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Safety and Efficacy of Ruxolitinib Cream for the Treatment of Vitiligo: 104-Week Data From a Phase 2 Study

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Background

- Vitiligo is a chronic autoimmune disease resulting in skin depigmentation[1,2]
- Disease pathogenesis is driven by interferon-γ, which activates signaling pathways regulated by Janus kinase (JAK) 1 and JAK2[3]
- Ruxolitinib cream, a JAK1/JAK2 inhibitor, demonstrated significant repigmentation over 52 weeks in a phase 2, dose-ranging, randomized study of adult patients with vitiligo[4]

Objective

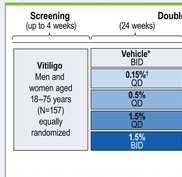
- To report the safety and efficacy of ruxolitinib cream following 104 weeks of treatment in a phase 2 study of adults with vitiligo

Methods

Patients and Study Design

- This phase 2 study (NCT03099304) enrolled adult patients (aged 18–75 years) with vitiligo that included depigmentation ≥0.5% of body surface area (BSA) on the face and ≥3% of BSA on nonfacial areas
- Key exclusion criteria included dermatologic disease confounding vitiligo assessment, previous use of JAK inhibitor therapy, and use of the following therapies for vitiligo: any biological or experimental therapy within 12 weeks (or 5 half-lives) of screening, phototherapy within 8 weeks of screening, or immunomodulating treatments within 4 weeks of screening
- Patients were equally randomized to receive ruxolitinib cream (1.5% twice daily [BID], 1.5% once daily [QD], 0.5% QD, or 0.15% QD) or vehicle BID for 24 weeks (**Figure 1**)
  - Patients were instructed to treat lesions constituting ≤20% of baseline total BSA for the duration of the study
- After 24 weeks, patients either were rerandomized (patients who initially received vehicle and those treated with 0.15% ruxolitinib cream QD who did not achieve ≥25% improvement from baseline in facial Vitiligo Area Scoring Index [F-VASI] at Week 24) to 1 of the 3 higher ruxolitinib cream doses or maintained their original dose until Week 52
- After Week 52, patients who completed baseline, Week 24, and Week 52 assessments could continue to receive open-label treatment with 1.5% ruxolitinib cream BID for an additional 104 weeks (total treatment duration of up to 156 weeks)
  - Patients were offered optional concomitant narrow-band ultraviolet-B phototherapy during open-label treatment (refer to poster 27636 for analyses of concomitant ruxolitinib cream and phototherapy)

Figure 1. Study Design



BID, twice daily; F-VASI, facial Vitiligo Area Scoring Index; NB-UVB, narrow-band ultraviolet-B; QD, once daily.
* Rerandomization to 0.5% QD, 1.5% QD, or 1.5% BID at Week 24 for vehicle group.
† Rerandomization to 0.5% QD, 1.5% QD, or 1.5% BID if <25% improvement in F-VASI at Week 24.
‡ Patients were offered optional concurrent NB-UVB phototherapy.

Assessments

- Efficacy assessments included the proportion of patients achieving the following endpoints with 1.5% ruxolitinib cream BID monotherapy at the Week 104 study visit
  - F-VASI response with improvements of ≥50%, ≥75%, and ≥90% (F-VASI50, F-VASI75, and F-VASI90, respectively)
  - Total Vitiligo Area Scoring Index (T-VASI) response with improvements of ≥50% and ≥75% (T-VASI50 and T-VASI75, respectively)
  - Facial Physician's Global Vitiligo Assessment (F-PhGVA) response, defined as achieving clear (completely repigmented, no signs of vitiligo) or almost clear (only specks of depigmentation) skin
  - Patient Global Impression of Change for Vitiligo (PaGIC-V) response, defined as achieving very much or much improvement
- Safety and tolerability assessments included the frequency of reported adverse events (AEs) and monitoring of hematologic parameters (ie, platelets and hemoglobin)

Statistical Analyses

- Data were summarized using descriptive statistics

Results

Patients

- A total of 94 patients were randomized to receive the 3 highest doses of ruxolitinib cream (0.5% QD, n=31; 1.5% QD, n=30; 1.5% BID, n=33)
- Of 80 patients who completed the 52-week randomized period, 77 entered the open-label period and applied 1.5% BID for 52 weeks (**Table 1**)
  - Mean (SD) age was 51.2 (12.0) years; 57.1% were male and 87.0% were White
- Of patients who entered the open-label period, 55 (71.4%) completed the Week 104 study visit and were included in these analyses
- At data cutoff for these analyses, 27 patients (35.1%) had discontinued open-label treatment (Weeks 52–156), most commonly because of withdrawal by patient (n=18)

Table 1. Patient Demographics and Baseline Characteristics for Patients Who Received 1.5% Ruxolitinib Cream BID

