43978

Presented at the
American Academy of Dermatology (AAD) Annual Meeting
New Orleans, LA
March 17–21, 2023

Treatment-Emergent Adverse Events of Interest for Janus Kinase Inhibitors: Pooled Analysis of the 52-Week TRuE-V Phase 3 Studies of Ruxolitinib Cream Treatment for Vitiligo

Amit G. Pandya, MD,[1,2*] Khaled Ezzedine, MD, PhD,[3] David Rosmarin, MD,[4] Thierry Passeron, MD, PhD,[5] Seemal R. Desai, MD,[1,6] Mark Lebwohl, MD,[7] Deanna Kornacki, PhD,[8] Kang Sun, PhD,[8] Kathleen Butler, MD,[8] Albert Wolkerstorfer, MD, PhD[9]

[1]University of Texas Southwestern Medical Center, Dallas, TX, USA; [2]Palo Alto Foundation Medical Group, Sunnyvale, CA, USA; [3]Henri Mondor University Hospital and Université Paris-Est Créteil Val de Marne, Paris, France; [4]Indiana University School of Medicine, Indianapolis, IN, USA; [5]Centre Hospitalier Universitaire de Nice, Université Côte d'Azur, Nice, France; [6]Innovative Dermatology, Plano, TX, USA; [7]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [8]Incyte Corporation, Wilmington, DE, USA; [9]Amsterdam University Medical Center, Amsterdam, Netherlands

* Presenting author

Introduction

- Vitiligo is a chronic autoimmune disease that targets melanocytes, resulting in patches of skin depigmentation[1]
- Disease pathogenesis is modulated by signaling through the Janus kinases (JAKs)[2]
- A cream formulation of ruxolitinib, a JAK1/JAK2 inhibitor, was recently approved by the US Food and Drug Administration for topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older[3]
- Prescribing information for ruxolitinib cream, similar to other JAK inhibitors,[4,5] contains a boxed warning for serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis[3]
- In two randomized phase 3 studies in adolescent and adult patients (TRuE-V1 [NCT04052425]/TRuE-V2 [NCT04057573]), ruxolitinib cream was statistically superior to vehicle at Week 24 in the primary and all key secondary endpoints, with a higher proportion of patients responding at Week 52[6]

Objective

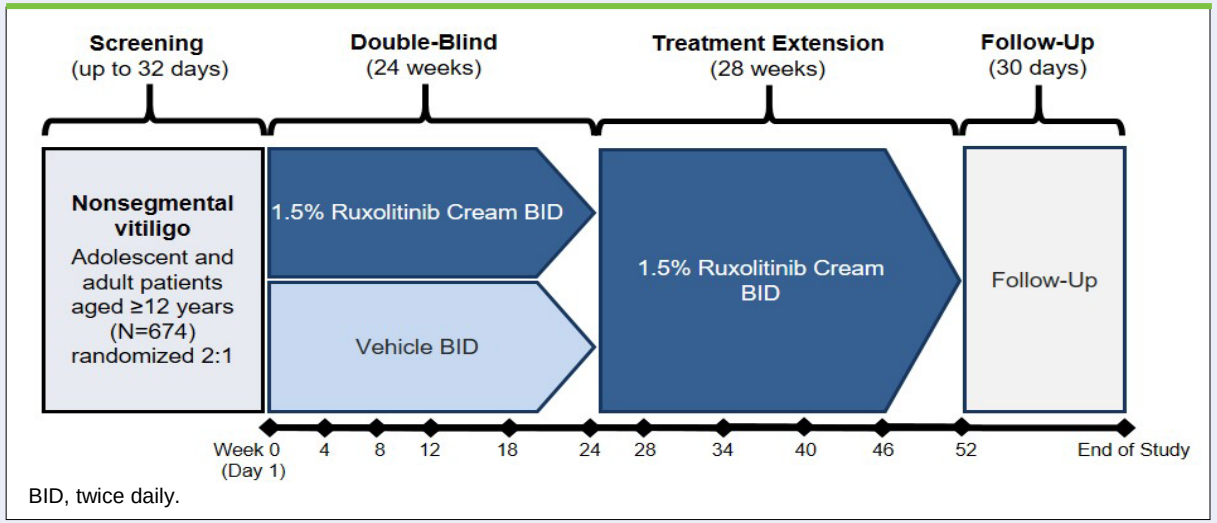
- To summarize the treatment-emergent adverse events (TEAEs) and evaluate JAK class TEAEs among patients who applied ruxolitinib cream in two 52-week phase 3 studies of adolescents and adults with vitiligo

Methods

Patients and Study Design

- For both studies, eligible patients were aged ≥12 years with a diagnosis of nonsegmental vitiligo and depigmented areas covering ≤10% total body surface area (BSA), including ≥0.5% BSA on the face and ≥3% BSA on non-facial areas, scores ≥0.5 on facial Vitiligo Area Scoring Index (F-VASI), and scores ≥3 on total VASI (T-VASI)
- Key exclusion criteria and study design (**Figure 1**) have been described previously[6]
  - Pooled data at Week 52 are reported here

Figure 1. Study Design



BID, twice daily.

