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Presented at
Revolutionizing Atopic Dermatitis
Washington, DC • April 29–May 1, 2023

Rapid, Substantial, and Sustained Reduction of Itch in Adults With Atopic Dermatitis Applying Ruxolitinib Cream

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Introduction

- Atopic dermatitis (AD) is a chronic, recurring, highly pruritic inflammatory skin disease[1]
- The mechanical injury from scratching contributes to skin inflammation and barrier disruption, exacerbating the itch–scratch cycle, which perpetuates the disease[2]
- Ruxolitinib cream is a topical formulation of ruxolitinib, a selective Janus kinase (JAK) 1/JAK2 inhibitor, approved in the United States for the short-term and non-continuous chronic treatment of mild to moderate AD in non-immunocompromised patients ≥12 years old whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable[3]
- In two pivotal phase 3 trials (TRuE-AD1 and TRuE-AD2) in adolescents and adults with AD, 1.5% ruxolitinib cream demonstrated significant improvement in itch vs vehicle cream, as early as 12 hours after initial application[4,5]

Objective

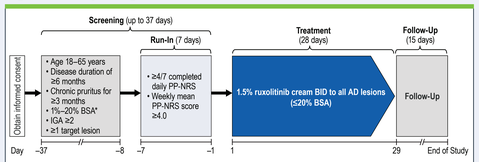
- To further understand the short-term clinical benefits of ruxolitinib cream to control pruritus and reduce disease severity in patients with AD in a phase 2, open-label, single-site study (SCRATCH-AD; NCT04839380)

Methods

Patients and Study Design

- In this single-site Canadian study, eligible patients were aged 18–65 years with AD for ≥6 months, chronic itch related to AD for ≥3 months, 1%–20% affected body surface area (excluding palms, soles, scalp, genitals, and folds), Investigator's Global Assessment (IGA) of ≥2, and a peak pruritus numerical rating scale (PP-NRS) score ≥4 at screening and baseline
  - PP-NRS is reported as the worst level of itch during the past 24-hour period from 0 (no itch) to 10 (worst imaginable itch)[6-8]
- Key exclusion criteria were unstable course of AD, clinically infected AD or use of antibiotics within 2 weeks of the run-in period, history of other skin conditions that could interfere with study assessments, history of hypertrophic scarring or keloid formation, clearly defined etiology for pruritus other than AD, immunocompromised status, use of AD systemic therapies (other than oral, nonsedative H_1 antihistamines) or phototherapy within 4 weeks prior to the run-in period and during the study, use of dupilumab within 26 weeks prior to the run-in period, use of other biologic that could interfere with the course or assessment of AD within 12 weeks or 5-half-lives (whichever is longer) of the run-in period, use of AD topical therapies (except bland emollients) within 2 weeks prior to the run-in 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
- Patients were given an electronic diary to record daily PP-NRS each morning from screening through Day –1 and from Day 2 through Day 29
  - In the 7-day run-in to Day 1, patients were required to complete ≥4 of 7 PP-NRS assessments and have a baseline mean PP-NRS ≥4.0 during this period
- All patients applied 1.5% ruxolitinib cream twice daily (BID) approximately 12 hours apart to all AD lesions identified on Day 1 for 28 days and any new lesions (**Figure 1**)

Figure 1. Study Design



* Excluding palms, soles, scalp, genitals, and folds.
AD, atopic dermatitis; BID, twice daily; BSA, body surface area; IGA, Investigator's Global Assessment; PP-NRS, peak pruritus numerical rating scale.

Assessments

- On Day 1, patients remained at the study center and reported modified PP-NRS (mPP-NRS; current itch intensity)[6-8] pre-dose and at 15 minutes, 30 minutes, 1 hour, 2 hours, 4 hours, and 6 hours post-application of ruxolitinib cream
  - Patients reported the 12-hour mPP-NRS assessment at home prior to the evening application
- On Day 2 (approximately 24 hours after initial application) through Day 29, patients reported PP-NRS in their electronic diaries prior to the morning application of ruxolitinib cream
- IGA was assessed at site visits on Days 1, 8, 15, and 29
- Transepidermal water loss (TEWL) was assessed at target lesions representative of overall disease during site visits on Days 1 and 29

