26884

Ruxolitinib Cream Rapidly Decreases Pruritus in Atopic Dermatitis: Pooled Results From Two Phase 3 Studies

Presented at the
American Academy of Dermatology Virtual Meeting Experience
April 23–25, 2021

Andrew Blauvelt, MD, MBA,[1] Jacek C. Szepietowski, MD, PhD, FRCP (Edin),[2] Kim Papp, MD, PhD,[3] Eric L. Simpson, MD, MCR,[4] Jonathan I. Silverberg, MD, PhD, MPH,[5] Brian S. Kim, MD, MTR,[6] Shawn G. Kwatra, MD,[7] Michael E. Kuligowski, MD, PhD, MBA,[8] May E. Venturanza, MD,[8] Kang Sun, PhD,[8] Leon Kircik, MD[9]

[1]Oregon Medical Research Center, Portland, OR, USA; [2]Department of Dermatology, Venereology, and Allergology, Wroclaw Medical University, Wroclaw, Poland; [3]K. Papp Clinical Research and Probity Medical Research, Waterloo, ON, Canada; [4]Oregon Health & Science University, Portland, OR, USA; [5]George Washington University, Washington, DC, USA; [6]Washington University School of Medicine, St. Louis, MO, USA; [7]Johns Hopkins University School of Medicine, Baltimore, MD, USA; [8]Incyte Corporation, Wilmington, DE, USA; [9]Icahn School of Medicine at Mount Sinai, New York, NY, USA

Background

- Atopic dermatitis (AD) is a highly pruritic, chronic, inflammatory skin disease[1]
- Itch is the most common and burdensome symptom of AD and is associated with eczematous lesions that are characteristic of the disease[1,2]
- Janus kinases (JAKs) act downstream of proinflammatory cytokines and itch mediators involved in the pathogenesis of AD[3,4]
- Ruxolitinib cream is a topical selective inhibitor of JAK1 and JAK2 in development for the treatment of AD[5]
- 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[6]

Objective

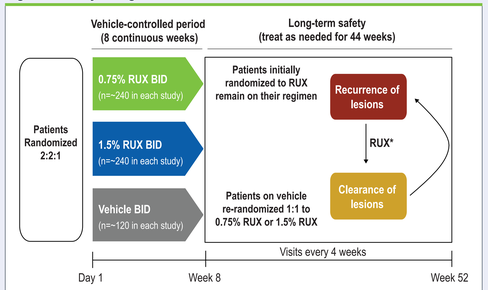
- To describe the impact of ruxolitinib cream on itch using pooled data from two phase 3 trials in adolescent and adult patients with AD

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-blinded 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

- Itch was primarily assessed using the itch numerical rating scale (NRS). Patients were given an electronic diary to be completed each evening and were instructed to report their worst level of itch during the past 24-hour period from 0 (no itch) to 10 (worst imaginable itch)
  - Minimal clinically important difference (MCID) in itch was defined as a 2–3-point change in itch NRS score from baseline (NRS2)[7]
  - Clinically meaningful improvement was defined as a ≥4-point change in itch NRS score from baseline (NRS4)[8]
- Itch was also assessed using item 1 of the Patient-Oriented Eczema Measure (POEM) at baseline and Weeks 2, 4, and 8
  - POEM is a 7-question quality-of-life assessment that evaluates how many days the patient has been bothered by various aspects of their disease during the past 7 days[9]

Statistical Analyses

- All analyses were conducted using the pooled data from the vehicle-controlled portion of both studies
- Statistical significance for daily itch NRS was assessed using analysis of variance
- The proportion of patients with itch NRS2 and NRS4 was analyzed by exact logistic regression
- For the assessment of NRS2 and NRS4, only patients with NRS scores ≥2 or ≥4, respectively, were included
- Cumulative incidence plots were created for time to NRS2 or NRS4; comparisons were made across treatment groups using a log-rank test
- The efficacy population consisted of 1208 patients (vehicle, n=244; 0.75% ruxolitinib cream, n=483; 1.5% ruxolitinib cream, n=481)

Results

Patients

- A total of 1249 patients (median age, 32 years) were randomized
- The mean (SD) itch NRS score at baseline was 5.1 (2.5)
  - 84.3% of patients had an itch NRS score ≥2 at baseline
  - 63.9% of patients had an itch NRS score ≥4 at baseline
- Distribution of baseline demographics and clinical characteristics was similar across treatment groups (**Table 1**)

Table 1. Patient Demographics and Baseline Clinical Characteristics

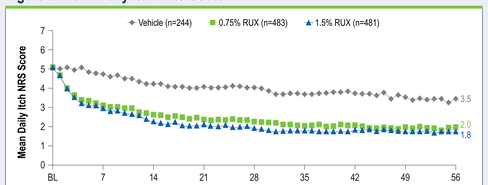
Characteristic	Vehicle (n=250)	0.75% RUX (n=500)	1.5% RUX (n=499)	Total (N=1249)
Age, median (range), y	34.0 (12–82)	33.0 (12–85)	31.0 (12–85)	32.0 (12–85)
Female, n (%)	159 (63.6)	304 (60.8)	308 (61.7)	771 (61.7)
Race, n (%)				
White	170 (68.0)	345 (69.0)	355 (71.1)	870 (69.7)
Black	61 (24.4)	118 (23.6)	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)
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)
≥2, n (%)	209 (83.6)	419 (83.8)	425 (85.2)	1053 (84.3)
≥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.