Endpoints and Assessments

- The safety and tolerability of ruxolitinib cream were assessed based on monitoring of adverse events (AEs) and laboratory data throughout the study
  - AEs were tabulated by Medical Dictionary for Regulatory Activities (MedDRA) preferred terms and their severity was evaluated using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v5.0

Statistical Analysis

- Data were summarized using descriptive statistics
- All patients who applied ≥1 dose of study drug were included in the safety analysis

Results

Patients

- A total of 637 patients applied ruxolitinib cream at any time during the TRuE-V studies (ruxolitinib cream from Day 1, n=449; crossover from vehicle to ruxolitinib cream after Week 24, n=188)
  - Mean (SD) age was 39.6 (15.2) years; 54.0% were female, and 72.5% had Fitzpatrick skin types I–III
  - Median (range) duration of disease was 12.1 (0–60.5) years
  - Baseline mean (SD) F-VASI and T-VASI scores were 0.91 (0.55) and 6.66 (2.07), respectively
  - Patients applied ruxolitinib cream for a median (range) of 364 (1–416) days for those who applied ruxolitinib cream from Day 1 and 196 (1–226) days for those who crossed over from vehicle to ruxolitinib cream after Week 24

TEAEs

- Over 52 weeks, TEAEs occurred in 332 patients (52.1%; grade ≥3, 3.0%), most commonly COVID-19 (6.1%; grade ≥3, 0.2%), application site acne (5.3%; grade ≥3, 0%), and nasopharyngitis (4.9%; grade ≥3, 0%; **Table 1**)
- 14 patients (2.2%) had serious TEAEs, none of which were considered by investigators to be treatment-related
- There were no fatal TEAEs

Table 1. TEAEs in Patients Applying ≥1 Dose of Ruxolitinib Cream During the 52-Week Study Period

Characteristic	Vehicle to Ruxolitinib Cream After Week 24* (n=188)	Ruxolitinib Cream Since Day 1 (n=449)	Total Ruxolitinib Cream (N=637)
Patients with any TEAE	69 (36.7)	263 (58.6)	332 (52.1)
Most common TEAEs†			
COVID-19	6 (3.2)	33 (7.3)	39 (6.1)
Application site acne	5 (2.7)	29 (6.5)‡	34 (5.3)
Nasopharyngitis	5 (2.7)	26 (5.8)	31 (4.9)
Application site pruritus	1 (0.5)	24 (5.3)	25 (3.9)
Headache	3 (1.6)	22 (4.9)	25 (3.9)
Upper respiratory tract infection	5 (2.7)	15 (3.3)	20 (3.1)
Sinusitis	1 (0.5)	13 (2.9)	14 (2.2)
Patients with a treatment-related AE	11 (5.9)	76 (16.9)	87 (13.7)
Most common treatment-related AEs†			
Application site acne	3 (1.6)	25 (5.6)	28 (4.4)
Application site pruritis	1 (0.5)	21 (4.7)	22 (3.5)
Patients with any application site reaction	12 (6.4)	78 (17.4)	90 (14.1)
Patients who discontinued due to a TEAE	0	3 (0.7)§	3 (0.5)
Patients with a serious TEAE¶	3 (1.6)	11 (2.4)	14 (2.2)

AE, adverse event; OLE, open-label extension; TEAE, treatment-emergent adverse event.
* Patients who were randomized to apply vehicle cream on Day 1 and crossed over to ruxolitinib cream during the OLE period (Weeks 24–52).
† Occurring in ≥2% of total patients in this analysis.
‡ Leading to interruption of treatment in 1 patient.
§ Discontinued due to application site eczema (n=1), application site rash (n=1), and fatigue (n=1)
¶ No serious TEAEs were considered by investigators to be related to treatment.

