Efficacy and Safety of Ruxolitinib Cream for the Treatment of Moderate to Severe Chronic Hand Eczema: Top-Line Results From a 16-Week, Multicenter, Randomized, Double-Blind Study

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Introduction

- Hand eczema is a common inflammatory disorder involving skin of the hands[1,2]
- Chronic hand eczema (CHE) is defined as hand eczema that persists for >3 months or recurs ≥2 times within a 12-month period[2]
  - Symptoms typically include pruritus, burning, pain, stinging, sleep disturbances, and/or mood disturbances[1]
  - Clinical signs include redness, skin thickening, scaling, edema, vesicles, hyperkeratosis, and fissures[2]
- Pathophysiology of hand eczema is mediated through multiple cytokines acting through the Janus kinase (JAK)-signal transducer and activator of transcription (STAT) signaling pathway[3,4]
- Ruxolitinib cream is a selective JAK1/JAK2 inhibitor designed for topical administration[5]

Objective

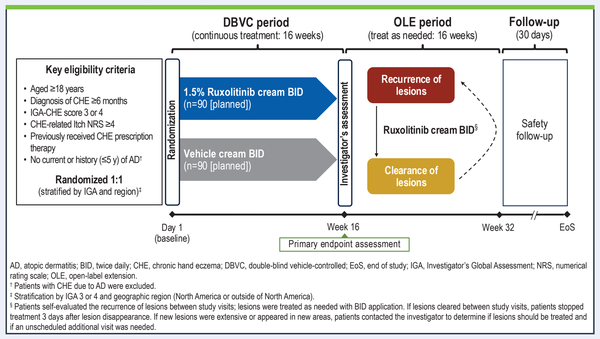
- To investigate the efficacy and safety of 1.5% ruxolitinib cream in adults with moderate to severe CHE (NCT05906628)

Methods

Patients and Study Design

- Eligible patients were randomized 1:1 to apply 1.5% ruxolitinib cream or vehicle cream twice daily (BID) for 16 weeks (double-blind vehicle-controlled period; **Figure 1**)
  - Patients with current atopic dermatitis (AD), history of AD within the past 5 years, or CHE as a result of AD were excluded from the study
- At Week 16, patients applied 1.5% ruxolitinib cream BID as needed for an additional 16 weeks (open-label extension period)

Figure 1. Study Design



AD, atopic dermatitis; BID, twice daily; CHE, chronic hand eczema; DBVC, double-blind vehicle-controlled; EoS, end of study; IGA, Investigator's Global Assessment; NRS, numerical rating scale; OLE, open-label extension.
† Patients with CHE due to AD were excluded.
‡ Stratification by IGA 3 or 4 and geographic region (North America or outside of North America).
§ Patients self-evaluated the recurrence of lesions between study visits; lesions were treated as needed with BID application. 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 lesions should be treated and if an unscheduled additional visit was needed.

Results

Patients

- A total of 186 patients were randomized (vehicle, n=92; ruxolitinib cream, n=94; **Table 1**)
- 7 (7.4%) and 14 (15.2%) patients in the ruxolitinib cream and vehicle groups, respectively, discontinued from the study; no discontinuations were due to treatment-emergent adverse events (TEAEs)

Table 1. Patient Demographics and Baseline Clinical Characteristics

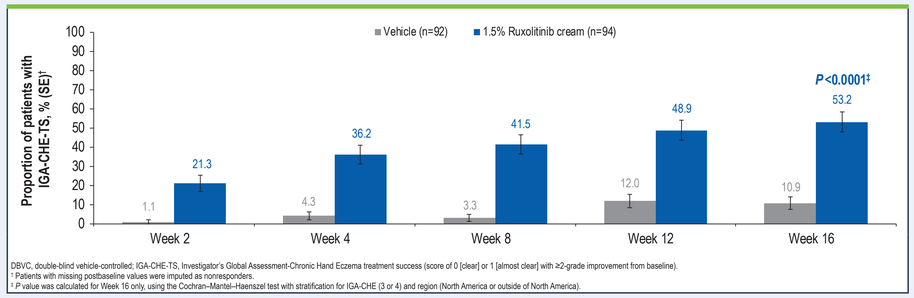
Characteristic	Total (N=186)
Age, median (range), y	50.0 (18–80)
18–64 y, n (%)	157 (84.4)
≥65 y, n (%)	29 (15.6)
Female, n (%)	111 (59.7)
White, n (%)	168 (90.3)
Geographic region, n (%)	
North America	114 (61.3)
Outside of North America	72 (38.7)
CHE type, n (%)†	
Irritant contact dermatitis	51 (27.4)
Allergic contact dermatitis	30 (16.1)
Vesicular (pompholyx)	28 (15.1)
Hyperkeratotic eczema	26 (14.0)
Contact urticaria/protein contact dermatitis	1 (0.5)
Unclassified‡	60 (32.3)
IGA-CHE score, n (%)	
3 (moderate)	135 (72.6)
4 (severe)	51 (27.4)
Itch NRS score, median (range)	6.6 (2.1–10)
Skin Pain NRS score, median (range)	6.3 (0.6–10)
Time since initial CHE diagnosis, median (range), y	6.0 (0.6–54.0)

CHE, chronic hand eczema; IGA, Investigator's Global Assessment; NRS, numerical rating scale.
† More than 1 CHE type could be selected.
‡ Defined by investigators as a CHE type that is not atopic hand eczema (exclusion criteria for the study) and does not fit other listed types.