Efficacy

- The mean itch NRS score decreased throughout the study, with lower scores for ruxolitinib cream vs vehicle as early as Day 1 (**Figure 2**)
  - Statistically significant greater reduction in itch was observed within 12 hours of the first application of ruxolitinib cream (mean change from baseline, –0.4 and –0.5 for 0.75% and 1.5% ruxolitinib creams, respectively) vs vehicle (–0.1; both $P<0.02$)
- Among patients with baseline itch NRS ≥2, statistically significant improvement for both ruxolitinib strengths vs vehicle was observed within 12 hours of first application and maintained through Week 8 (**Figure 3**)
  - Median time to NRS2 response (MCID) was shorter for patients who applied 0.75% and 1.5% ruxolitinib creams (5.0 and 4.0 days, respectively) vs vehicle (17.0 days)
- Among patients with baseline itch NRS ≥4, clinically meaningful (≥4-point) reduction in itch was achieved by significantly more patients who applied ruxolitinib cream vs vehicle by Day 2 (~36 hours after first application); significantly higher rates of achieving NRS4 were observed at Week 8 for ruxolitinib creams (41.5% and 51.5% for 0.75% and 1.5% ruxolitinib creams, respectively) vs vehicle (15.8%; $P<0.0001$; **Figure 4**)

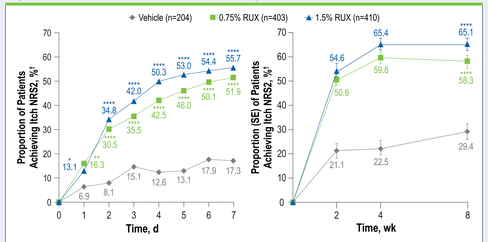
Figure 2. Mean Daily Itch NRS Score



Number of Patients	Day 14	Day 28	Day 56
Vehicle	214	198	131
0.75% RUX	420	405	289
1.5% RUX	421	416	314

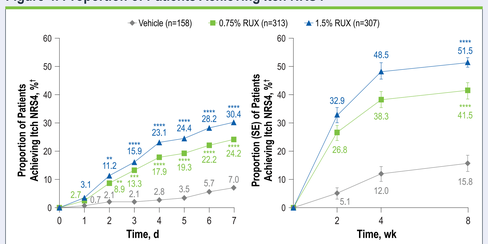
BL, baseline; NRS, numerical rating scale; RUX, ruxolitinib cream.

Figure 3. Proportion of Patients Achieving Itch NRS2



NRS2, ≥2-point improvement in numerical rating scale score from baseline; RUX, ruxolitinib cream.
* $P<0.05$ vs vehicle; ** $P<0.01$ vs vehicle; **** $P<0.0001$ vs vehicle.
† Patients in the analysis had an itch NRS score ≥2 at baseline. Patients with missing post-baseline values were imputed as nonresponders at Weeks 2, 4, and 8.

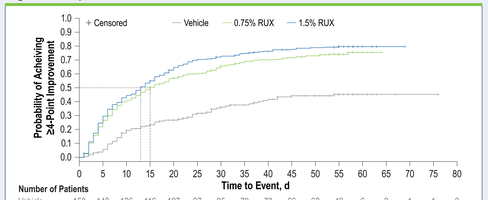
Figure 4. Proportion of Patients Achieving Itch NRS4



NRS4, ≥4-point improvement in itch numerical rating scale score from baseline; RUX, ruxolitinib cream.
** $P<0.01$ vs vehicle; *** $P<0.001$ vs vehicle; **** $P<0.0001$ 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.

- Median time to NRS4 was shorter for ruxolitinib cream (15.0 and 13.0 days for 0.75% and 1.5% ruxolitinib creams, respectively) vs vehicle (not reached; **Figure 5**); cumulative incidence rates for achieving NRS4 were significantly higher for ruxolitinib cream (log-rank $P<0.0001$)
- More patients reported *no days of itch* with ruxolitinib creams at Week 8 (28.0% and 32.7% for 0.75% and 1.5% ruxolitinib creams, respectively) vs vehicle (9.0%) as assessed by POEM item 1 (**Figure 6**)
- Representative clinical images from baseline to Week 8 are shown in **Figure 7**

