24916

Efficacy of Ruxolitinib Cream in Patients With Atopic Dermatitis Who Demonstrated Partial Responses: Pooled Analysis From Two Randomized Phase 3 Studies

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

Eric L. Simpson, MD, MCR,[1] Leon Kircik, MD,[2] Andrew Blauvelt, MD, MBA,[3] Michael E. Kuligowski, MD, PhD, MBA,[4] May E. Venturanza, MD,[4] Kang Sun, PhD,[4] Lawrence F. Eichenfield, MD[5]

[1]Oregon Health & Science University, Portland, OR; [2]Icahn School of Medicine at Mount Sinai, New York, NY; [3]Oregon Medical Research Center, Portland, OR; [4]Incyte Corporation, Wilmington, DE; [5]Departments of Dermatology and Pediatrics, University of California San Diego, San Diego, CA

Background

- Atopic dermatitis (AD) is a highly pruritic, chronic, inflammatory skin disease[1]
- Janus kinases (JAKs) act downstream of proinflammatory cytokines and itch mediators involved in AD pathogenesis[2,3]
- Ruxolitinib cream is a topical selective inhibitor of JAK1 and JAK2 in development for the treatment of AD[4]
- In two phase 3 AD studies of identical design (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651]), significantly more patients who applied ruxolitinib cream vs vehicle cream achieved Investigator's Global Assessment-treatment success at Week 8 (IGA-TS; score of 0 or 1 with ≥2-grade improvement from baseline), the primary endpoint of the study (44.7%/52.6% for 0.75%/1.5% ruxolitinib cream, respectively, vs 11.5% for vehicle; *P*<0.0001)[5]
  - Patients not achieving IGA scores of 0 or 1 may still experience clinically relevant improvement in their disease; thus, we sought to quantify the proportion of patients who achieved relevant treatment responses in the subgroup of patients who did not achieve IGA 0 or 1 with ≥2-grade improvement from baseline

Objective

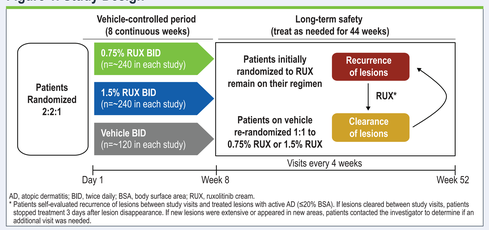
- To evaluate the efficacy of ruxolitinib cream in patients who did not achieve IGA-TS at Week 8 in two phase 3 studies in adolescent and adult patients with AD

Methods

Study Design and Patients

- Eligible patients were aged ≥12 years with AD for ≥2 years and had an 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-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 strength

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

- Analyses were performed on patients who did not achieve IGA-TS at Week 8
- Efficacy endpoints for clinically relevant partial responses using minimal clinically important differences included the following:
  - Proportion of patients achieving ≥50% improvement in Eczema Area and Severity Index (EASI-50)
  - ≥2-point reduction in itch numerical rating scale score (NRS2)
  - ≥4-point reduction in Dermatology Life Quality Index (DLQI; patients aged ≥16 years)
  - ≥6-point reduction in Children's DLQI (CDLQI; patients aged 12–15 years) from baseline
  - 1-point reduction in IGA from baseline (IGA score change from 3 to 2 or 2 to 1) was added as an additional component of the partial response definition
- To evaluate whether any clinically meaningful outcome occurred, a composite partial response endpoint was used and was defined as achievement of ≥1 of the described efficacy parameters

Statistical Analyses

- Data were analyzed by logistic regression

Results

Patients

- Of 1208 patients in the efficacy-evaluable overall population, 584 did not achieve IGA-TS at Week 8; demographics and baseline clinical characteristics were similar across treatment groups (**Table 1**)

