Black	61 (24.4)	118 (23.6)	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)
EASI HN score*	1.2 (0.9)	1.2 (1.0)	1.1 (0.8)	NA
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; HN, head and/or neck; IGA, Investigator's Global Assessment; NA, not available; NRS, numerical rating scale; RUX, ruxolitinib cream.
* Patients with HN involvement in the efficacy-evaluable population (vehicle, n=136; 0.75% RUX, n=265; 1.5% RUX, n=262).
† Patient reported.

Efficacy

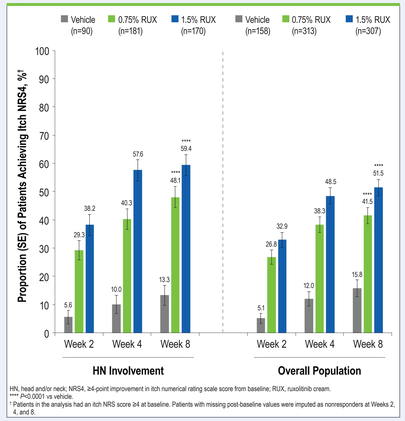
- IGA-TS (**Figure 2**) and itch NRS4 (**Figure 3**) were achieved by significantly more patients who applied ruxolitinib cream compared with vehicle at Week 8 ($P<0.0001$)
  - Response rates were numerically greater among patients with HN involvement vs the overall population
- Significantly greater improvements from baseline in total EASI and HN region scores were observed with ruxolitinib cream vs vehicle at Week 8 ($P<0.0001$; **Figure 4**)
- Significantly more patients who received ruxolitinib cream vs vehicle achieved EASI-50 (**Figure 5**; $P<0.0001$), EASI-75 (**Figure 6**; $P<0.0001$), and EASI-90 (**Figure 7**; $P<0.0001$) at Week 8
  - Response rates were numerically greater among patients with HN involvement vs the overall population

Figure 2. IGA-TS in the HN and Overall Populations



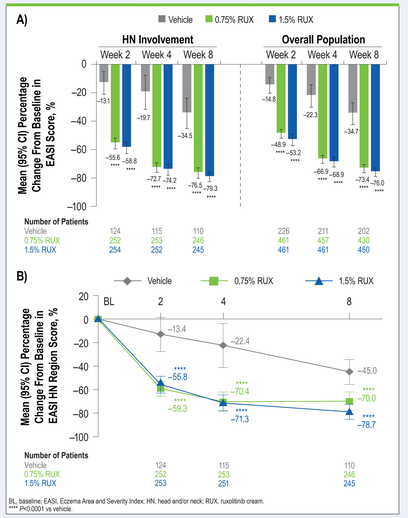
HN, head and/or neck; IGA-TS, Investigator's Global Assessment-treatment success; RUX, ruxolitinib cream.
**** $P<0.0001$ vs vehicle.
† Defined as patients achieving an IGA score of 0 or 1 with an improvement of ≥2 points from baseline. Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

Figure 3. Itch NRS4 in the HN and Overall Populations



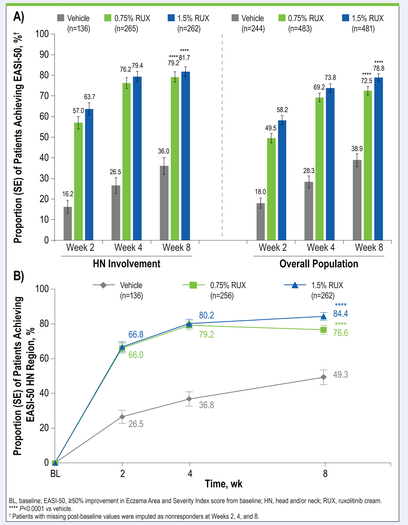
HN, head and/or neck; NRS4, ≥4-point improvement in itch numerical rating scale score from baseline; RUX, ruxolitinib cream.
**** $P<0.0001$ vs vehicle.
† Patients in the analysis had an itch NRS score ≥4 at baseline. Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

Figure 4. EASI Percentage Change From Baseline in the (A) HN and Overall Populations and (B) Based on HN Region Score



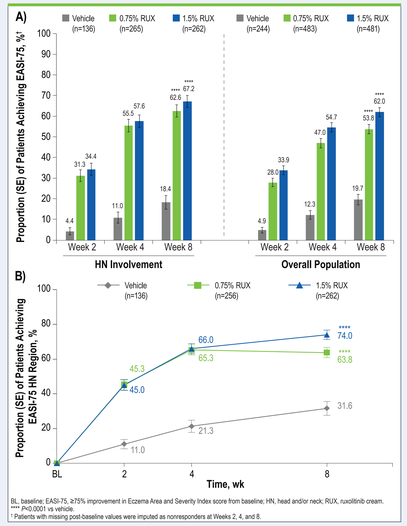
BL, baseline; EASI, Eczema Area and Severity Index; HN, head and/or neck; RUX, ruxolitinib cream.
**** $P<0.0001$ vs vehicle.

