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Addition of Narrow-Band Ultraviolet Light B Phototherapy to Ruxolitinib Cream in Patients With Vitiligo

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Background

- Vitiligo is a chronic autoimmune disease resulting in patches of skin depigmentation[1] and reduced quality of life[2]
- Disease pathogenesis is driven by interferon-γ signaling through Janus kinase (JAK) 1 and JAK2[3]
- Previous reports with JAK inhibitors have suggested additional therapeutic benefit with concomitant phototherapy in patients with vitiligo[4,5]
- In a phase 2, randomized, dose-ranging study in adult patients with vitiligo (NCT03099304), treatment with ruxolitinib cream, a JAK1/JAK2 inhibitor, was associated with substantial repigmentation over 52 weeks[6]

Objective

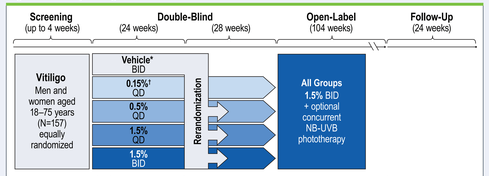
- To report the safety and efficacy of concomitant therapy with ruxolitinib cream and narrow-band ultraviolet-B (NB-UVB) phototherapy during the open-label phase of the phase 2 study

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 were offered optional concomitant NB-UVB phototherapy while continuing open-label treatment with 1.5% ruxolitinib cream BID

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.

Assessments

- Efficacy assessments included change from baseline in F-VASI and total body (including the face) Vitiligo Area Scoring Index (T-VASI), the proportion of patients achieving F-VASI improvements of ≥50%, ≥75%, and ≥90% (F-VASI50, F-VASI75, and F-VASI90, respectively), and the proportion of patients achieving T-VASI improvements of ≥25%, ≥50%, and ≥75% (T-VASI25, T-VASI50, and T-VASI75, respectively) with concomitant use of 1.5% ruxolitinib cream BID and NB-UVB phototherapy
  - The subpopulation of patients who had not achieved the primary endpoint of F-VASI50 at Week 24 was also evaluated
- Safety and tolerability of concomitant 1.5% ruxolitinib cream BID and NB-UVB phototherapy were assessed, including the frequency of reported adverse events (AEs)

Statistical Analyses

- Data were summarized using descriptive statistics

Results

Patient Characteristics

- Nineteen patients (mean age, 47.2 years; male, 63.2%) received add-on NB-UVB for ≥12 weeks during open-label treatment at various frequencies based on the standard phototherapy protocols of each investigator site, most commonly thrice weekly (47.4%)
  - Patient demographics and clinical characteristics for the subpopulation of 12 patients who did not achieve F-VASI50 at Week 24 (mean age, 45.4 years; male, 66.7%) were comparable (**Table 1**)

Table 1. Patient Demographics and Baseline Disease Characteristics Among Patients Who Received Combination 1.5% Ruxolitinib Cream BID and NB-UVB Phototherapy After Week 52

Parameter	All Patients (N=19)	Patients Who Did Not Achieve F-VASI50 at Week 24 (n=12)
Age, mean (SD), y	47.2 (10.8)	45.4 (11.9)
Male, n (%)	12 (63.2)	8 (66.7)
White, n (%)	15 (78.9)	10 (83.3)
Skin type, n (%)		
I	0	0
II	5 (26.3)	5 (41.7)
III	8 (42.1)	4 (33.3)
IV	3 (15.8)	1 (8.3)
V	0	0
VI	3 (15.8)	2 (16.7)
Baseline F-VASI, mean (SD)	1.39 (0.91)	1.51 (0.98)
Baseline T-VASI, mean (SD)	17.0 (11.9)	19.0 (13.8)
Facial BSA,* mean (SD), %	1.43 (0.9)	1.54 (1.0)
Total BSA, mean (SD), %	19.5 (12.9)	22.2 (14.8)
Disease duration, median (range), y	23.0 (3.0–56.8)	25.5 (3.0–56.8)
Diagnosed in childhood, n (%)	4 (21.1)	3 (25.0)
Other autoimmune disorders,† n (%)	4 (21.1)	3 (25.0)
Prior therapy, n (%)		
Topical corticosteroids	11 (57.9)	6 (50.0)
Topical calcineurin inhibitors	11 (57.9)	5 (41.7)
Phototherapy‡	15 (78.9)	8 (66.7)
Duration of concomitant ruxolitinib cream and NB-UVB phototherapy, mean (range), wk	40 (15–51)	39 (15–47)
Frequency of NB-UVB during concomitant ruxolitinib cream therapy, n (%)		
Once weekly	1 (5.3)	0
Twice weekly	7 (36.8)	4 (33.3)
Thrice weekly	9 (47.4)	6 (50.0)
Every other day	2 (10.5)	2 (16.7)