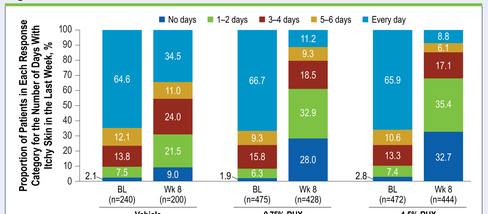
Figure 5. Kaplan-Meier Curve of Time to Itch NRS4



Number of Patients														
Vehicle	158	148	126	116	107	97	85	79	72	66	62	49	6	2	1	1	0
0.75% RUX	312	243	187	159	132	120	106	90	84	80	75	61	4	0			
1.5% RUX	307	228	173	141	111	90	81	73	66	60	56	52	5	1	0		

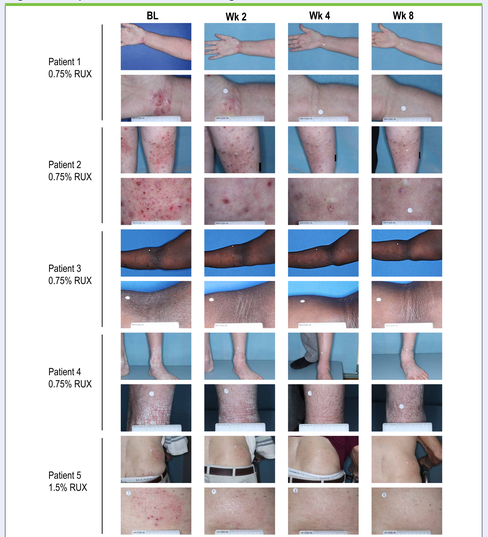
NRS4, ≥4-point improvement in itch numerical rating scale score from baseline; RUX, ruxolitinib cream.

Figure 6. POEM Item 1



BL, baseline; POEM, Patient-Oriented Eczema Measure; RUX, ruxolitinib cream.

Figure 7. Representative Clinical Images



BL, baseline; RUX, ruxolitinib cream.

Safety

- Ruxolitinib cream was well tolerated with an adverse event (AE) profile similar to vehicle[6]; no serious AEs were related to ruxolitinib cream

Conclusions

- **Ruxolitinib cream demonstrated rapid, clinically meaningful, and sustained improvement in itch in patients with AD**
  - **Statistically significant improvement vs vehicle in itch NRS2 and NRS4 was observed within 12 and 36 hours, respectively**
  - **At Week 8, considerably more patients who applied ruxolitinib cream vs vehicle reported no days of itch within the past week**
- **The rapidity and magnitude of itch relief across multiple measures of itch supports the dual antipruritic and anti-inflammatory mode of action for ruxolitinib cream**

Disclosures

AB has served as a scientific advisor and/or clinical study investigator for AbbVie, Aligos, Almirall, Amgen, Arcutis, Arena, 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. JCS has served as an advisor for AbbVie, LEO Pharma, Novartis, Pierre Fabre, Menlo Therapeutics, 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. 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 Pharma, 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. 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. 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 Galderma and GlaxoSmithKline. BSK has served as a consultant to AbbVie, Almirall, Amagma, Cara Therapeutics, Daewoong, Incyte Corporation, OM Pharma, and Pfizer; has served on advisory boards for AstraZeneca, Boehringer Ingelheim, Cara Therapeutics, Celgene Corporation, Regeneron Pharmaceuticals, Sanofi Genzyme, and Trevi Therapeutics; is a shareholder in Locus Biosciences; and has a pending patent for JAK inhibitors in chronic itch. SGK has served as an advisory board member or consultant for AbbVie, Galderma, Incyte Corporation, Kiniksa Pharmaceuticals, Regeneron Pharmaceuticals, and Pfizer Inc and has received grant funding from Pfizer Inc, Galderma, and Kiniksa Pharmaceuticals. MEK, MEV, and KS are employees and shareholders of Incyte Corporation. 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, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and Taro.

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 Mayur Kapadia, MD, an employee of ICON (North Wales, PA, USA), and was funded by Incyte Corporation.

References

1. Langan SM, et al. *Lancet*. 2020;396(10247):345-360. **2.** Chrostowska-Plak D, et al. *J Eur Acad Dermatol Venereol*. 2013;27(2):e239-e242. **3.** Bao L, et al. *JAKSTAT*. 2013;2(3):e24137. **4.** Oetjen LK, et al. *Cell*. 2017;171(1):217-228. **5.** Quintas-Cardama A, et al. *Blood*. 2010;115(15):3109-3117. **6.** Papp K, et al. *Br J Dermatol*. 2020;183(4):e116. **7.** Reich A, et al. *Acta Derm Venereol*. 2016;96(7):978-980. **8.** Yosipovitch G, et al. *Br J Dermatol*. 2019;181(4):761-769. **9.** Charman CR, et al. *Arch Dermatol*. 2004;140(12):1513-1519.

To download a copy of this poster, scan code.