Figure 5. EASI-50 in the (A) HN and Overall Populations and (B) Based on HN Region Score



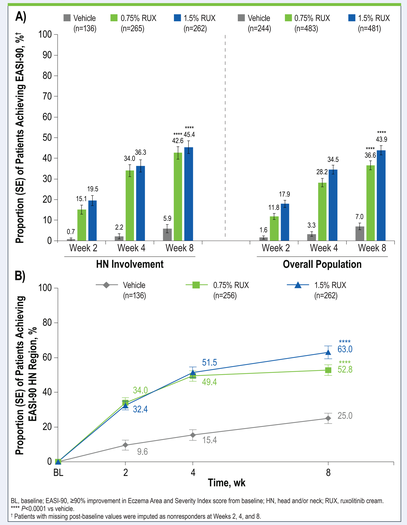
BL, baseline; EASI-50, ≥50% improvement in Eczema Area and Severity Index score from baseline; HN, head and/or neck; RUX, ruxolitinib cream.
**** $P<0.0001$ vs vehicle.
† Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

Figure 6. EASI-75 in the (A) HN and Overall Populations and (B) Based on HN Region Score



BL, baseline; EASI-75, ≥75% improvement in Eczema Area and Severity Index score from baseline; HN, head and/or neck; RUX, ruxolitinib cream.
**** $P<0.0001$ vs vehicle.
† Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

Figure 7. EASI-90 in the (A) HN and Overall Populations and (B) Based on HN Region Score



BL, baseline; EASI-90, ≥90% improvement in Eczema Area and Severity Index score from baseline; HN, head and/or neck; RUX, ruxolitinib cream.
**** $P<0.0001$ vs vehicle.
† Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

Safety

- Application site reactions were less frequent in patients who applied ruxolitinib cream regardless of HN involvement compared with vehicle (**Table 2**)
- Among patients who applied ruxolitinib cream, application site pain (ie, stinging/burning) was reported in 5/555 patients (0.9%) with HN involvement and 7/999 (0.7%) in the overall population (vs 8/141 [5.7%] and 12/250 [4.8%] among patients who applied vehicle, respectively)
  - No application site reactions were serious

Table 2. Application Site Reactions in the HN and Overall Populations

	HN Population		Overall Population	
AE, n (%)	Vehicle (n=141)	RUX (Combined) (n=555)	Vehicle (n=250)	RUX (Combined) (n=999)
Application site reactions*	13 (9.2)	14 (2.5)	18 (7.2)	19 (1.9)
Pain	8 (5.7)	5 (0.9)	12 (4.8)	7 (0.7)
Pruritus	5 (3.5)	4 (0.7)	7 (2.8)	6 (0.6)
Irritation	2 (1.4)	2 (0.4)	2 (0.8)	2 (0.2)
Erythema	2 (1.4)	0	2 (0.8)	1 (0.1)
Dryness	0	1 (0.2)	0	1 (0.1)
Folliculitis	0	1 (0.2)	0	2 (0.2)
Exfoliation	0	1 (0.2)	0	1 (0.1)
Papules	0	1 (0.2)	0	1 (0.1)
Swelling	0	0	1 (0.4)	0

AE, adverse event; RUX, ruxolitinib cream.
* Patients may report more than 1 type of application site reaction.

Conclusions

- **In patients with AD with HN involvement, ruxolitinib cream showed superior efficacy compared with vehicle**
- **Ruxolitinib cream was well tolerated (ie, low rates of stinging/burning) in patients with HN involvement with a safety profile comparable to the overall population**

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. RB is a consultant with honoraria for AbbVie, Arena, Bluefin, Boehringer Ingelheim, CARA Therapeutics, Kyowa Kirin, Pfizer, and Respivant; an investigator with grants/research funding for AbbVie, Arcutis, Arena, Asana BioSciences, Bellus, Boehringer Ingelheim, CARA Therapeutics, Eli Lilly, Incyte Corporation, Pfizer, RAPT, and Sanofi Genzyme; an advisor with honoraria for Arena, Eli Lilly, Galderma, Incyte Corporation, LEO Pharma, Pfizer, and RAPT; and an employee and shareholder of Innovaderm Research. MEK, MEV, and KS are employees and shareholders of Incyte Corporation. JIS 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 Galderma and GlaxoSmithKline.

Acknowledgments

The authors thank the patients, investigators, and investigational sites whose participation made the study possible. Support for this study was provided by Incyte Corporation (Wilmington, DE, USA). Writing assistance was provided by Tania Iqbal, PhD, an employee of ICON (North Wales, PA, USA), and was funded by Incyte Corporation.

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