Table 1. Patient Demographics and Baseline Clinical Characteristics

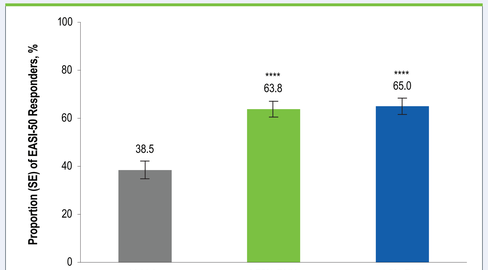
Characteristic	Patients Who Did Not Achieve IGA-TS at Week 8				Overall Population (N=1208)
	Vehicle (n=174)	0.75% RUX (n=213)	1.5% RUX (n=197)	Total (N=584)	
Age, median (range), y	34.5 (12–82)	37.0 (12–85)	28.0 (12–84)	33.0 (12–85)	32.0 (12–85)
Female, n (%)	113 (64.9)	117 (54.9)	127 (64.5)	357 (61.1)	739 (61.2)
Race, n (%)					
White	117 (67.2)	138 (64.8)	124 (62.9)	379 (64.9)	829 (68.6)
Black	43 (24.7)	62 (29.1)	61 (31.0)	166 (28.4)	292 (24.2)
Asian	8 (4.6)	7 (3.3)	10 (5.1)	25 (4.3)	46 (3.8)
Other	6 (3.4)	6 (2.8)	2 (1.0)	14 (2.4)	41 (3.4)
Region, n (%)					
North America	121 (69.5)	171 (80.3)	154 (78.2)	446 (76.4)	855 (70.8)
Europe	53 (30.5)	42 (19.7)	43 (21.8)	138 (23.6)	353 (29.2)
BSA, mean (SD), %	9.3 (5.3)	9.9 (5.2)	9.1 (5.1)	9.5 (5.2)	9.6 (5.2)
EASI, mean (SD)	7.9 (4.9)	7.8 (5.3)	7.2 (4.7)	7.6 (5.0)	7.9 (4.9)
IGA, n (%)					
2	55 (31.6)	83 (39.0)	80 (40.6)	218 (37.3)	312 (25.8)
3	119 (68.4)	130 (61.0)	117 (59.4)	366 (62.7)	896 (74.2)
Itch NRS score, mean (SD)	5.1 (2.4)	5.1 (2.4)	4.9 (2.4)	5.1 (2.4)	5.1 (2.4)
≥2, n (%)	148 (85.1)	177 (83.1)	165 (83.8)	490 (83.9)	1017 (84.2)
≥4, n (%)	112 (64.4)	148 (69.5)	127 (64.5)	387 (66.3)	778 (64.4)
Duration of disease, median (range), y	15.5 (0.8–79.1)	14.0 (1.8–68.6)	14.9 (0.2–69.2)	14.9 (0.2–79.1)	15.3 (0–79.1)
Facial involvement, n (%)*	72 (41.4)	77 (36.2)	77 (39.1)	226 (38.7)	476 (39.4)
Number of flares in last 12 mo, mean (SD)*	5.7 (13.6)	4.6 (4.5)	5.5 (8.4)	5.3 (9.3)	5.8 (16.8)

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

Efficacy in Patients Who Did Not Achieve IGA-TS

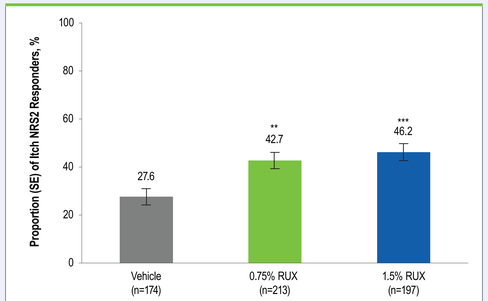
- Analysis of each endpoint of the definition for partial response indicated significant improvement for ruxolitinib cream vs vehicle at Week 8 in EASI-50 (**Figure 2**), itch NRS2 (**Figure 3**), DLQI/CDLQI (**Figure 4**), and 1-point reduction in IGA from baseline (**Figure 5**)
- Among patients who did not achieve IGA-TS, a clinically meaningful response in ≥1 of the above endpoints (composite partial response endpoint) was achieved in significantly more patients who applied ruxolitinib cream (88.3%/85.3% for 0.75%/1.5% ruxolitinib cream, respectively) vs vehicle (63.2%; both *P*<0.0001) at Week 8 (**Figure 6**)
- Similarly, more patients who applied ruxolitinib cream achieved a response vs vehicle when a 1-point reduction in IGA from baseline was added to the composite partial response definition (93.4%/90.9% for 0.75%/1.5% ruxolitinib cream, respectively; vehicle, 69.0%; both *P*<0.0001; **Figure 7**)