Parameter	All Patients in the Open-Label Period* n=77	Patients Initially Randomized to 1.5% BID n=33
Age, mean (SD), y	51.2 (12.0)	49.5 (12.3)
Male, n (%)	44 (57.1)	18 (54.5)
White, n (%)	67 (87.0)	29 (87.9)
Skin type, n (%)		
I	3 (3.9)	1 (3.0)
II	28 (36.4)	12 (36.4)
III	27 (35.1)	13 (39.4)
IV	11 (14.3)	4 (12.1)
V	4 (5.2)	1 (3.0)
VI	4 (5.2)	2 (6.1)
Baseline F-VASI, mean (SD)	1.29 (0.78)	1.26 (0.81)
Baseline T-VASI, mean (SD)	18.7 (16.1)	16.9 (14.3)
Facial BSA,† mean (SD), %	1.52 (0.83)	1.55 (0.89)
Total BSA, mean (SD), %	23.2 (19.5)	21.5 (16.8)
Disease duration, median (range), y	13.1 (0.3–59.0)	13.5 (0.8–47.8)
Diagnosed in childhood, n (%)	16 (20.8)	10 (30.3)
Other autoimmune disorders, n (%)		
Thyroid disorders	21 (27.3)	8 (24.2)
Juvenile diabetes mellitus	1 (1.3)	2 (6.1)
Prior therapy, n (%)		
Topical corticosteroids	35 (45.5)	14 (42.4)
Calcineurin inhibitors	32 (41.6)	14 (42.4)
Phototherapy‡	32 (41.6)	12 (36.4)

BID, twice daily; BSA, body surface area; F-VASI, facial Vitiligo Area Scoring Index; NA, not available; NB-UVB, narrow-band ultraviolet-B; PUVA, psoralen ultraviolet-A; T-VASI, total Vitiligo Area Scoring Index.
* Includes patients initially randomized to 0.5% QD (n=28), 1.5% QD (n=21), and 1.5% BID (n=28).
† Percentage of total BSA.
‡ Phototherapy includes NB-UVB phototherapy, excimer laser, and PUVA photochemotherapy.

Efficacy

All Evaluable Patients

- Among all evaluable patients with a Week 104 study visit (n=55), F-VASI50, F-VASI75, and F-VASI90 were achieved by 83.6%, 65.5%, and 52.7% of patients, respectively
  - Responses at Weeks 24 and 52 are shown in **Table 2**
- T-VASI50 and T-VASI75 were achieved by 58.2% and 27.3% of patients, respectively, at Week 104
- Patients also achieved responses on the F-PhGVA (43.6%) and PaGIC-V (55.6%) with 1.5% ruxolitinib cream BID at Week 104

Table 2. Efficacy of 1.5% Ruxolitinib Cream BID Among All Evaluable Patients

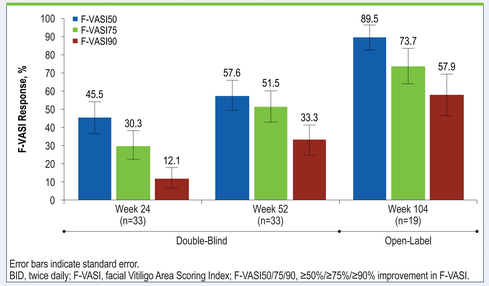
Endpoint	Week 24 n/N (%)	Week 52 n/N (%)	Week 104 n/N (%)
F-VASI response			
F-VASI50	38/94 (40.4)	47/94 (50.0)	46/55 (83.6)
F-VASI75	20/94 (21.3)	35/94 (37.2)	36/55 (65.5)
F-VASI90	11/94 (11.7)	21/94 (22.3)	29/55 (52.7)
T-VASI response			
T-VASI50	13/94 (13.8)	29/94 (30.9)	32/55 (58.2)
T-VASI75	2/94 (2.1)	9/94 (9.6)	15/55 (27.3)
F-PhGVA of clear or almost clear	10/94 (10.6)	17/79 (21.5)	24/55 (43.6)
PaGIC-V of very much or much improved	23/87 (26.4)	33/78 (42.3)	30/54 (55.6)

BID, twice daily; F-PhGVA, facial Physician's Global Vitiligo Assessment; F-VASI, facial Vitiligo Area Scoring Index; F-VASI50/75/90, ≥50%/≥75%/≥90% improvement in F-VASI; PaGIC-V, Patient Global Impression of Change for Vitiligo; T-VASI, total Vitiligo Area Scoring Index; T-VASI50/75, ≥50%/≥75% improvement in T-VASI.