Results *(cont.)*

TEAEs of Interest

- JAK-related TEAEs of interest were reported in <1% of patients with vitiligo who applied ruxolitinib cream for up to 52 weeks and included (**Table 2**):
  - Serious infections (n=3 [0.5%])
    - Appendiceal abscess (n=1, grade 4)
    - Appendicitis (n=1, grade 4)
    - Hepatitis infectious mononucleosis (n=1, grade 3)
  - Malignancies (n=4 [0.6%])
    - Basal cell carcinoma (n=1; not at the application site)
    - Ovarian cancer (n=1, grade 3)
    - Papillary thyroid cancer (n=1, serious, grade 3)
    - Prostate cancer (n=1, serious, grade 3)
  - Thromboembolic events (n=1 [0.2%])
    - Transient ischemic attack (n=1)
- No major adverse cardiovascular events were reported

Table 2. TEAEs of Interest in Patients Applying ≥1 Dose of Ruxolitinib Cream During the 52-Week Study Period

Characteristic*	Vehicle to Ruxolitinib Cream After Week 24† (n=188)	Ruxolitinib Cream Since Day 1 (n=449)	Total Ruxolitinib Cream (N=637)
Serious infections	1 (0.5)	2 (0.4)	3 (0.5)
Skin infections			
Application site folliculitis	0	4 (0.9)‡	4 (0.6)‡
Folliculitis	0	3 (0.7)	3 (0.5)
Acarodermatitis	0	2 (0.4)	2 (0.3)
Body tinea	1 (0.5)	1 (0.2)	2 (0.3)
Herpes zoster	0	2 (0.4)	2 (0.3)
Herpes simplex	1 (0.5)§	4 (0.9)§	5 (0.7)§
Cellulitis	0	1 (0.2)	1 (0.2)
Fungal skin infection	0	1 (0.2)	1 (0.2)
Infected dermal cyst	0	1 (0.2)	1 (0.2)
Paronychia	0	1 (0.2)	1 (0.2)
Skin bacterial infection	1 (0.5)	0	1 (0.2)
Tinea versicolor	0	1 (0.2)	1 (0.2)
Varicella	1 (0.5)	0	1 (0.2)
Malignancies	1 (0.5)	3 (0.7)	4 (0.6)
Thromboembolic events	0	1 (0.2)	1 (0.2)

AE, adverse event; OLE, open-label extension; TEAE, treatment-emergent adverse event.
* All TEAEs are non-serious, grade <3, and unrelated to treatment, except as noted.
† Patients who were randomized to apply vehicle cream on Day 1 and crossed over to ruxolitinib cream during the OLE period (Weeks 24–52).
‡ Treatment-related AE in 3 patients.
§ Possibly treatment-related AE in 2 patients.

Results *(cont.)*

- Hematopoietic TEAEs included erythropenia (0.8%), leukopenia (0.8%), thrombocytopenia (0.2%), and thrombocytosis (0.3%; **Table 3**)

Table 3. Hematopoietic TEAEs in Patients Applying ≥1 Dose of Ruxolitinib Cream During the 52-Week Study Period

Hematopoietic TEAE	Vehicle to Ruxolitinib Cream After Week 24* (n=188)	Ruxolitinib Cream Since Day 1 (n=449)	Total Ruxolitinib Cream (N=637)
Erythropenia	1 (0.4)	4 (0.9)	5 (0.8)
Neutropenia	4 (2.1)	1 (0.2)	5 (0.8)
Thrombocytopenia	0	1 (0.2)	1 (0.2)
Thrombocytosis	0	2 (0.4)	2 (0.3)

AE, adverse event; OLE, open-label extension; TEAE, treatment-emergent adverse event.
* Patients who were randomized to apply vehicle cream on Day 1 and crossed over to ruxolitinib cream during the OLE period (Weeks 24–52).

- Liver function tests were elevated in 2.2% of patients (**Table 4**)

Table 4. Liver Function TEAEs in Patients Applying ≥1 Dose of Ruxolitinib Cream During the 52-Week Study Period

Characteristic	Vehicle to Ruxolitinib Cream After Week 24* (n=188)	Ruxolitinib Cream Since Day 1 (n=449)	Total Ruxolitinib Cream (N=637)
Liver function test elevations	2 (1.1)	12 (2.7)	14 (2.2)
Alanine aminotransferase increased	1 (0.5)	8 (1.8)	9 (1.4)
Aspartate aminotransferase increased	0	5 (1.1)	5 (0.8)
Blood alkaline phosphatase increased	1 (0.5)	1 (0.2)	2 (0.3)
Transaminases increased	0	2 (0.4)	2 (0.3)

AE, adverse event; OLE, open-label extension; TEAE, treatment-emergent adverse event.
* Patients who were randomized to apply vehicle cream on Day 1 and crossed over to ruxolitinib cream during the OLE period (Weeks 24–52).