Figure 2. Proportion of Patients Achieving EASI-50 Who Did Not Achieve IGA-TS at Week 8



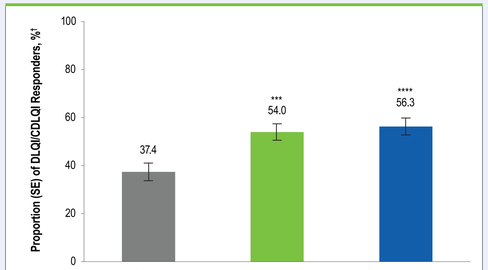
EASI-50, ≥50% improvement in Eczema Area and Severity Index from baseline; IGA-TS, Investigator's Global Assessment-treatment success; RUX, ruxolitinib cream.
**** *P*<0.0001 vs vehicle.

Figure 3. Proportion of Patients Achieving Itch NRS2 Who Did Not Achieve IGA-TS at Week 8



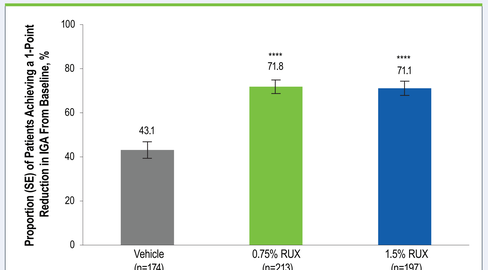
IGA-TS, Investigator's Global Assessment-treatment success; NRS2, ≥2-point reduction in itch numerical rating scale score from baseline; RUX, ruxolitinib cream.
** *P*<0.01 vs vehicle; *** *P*<0.001 vs vehicle.

Figure 4. Proportion of Patients Achieving DLQI/CDLQI Response Who Did Not Achieve IGA-TS at Week 8



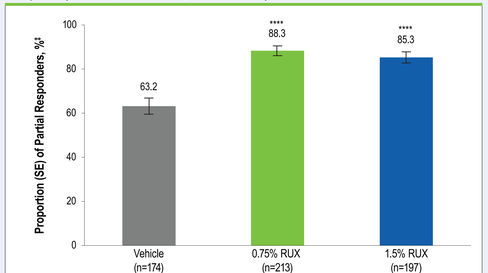
CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; IGA-TS, Investigator's Global Assessment-treatment success; RUX, ruxolitinib cream.
† Defined as a 24-point reduction in DLQI score or ≥6-point reduction in CDLQI score.
*** *P*<0.001 vs vehicle; **** *P*<0.0001 vs vehicle.

Figure 5. Proportion of Patients Achieving a 1-Point Reduction in IGA From Baseline Who Did Not Achieve IGA-TS at Week 8



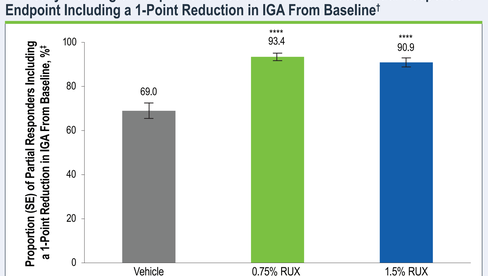
IGA, Investigator's Global Assessment; IGA-TS, IGA-treatment success; RUX, ruxolitinib cream.
**** *P*<0.0001 vs vehicle.