Patients Initially Randomized to 1.5% Ruxolitinib Cream BID

- Among patients randomized to 1.5% ruxolitinib cream BID on Day 1 (n=33), the proportion who achieved F-VASI50, F-VASI75, and F-VASI90 responses increased steadily from Week 24 through Week 104 (**Figure 2**)

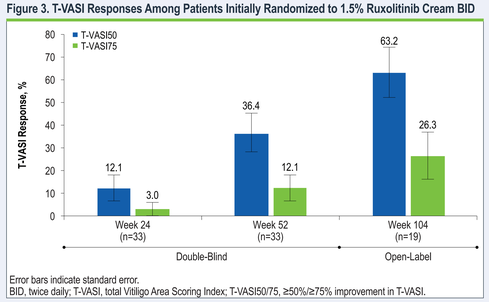
Figure 2. F-VASI Responses Among Patients Initially Randomized to 1.5% Ruxolitinib Cream BID



Error bars indicate standard error.
BID, twice daily; F-VASI, facial Vitiligo Area Scoring Index; F-VASI50/75/90, ≥50%/≥75%/≥90% improvement in F-VASI.

- The proportion of patients randomized to 1.5% ruxolitinib cream BID on Day 1 who achieved T-VASI50 and T-VASI75 responses increased from Week 24 through Week 104 (**Figure 3**)

Figure 3. T-VASI Responses Among Patients Initially Randomized to 1.5% Ruxolitinib Cream BID

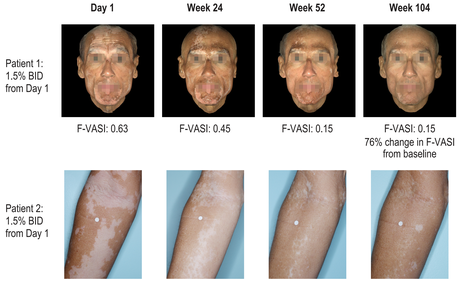


Error bars indicate standard error.
BID, twice daily; T-VASI, total Vitiligo Area Scoring Index; T-VASI50/75, ≥50%/≥75% improvement in T-VASI.

Clinical Images

- Representative clinical images of patients who received 1.5% ruxolitinib cream BID during the open-label period are shown in **Figure 4**

Figure 4. Representative Clinical Images of Patients Who Received 1.5% Ruxolitinib Cream BID During the Open-Label Period



BID, twice daily; F-VASI, facial Vitiligo Area Scoring Index.

Safety

- No significant safety signals were observed during 52 weeks of open-label treatment; 51.9% of 77 patients in the open-label period and 78.8% of 33 patients initially randomized to 1.5% ruxolitinib cream BID experienced treatment-emergent AEs (TEAEs; **Table 3**)
  - Regardless of dose at initial randomization, no accumulation of AEs was observed over the 104-week treatment period
- Among all patients in the open-label period, 7 (9.1%) had a treatment-related AE (all grade 1 or 2)
- Among patients initially randomized to receive 1.5% ruxolitinib cream BID, treatment-related AEs were reported in 11 patients (33.3%) over the 104-week study period, all of which were grades 1 (n=10) or 2 (n=1)

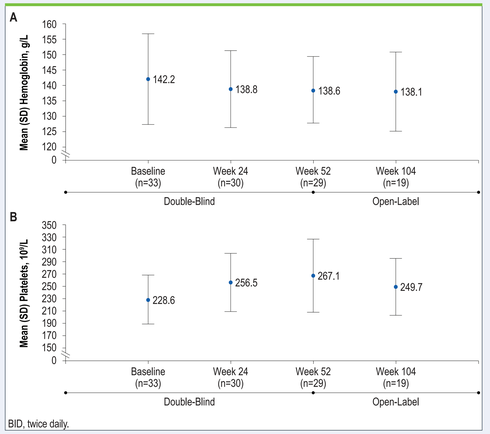
Table 3. TEAEs in Patients Who Received 1.5% Ruxolitinib Cream BID

Parameter, n (%)	All Patients in the Open-Label Period* (Weeks 52–104) n=77	Patients Initially Randomized to 1.5% BID (Day 1–Week 104) n=33
Patients with TEAE	40 (51.9)	26 (78.8)
Most common TEAEs†		
Acne	2 (2.6)	6 (18.2)
Upper respiratory tract infection	3 (3.9)	4 (12.1)
Sinusitis	4 (5.2)	2 (6.1)
Pruritus	2 (2.6)	3 (9.1)
Nasopharyngitis	3 (3.9)	1 (3.0)
Oral herpes	3 (3.9)	1 (3.0)
Erythema	0	3 (9.1)
Patients with treatment-related AE	7 (9.1)	11 (33.3)
Most common treatment-related AEs†		
Acne	2 (2.6)	6 (18.2)
Erythema	0	3 (9.1)
Patients with TEAE leading to discontinuation	2 (2.6)‡	0
Patients with serious TEAE§	1 (1.3)	1 (3.0)

AE, adverse event; BID, twice daily; TEAE, treatment-emergent adverse event.
* Includes patients initially randomized to 0.5% QD (n=28), 1.5% QD (n=21), and 1.5% BID (n=28).
† Occurring in ≥3 patients in either population presented.
‡ Basal cell carcinoma (n=1) related to treatment per investigator judgment; migraine (n=1) not related to treatment.
§ Arthralgia (n=1, all patients in the open-label period) not related to treatment; subdural hematoma (n=1, patients initially randomized to 1.5% BID) not related to treatment.