Endpoints

- The primary endpoint was change from baseline in PP-NRS on Day 2
- Secondary endpoints included:
  - Change from baseline in mPP-NRS at 15 and 30 minutes and at 1, 2, 4, 6, and 12 hours post-treatment on Day 1
  - Change from baseline in PP-NRS on Days 3–29
  - Change from baseline in IGA at Days 8, 15, and 29
- Safety and tolerability assessments included frequency of treatment-emergent adverse events (AEs), treatment-related AEs, serious AEs, and AEs leading to treatment discontinuation

Statistical Analyses

- Data were summarized using descriptive statistics, reported as observed
- All patients who applied ≥1 application of ruxolitinib cream were included in the safety analysis

Results

Patients

- Of 49 enrolled patients who applied ruxolitinib cream at least once, 46 patients completed the run-in period, met the inclusion and exclusion criteria, and had both baseline and ≥1 post-baseline assessment of PP-NRS or mPP-NRS (modified intent-to-treat population; **Table 1**)
- Baseline demographics were similar to those of patients in the phase 3 TRuE-AD studies[4,5]
  - Mean (SD) 7-day average PP-NRS during the run-in period was 6.7 (1.36)
  - Mean (SD) pre-treatment mPP-NRS score was 6.4 (1.72)
  - 89.1% had an IGA score of 3

Table 1. Patient Demographics and Baseline Clinical Characteristics (mITT Population)

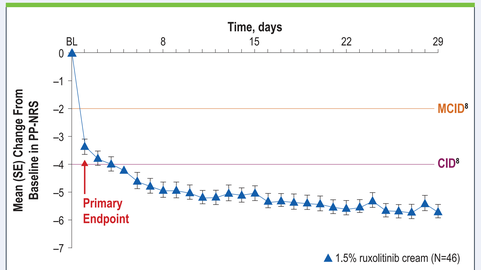
Characteristic	1.5% Ruxolitinib Cream (N=46)
Age, median (range), y	30.0 (18–64)
Female, n (%)	32 (69.6)
Race, n (%)	
White	41 (89.1)
Black	4 (8.7)
Asian	1 (2.2)
BSA affected, mean (SD), %	9.5 (4.94)
PP-NRS, mean (SD)*	6.7 (1.36)
mPP-NRS, mean (SD)	6.4 (1.72)
IGA, n (%)	
2	5 (10.9)
3	41 (89.1)
EASI, mean (SD)	6.9 (2.94)
Median TEWL score, mean (SD)	
Lesional	35.0 (17.47)
Non-lesional	15.1 (7.42)

* Mean over the run-in period.
BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; mITT, modified intent-to-treat; mPP-NRS, modified peak pruritus numerical rating scale; PP-NRS, peak pruritus numerical rating scale; TEWL, transepidermal water loss.

Efficacy

- The mean (SE) change from baseline in PP-NRS on Day 2 was –3.4 (0.28) (**Figure 2**)
- Mean (SE) change from baseline PP-NRS continued to increase through Day 29 (–5.7 [1.60]) (**Figure 2**)

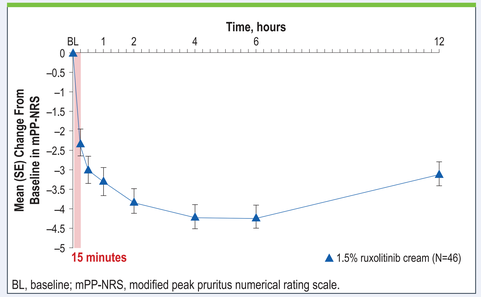
Figure 2. Mean (SE) Change From Baseline in PP-NRS Score



BL, baseline; CID, clinically important difference; MCID, minimal clinically important difference; PP-NRS, peak pruritus numerical rating scale.

- Mean (SE) change from baseline in mPP-NRS at 15 minutes post-treatment was –2.3 (0.35), peaking at –4.2 (0.31) at 4 hours, and was –3.1 (0.31) at 12 hours (**Figure 3**)

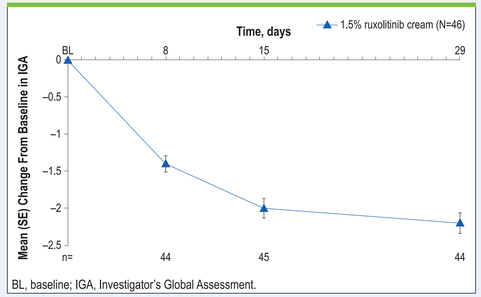
Figure 3. Mean (SE) Change From Baseline in mPP-NRS Score



BL, baseline; mPP-NRS, modified peak pruritus numerical rating scale.