Efficacy

- At Week 16, significantly more patients who applied ruxolitinib cream vs vehicle achieved Investigator's Global Assessment-Chronic Hand Eczema (IGA-CHE) treatment success (P<0.0001; primary endpoint), defined as an IGA-CHE score of 0 (clear) or 1 (almost clear) with a ≥2-grade improvement from baseline (**Figure 2**)

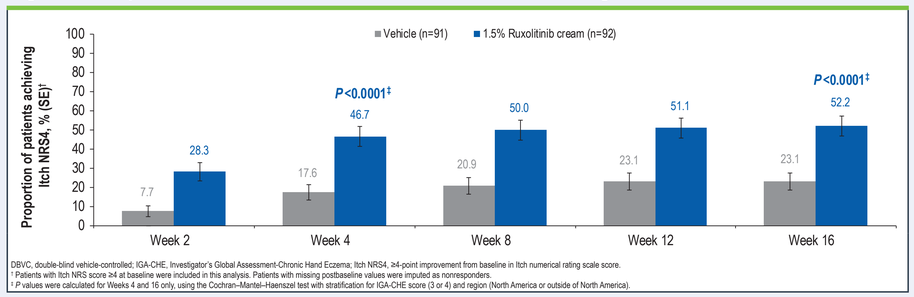
Figure 2. Proportion of Patients Who Achieved IGA-CHE-TS During the DBVC Period



DBVC, double-blind vehicle-controlled; IGA-CHE-TS, Investigator's Global Assessment-Chronic Hand Eczema treatment success (score of 0 [clear] or 1 [almost clear] with ≥2-grade improvement from baseline).
† Patients with missing postbaseline values were imputed as nonresponders.
‡ P value was calculated for Week 16 only, using the Cochran–Mantel–Haenszel test with stratification for IGA-CHE (3 or 4) and region (North America or outside of North America).

- Significantly more patients who applied ruxolitinib cream vs vehicle achieved a ≥4-point improvement from baseline in Itch numerical rating scale score (Itch NRS4) at Weeks 4 and 16 (P<0.0001; key secondary endpoints; **Figure 3**)
  - Numerical improvements with ruxolitinib cream vs vehicle were observed on Day 2, with statistically significant improvement observed on Day 7 (27.4% vs 9.0% [multiple imputation of missing postbaseline values]; P=0.0024; key secondary endpoint)

Figure 3. Proportion of Patients Who Achieved Itch NRS4 During the DBVC Period



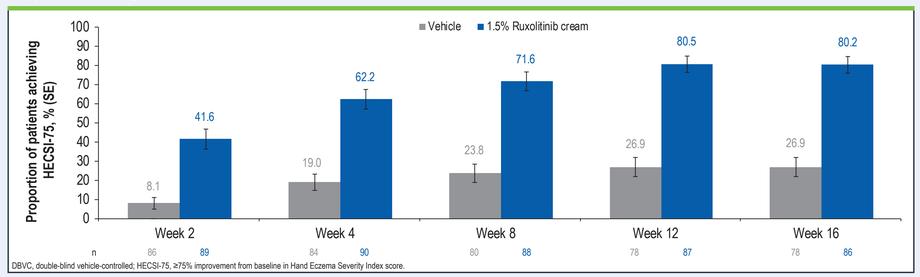
DBVC, double-blind vehicle-controlled; IGA-CHE, Investigator's Global Assessment-Chronic Hand Eczema; Itch NRS4, ≥4-point improvement from baseline in Itch numerical rating scale score.
† Patients with Itch NRS score ≥4 at baseline were included in this analysis. Patients with missing postbaseline values were imputed as nonresponders.
‡ P values were calculated for Weeks 4 and 16 only, using the Cochran–Mantel–Haenszel test with stratification for IGA-CHE score (3 or 4) and region (North America or outside of North America).