Figure 6. Composite Partial Response: Proportion of Patients Achieving a Clinically Meaningful Response at Week 8 in ≥1 Individual Partial Response Endpoint (EASI-50, Itch NRS2, DLQI/CDLQI)†



CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI-50, ≥50% improvement in Eczema Area and Severity Index from baseline; IGA-TS, Investigator's Global Assessment-treatment success; NRS2, ≥2-point reduction in itch numerical rating scale score from baseline; RUX, ruxolitinib cream.
† Among patients who did not achieve IGA-TS at Week 8.
‡ Defined as patients who achieved ≥1 of the following clinically meaningful responses: EASI-50, itch NRS2, ≥4-point reduction in DLQI score, or ≥6-point reduction in CDLQI score.
**** *P*<0.0001 vs vehicle.

Figure 7. Composite Partial Response: Proportion of Patients Achieving a Clinically Meaningful Response at Week 8 in ≥1 Individual Partial Response Endpoint Including a 1-Point Reduction in IGA From Baseline†



CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI-50, ≥50% improvement in Eczema Area and Severity Index from baseline; IGA-TS, Investigator's Global Assessment-treatment success; NRS2, ≥2-point reduction in itch numerical rating scale score from baseline; RUX, ruxolitinib cream.
† Among patients who did not achieve IGA-TS at Week 8.
‡ Defined as patients who achieved ≥1 of the following clinically meaningful responses: EASI-50, itch NRS2, ≥4-point reduction in DLQI score, ≥6-point reduction in CDLQI score, or a 1-point reduction in IGA from baseline.
**** *P*<0.0001 vs vehicle.

Efficacy in All Patients

- Among all patients in the efficacy-evaluable population, significantly more patients who applied ruxolitinib cream achieved IGA-TS or a partial response by EASI-50, itch NRS2, or DLQI/CDLQI at Week 8 (94.2%/93.6% for 0.75%/1.5% ruxolitinib cream, respectively; vehicle, 68.3%; both *P*<0.0001); results were similar with the addition of a 1-point reduction in IGA from baseline as a partial response parameter (96.7%/96.0% for 0.75%/1.5% ruxolitinib cream, respectively, vs 73.3% for vehicle; both *P*<0.0001)
  - Among all patients in the efficacy-evaluable population, a 1-point reduction in IGA from baseline at Week 8 was achieved by substantially more patients who applied ruxolitinib cream (86.0%/87.3% for 0.75%/1.5% ruxolitinib cream, respectively) vs vehicle (51.0%)
    - Although less stringent than the more challenging 2-point reduction required for IGA-TS, a 1-point reduction denotes a relevant decrease in disease severity (ie, moderate to mild [3 to 2] or mild to almost clear [2 to 1])

Safety

- In the overall population, ruxolitinib cream was well tolerated with an adverse event (AE) profile similar to vehicle[5]; no serious AEs were related to ruxolitinib cream

Conclusions

- **These data show that ruxolitinib cream provides clinically relevant improvements in the majority of patients who did not achieve IGA 0/1 with ≥2-grade improvement from baseline**
- **Significant differences with ruxolitinib cream vs vehicle were observed for EASI-50, itch NRS2, DLQI/CDLQI, and a 1-point reduction in IGA from baseline**
- **In the overall population of patients who applied ruxolitinib cream, ≥95% of patients achieved ≥1 clinically relevant response in signs, symptoms, or quality-of-life measures at Week 8**
- **Importantly, nearly 90% of all patients treated with ruxolitinib cream showed a relevant clinical benefit per reduction in disease severity assessed by IGA at Week 8**

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. 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. AB has served as a scientific adviser 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. MEK, MEV, and KS are employees and shareholders of Incyte Corporation. 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.

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). Writing assistance was provided by Sonia Mohinta, PhD, an employee of ICON (North Wales, PA), and was funded by Incyte Corporation.

References

1. Langan SM, et al. *Lancet*. 2020;396(10247):345-360. **2.** Bao L, et al. *JAKSTAT*. 2013;2(3):e24137. **3.** Oetjen LK, et al. *Cell*. 2017;171(1):217-228. **4.** Quintas-Cardama A, et al. *Blood*. 2010;115(15):3109-3117. **5.** Papp K, et al. *Br J Dermatol*. 2020;183(4):e116.

To download a copy of this poster, scan code.