- The mean (SE) changes from baseline in IGA score on Days 8, 15, and 29 were –1.4 (0.11), –2.0 (0.13), and –2.2 (0.14), respectively (**Figure 4**)

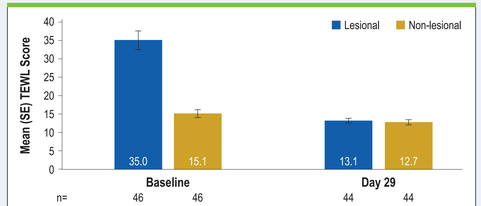
Figure 4. Mean (SE) Change From Baseline in IGA



BL, baseline; IGA, Investigator's Global Assessment.

- Lesional skin treated with 1.5% ruxolitinib cream BID showed substantial decrease in TEWL from a baseline mean (SE) score of 35.0 (2.58) to 13.1 (0.67) through Day 29, thus reaching similar levels to the non-lesional skin score of 12.7 (0.69) (**Figure 5**)

Figure 5. Mean (SE) TEWL* Score at Baseline and Day 29



AD, atopic dermatitis; TEWL, transepidermal water loss.
* Used to quantify the clinical severity of AD and the associated effect on skin barrier function.

Safety

- Treatment-emergent AEs (TEAEs) were reported in 15/49 (30.6%) participants; all were grade 1 or 2; none were serious (**Table 2**)
- 1 participant had a treatment-related TEAE (grade 1 application site reaction [acne])
- No patient discontinued treatment due to a TEAE

Table 2. TEAEs (Safety Population)

Parameter, n (%)	Ruxolitinib Cream (N=49)
Patients with TEAE	15 (30.6)
Most common TEAEs*	
COVID-19	3 (6.1)
Back pain	2 (4.1)
Headache	2 (4.1)
Nasopharyngitis	2 (4.1)
Upper respiratory tract infection	2 (4.1)
Patients with treatment-related TEAE†	1 (2.0)
Patients with serious TEAE	0
Patients with TEAE leading to discontinuation	0

* Occurring in ≥2 patients.
† One patient had application site acne.
TEAE, treatment-emergent adverse event.

Conclusions

- **Participants with AD applying 1.5% ruxolitinib cream in this study experienced rapid, substantial improvement in itch, which was sustained and further improved through 28 days of treatment**
  - **Itch reduction was observed as early as 15 minutes after first ruxolitinib cream application, and peak reduction was observed at 4 hours after first application**
- **These results are consistent with the established data on ruxolitinib cream as an effective, well-tolerated topical treatment for AD**

Disclosures

RB is an employee and shareholder of Innovaderm Research, has served as an advisory board member, consultant, speaker and/or investigator and received honoraria and/or grants from AbbVie, Arcutis, Arena Pharma, Aristea, Asana BioSciences, Bellus Health, Bluefin Biomedicine, Boehringer Ingelheim, CARA, Dermavant, Eli Lilly, EMD Serono, Evidera, Galderma, GlaxoSmithKline, Incyte, Inmagene Bio, Kiniksa, Kyowa Kirin, LEO Pharma, Novan, Pfizer, Ralexar, RAPT Therapeutics, Regeneron, Respivant, Sanofi-Genzyme, Sienna, Target RWE, and Vyne Therapeutics. HR, HN, and PH are employees and shareholders of Incyte Corporation. ES-CP has served as an advisory board member, consultant, speaker and/or investigator and received honoraria and/or grants from AbbVie, Arcutis, Arena Pharma, Aristea, Asana BioSciences, Bellus Health, Boehringer Ingelheim, Bristol Myers Squibb, CARA, Celgene, Dermavant, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Kiniksa, LEO Pharma, Neokera, Pfizer, Regeneron, Sanofi-Genzyme, Sienna, Target RWE, and UCB Pharma.

Acknowledgments

This study was funded by Incyte (Wilmington, DE, USA). Writing assistance was provided by Joshua Solomon, PhD, an employee of ICON (Blue Bell, PA, USA) and was funded by Incyte Corporation.

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