- Substantially more patients who applied ruxolitinib cream vs vehicle achieved a ≥75% (**Figure 4**) or ≥90% (**Figure 5**) improvement from baseline in Hand Eczema Severity Index (HECSI) score

Safety

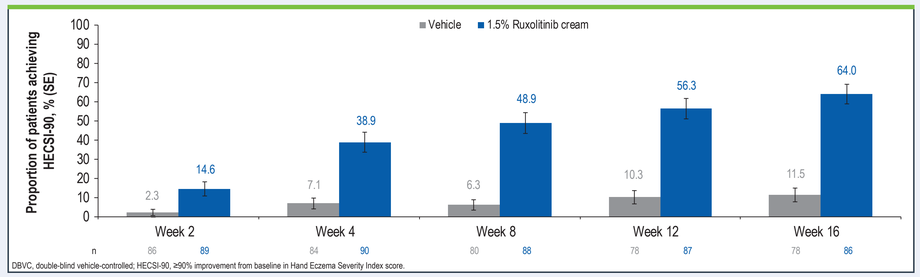
- No new safety signals emerged in the 16-week, double-blind, vehicle-controlled period (**Table 2**); no serious infections, major adverse cardiovascular events, malignancies, or thromboses were observed

Figure 4. Proportion of Patients Who Achieved HECSI-75 During the DBVC Period



DBVC, double-blind vehicle-controlled; HECSI-75, ≥75% improvement from baseline in Hand Eczema Severity Index score.

Figure 5. Proportion of Patients Who Achieved HECSI-90 During the DBVC Period



DBVC, double-blind vehicle-controlled; HECSI-90, ≥90% improvement from baseline in Hand Eczema Severity Index score.

Table 2. Safety in the DBVC Period

n (%)	Vehicle (n=92)	1.5% Ruxolitinib cream (n=94)
Patients with TEAE	29 (31.5)	36 (38.3)
Most common TEAEs†		
Nasopharyngitis	9 (9.8)	7 (7.4)
Upper respiratory tract infection	3 (3.3)	4 (4.3)
Arthralgia	2 (2.2)	2 (2.1)
COVID-19	3 (3.3)	1 (1.1)
Hypertension	2 (2.2)	1 (1.1)
Bronchitis	0	2 (2.1)
Helicobacter infection	0	2 (2.1)
Tonsillitis	2 (2.2)	0
Patients with treatment-related TEAE	3 (3.3)	6 (6.4)
Application site pain	1 (1.1)	1 (1.1)
Application site paresthesia	0	1 (1.1)
Application site reaction	0	1 (1.1)
Arthralgia	1 (1.1)	0
Drug hypersensitivity	1 (1.1)	0
Eczema	0	1 (1.1)
Hand dermatitis	1 (1.1)	0
Skin papilloma	0	1 (1.1)
Upper respiratory tract infection	0	1 (1.1)
Patients with grade ≥3 TEAE‡	1 (1.1)	2 (2.1)
Patients with serious TEAE§	1 (1.1)	2 (2.1)
Patients with TEAE leading to discontinuation of study drug	0	0
Patients with TEAE leading to dose reduction/interruption	0	0

DBVC, double-blind vehicle-controlled; TEAE, treatment-emergent adverse event.
† Occurred in ≥2% of patients in either treatment group.
‡ No events were considered related to treatment.
§ Serious TEAEs included retinal artery embolism (n=1) in the vehicle group and prostatic obstruction and sinus node dysfunction (both n=1) in the ruxolitinib cream group. None were considered related to treatment.

Conclusions

- **Ruxolitinib cream demonstrated significant reductions of CHE signs and symptoms vs vehicle at Week 16**
- **Significantly more patients achieved Itch NRS4 response vs vehicle during the first 7 days of treatment, with numerical increases observed by Day 2**
- **Ruxolitinib cream was generally well tolerated and consistent with the known safety profile[6,7]**
- **Ruxolitinib cream may represent a novel approach for the treatment of adults with CHE**

Disclosures

MZ has served as an investigator for AbbVie, Acrotech, Aldeyra, Amgen, AnaptysBio, Arcutis, Biocon, Bristol Myers Squibb, Cara Therapeutics, Dermavant, Edessa Biotech, Evelo, Galderma, Incyte Corporation, Janssen, LEO Pharma, Lilly, Nimbus, Novan, Pfizer, Q32 Bio, Regeneron, Sanofi, Sun Pharma, Takeda, and UCB; as a consultant for AbbVie, Advanced Derm Solutions, Aldeyra, All Free Clear/Sun Laundry Products, Apogee, Arcutis, Basuch and Lomb, Beiersdorf, Cara Therapeutics, Dermavant, Galderma, Google, Incyte Corporation, Janssen, L'Oreal, LEO Pharma, Level-Ex, Lilly, LUUM, Meta, Novan, Novartis, Pfizer, Regeneron, Sanofi, Supernus, Takeda, Trevi, Trifecta, and Verrica; and as a speaker for AbbVie, Advanced Derm Solutions, Dermavant, Incyte Corporation, LEO Pharma, Lilly, Novan, Pfizer, Regeneron, Sanofi, and Verrica. PH is an employee of Incyte Biosciences International Sàrl and a shareholder of Incyte Corporation. ZL, YK, and HN are employees and shareholders of Incyte Corporation. LFSG has served as an investigator, advisor, and/or speaker for AbbVie, Arcutis, Bristol Myers Squibb, Dermavant, Eli Lilly, Incyte Corporation, Ortho Dermatologics, Pfizer, Regeneron, and Sanofi.

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