- No clinically relevant changes in hemoglobin or platelet levels were observed over the 104-week treatment period, regardless of dose at initial randomization
  - Mean (SD) hemoglobin and platelet levels among patients initially randomized to 1.5% ruxolitinib cream BID are shown in **Figure 5**

Figure 5. Mean (SD) Hemoglobin (A) and Platelet (B) Levels Among Patients Initially Randomized to 1.5% Ruxolitinib Cream BID



BID, twice daily.

Conclusions

- **Treatment with ruxolitinib cream produced substantial facial and total body repigmentation of vitiligo lesions through 104 weeks of treatment**
  - **Longer duration of therapy was associated with greater repigmentation per assessment of F-VASI and T-VASI responses at Weeks 24, 52, and 104**
- **Ruxolitinib cream was well tolerated over a 2-year period, and no treatment-related serious AEs were reported**

Disclosures

JEH has served as a consultant for AbbVie, Aclaris Therapeutics, BiologicsMD, EMD Serono, Genzyme/Sanofi, Janssen, Pfizer, Rheos Medicines, Sun Pharmaceuticals, TeVido BioDevices, The Expert Institute, 3rd Rock Ventures, and Villaris Therapeutics; has served as an investigator for Aclaris Therapeutics, Celgene, Dermira, EMD Serono, Genzyme/Sanofi, Incyte Corporation, LEO Pharma, Pfizer, Rheos Medicines, Stiefel/GlaxoSmithKline, Sun Pharmaceuticals, TeVido BioDevices, and Villaris Therapeutics; holds equity in Rheos Medicines, TeVido BioDevices, and Villaris Therapeutics; is a scientific founder of Villaris Therapeutics; and has patents pending for IL-15 blockade for treatment of vitiligo, JAK inhibition with light therapy for vitiligo, and CXCR3 antibody depletion for treatment of vitiligo. AGP has served as an investigator for Aclaris Therapeutics, Immune Tolerance Network, Incyte Corporation, and Pfizer; a consultant for Arcutis, Avita, Chromaderm, Immune Tolerance Network, Incyte Corporation, Pfizer, Viela Bio, and Villaris; and a board member who also holds stock options for Clarify Medical and Tara Medical. ML is an employee of Mount Sinai Hospital, which receives research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant, Eli Lilly, Incyte Corporation, 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, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, and Verrica. PG has served as a consultant for Aclaris Therapeutics, Clarify Medical, DermaForce, Incyte Corporation, Proctor & Gamble, and Versicolor Technologies; and a principal investigator for Aclaris Therapeutics, Allergan/SkinMedica, Clinuvel Pharmaceuticals, Incyte Corporation, Johnson & Johnson, L'Oreal, Merz Pharma, Pfizer, Thync Global Inc., and VT Cosmetics. ABG has received honoraria as an advisory board member and consultant for AnaptysBio, Avotres Therapeutics, Beiersdorf, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Incyte Corporation, Janssen, LEO Pharma, Novartis, Sun Pharmaceuticals, and UCB; has stock options in Xbiotech; and has received institutional research/educational grants from Boehringer Ingelheim, Incyte Corporation, Janssen, Novartis, UCB, Xbiotech, and Sun Pharmaceuticals to Mount Sinai School of Medicine. HLS has served as a consultant and/or investigator for AbbVie, Amgen, Asana, Boehringer Ingelheim, Celgene, Dermira, Dermavant, Eli Lilly and Company, Incyte Corporation, Janssen/Johnson & Johnson, Kiniksa, LEO Pharma, Sun Pharmaceuticals, UCB, and Xbiotech. AYM has received research grants from Arcutis and Incyte Corporation. KB, FIK, and KS are employees and shareholders of Incyte Corporation. DR has received honoraria as a consultant for AbbVie, Celgene, Dermavant Sciences, Dermira, Eli Lilly and Company, Janssen, Kyowa Kirin, Novartis, Pfizer, Regeneron Pharmaceuticals, Sanofi, Sun Pharmaceuticals, UCB, and VielaBio; research support from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly and Company, Incyte Corporation, Janssen, Merck, Novartis, Pfizer, and Regeneron Pharmaceuticals; and has served as a paid speaker for AbbVie, Celgene, Eli Lilly and Company, Janssen, Novartis, Pfizer, Regeneron Pharmaceuticals, and Sanofi.

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