Conclusions

- **Ruxolitinib cream was well tolerated among patients with vitiligo for up to 52 weeks, and no serious treatment-related TEAEs were reported**
- **TEAEs of interest suggestive of systemic JAK inhibition as included in the boxed warning for JAK inhibitors were limited, occurring in <1% of patients with vitiligo who applied ruxolitinib cream for up to 52 weeks**
  - **There were no fatal TEAEs or major adverse cardiovascular events**

Disclosures

AGP has served as an investigator for Aclaris Therapeutics, Immune Tolerance Network, Incyte Corporation, and Pfizer; a consultant for AbbVie, Arcutis, Avita Medical, Chromaderm, Immune Tolerance Network, Incyte, Pfizer, TWi, Viela Bio, and Villaris; and holds stock options for Tara Medical and Zerigo Health. KE is a consultant for AbbVie, Incyte, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio. DR has received honoraria as a consultant for AbbVie, Abcuro, AltruBio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Concert, Dermavant Sciences, Dermira, Incyte, Janssen, Kyowa Kirin, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, Revolo Biotherapeutics, Sanofi, Sun Pharmaceuticals, UCB, and Viela Bio; has received research support from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Dermira, Galderma, Incyte, Janssen, Lilly, Merck, Novartis, Pfizer, and Regeneron Pharmaceuticals; and has served as a paid speaker for AbbVie, Amgen, Celgene, Janssen, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, and Sanofi. TP has received grants and/or honoraria from AbbVie, ACM Pharma, Almirall, Amgen, Astellas, Bristol Myers Squibb, Celgene, Galderma, Genzyme/Sanofi, GlaxoSmithKline, Incyte, Janssen, LEO Pharma, Eli Lilly, Novartis, Pfizer, Sun Pharmaceuticals, and UCB; is the cofounder of YUKIN Therapeutics; and has patents on WNT agonists or GSK3b antagonist for repigmentation of vitiligo and on the use of CXCR3B blockers in vitiligo. SRD has received fees and/or honoraria as a consultant for Almirall, Avita, Bristol Myers Squibb, Cassiopea SpA, Dermavant Sciences, Dermira, Ferndale Laboratories, Foamix, Galderma Laboratories LP, Incyte, MC2 Therapeutics, Ortho Dermatologics, Pfizer, Scientis, Sente Labs, SkinCeuticals LLC, UCB, and Verrica Pharmaceuticals; has received stock options as a consultant for Gore Range Capital; has received honoraria as a speaker for Almirall and Ortho Dermatologics; has received grants/research funding as an investigator for AbbVie, AOBiome LLC, Atacama Therapeutics, Brickell Biotech, Dermavant Sciences, Incyte, Novan, and SkinMedica; has served as an advisory board member for the Foundation for Research & Education of Dermatology; is a stockholder of Gore Range Capital; and is a shareholder in PDP of Texas. ML is an employee of Mount Sinai Hospital, which receives research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte, Janssen Research & Development, LLC, Ortho Dermatologics, Regeneron, and UCB, Inc; and is a consultant for Aditum Bio, Almirall, AnaptysBio, Arcutis, Aristea, Arrive Technology, Avotres Therapeutics, BioMX, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Dr. Reddy's Laboratories, Evelo, Evommune, Facilitate International Dermatologic Education, Forte, Foundation for Research and Education in Dermatology, Helsinn, Incyte, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, and Verrica. DK, KS, and KB are employees and shareholders of Incyte. AW is a dermatologist at the Netherlands Institute for Pigment Disorders and the Department of Dermatology at the Amsterdam University Medical Center; has served as principal investigator for Avita Medical, Incyte, and Novartis; has served as an advisory board member for Incyte; has received research grants from Avita Medical and Lumenis; and has received devices from Humeca and PerfAction.

Acknowledgments

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

References

1. Rodrigues M, et al. *J Am Acad Dermatol*. 2017;77(1):1-13. **2.** Rashighi M, Harris JE. *Ann Transl Med*. 2015;3(21):343. **3.** OPZELURA™ (ruxolitinib cream). Full Prescribing Information, Incyte Corporation, Wilmington, DE, 2022. **4.** Qian J, et al. *J Manag Care Spec Pharm*. 2022;28(9):1046-1052. **5.** US Food and Drug Administration. FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions. US Food & Drug Administration. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-warnings-about-increased-risk-serious-heart-related-events-cancer-blood-clots-and-death. Accessed December 12, 2022. **6.** Rosmarin D, et al. *N Engl J Med*. 2022;387:1445-1455.

To download a copy of this poster, scan code.