BID, twice daily; BSA, body surface area; F-VASI, facial Vitiligo Area Scoring Index; NB-UVB, narrow-band ultraviolet-B; PUVA, psoralen ultraviolet-A; T-VASI, total Vitiligo Area Scoring Index.
* Percentage of total BSA.
† Thyroid disorders for all patients.
‡ Phototherapy includes NB-UVB phototherapy, excimer laser, and PUVA photochemotherapy.

Efficacy

- Among 71 patients who received ruxolitinib cream alone, 62% achieved F-VASI75 and 56% achieved T-VASI50 at Week 104 (**Table 2**)
  - Continued treatment with ruxolitinib cream was also beneficial among 28 patients who did not achieve F-VASI50 at Week 24 (primary endpoint), with 71% achieving F-VASI50 at Week 104

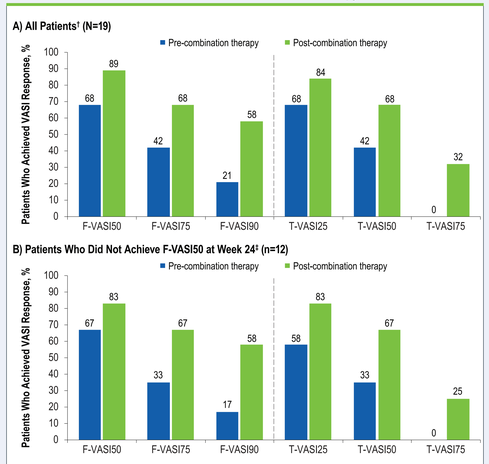
Table 2. Proportion of Patients Treated With Ruxolitinib Cream Alone Who Achieved VASI Response at Week 104

Patients, %	F-VASI50	F-VASI75	F-VASI90	T-VASI25	T-VASI50	T-VASI75
All patients* (N=71)	83	62	49	77	56	25
Received 1.5% ruxolitinib cream BID† (n=16)	88	63	50	81	56	25
Did not achieve F-VASI50 at Week 24‡ (n=28)	71	39	32	50	32	11

BID, twice daily; F-VASI, facial Vitiligo Area Scoring Index; NB-UVB, narrow-band ultraviolet-B; T-VASI, total Vitiligo Area Scoring Index; QD, once daily; VASI, Vitiligo Area Scoring Index.
* Includes all treatment groups, including patients who received vehicle and 0.15% ruxolitinib cream QD through Week 24.
† Patients who received 1.5% ruxolitinib cream BID since Day 1.
‡ Patients who received any dose of ruxolitinib cream since Day 1.

- Among 19 patients who received 1.5% ruxolitinib cream BID with concomitant phototherapy, the proportion of patients who achieved F-VASI and T-VASI response after add-on NB-UVB increased for all response parameters (**Figure 2**)
  - The benefit was also apparent in the 12 patients who did not achieve F-VASI50 at Week 24

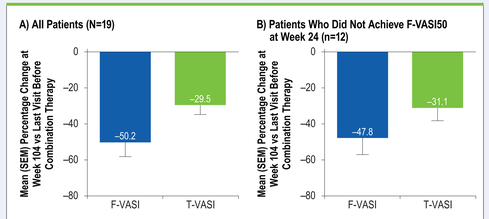
Figure 2. Proportion of Patients Who Achieved VASI Response Before and After Combination 1.5% Ruxolitinib Cream BID and NB-UVB Phototherapy*



BID, twice daily; F-VASI50/75/90, ≥50%/≥75%/≥90% improvement in facial VASI; NB-UVB, narrow-band ultraviolet-B; T-VASI, total Vitiligo Area Scoring Index; T-VASI25/50/75, ≥25%/≥50%/≥75% improvement in total VASI; QD, once daily; VASI, Vitiligo Area Scoring Index.
* Patients could start combination phototherapy at any time after the Week-52 study visit.
† Includes all treatment groups, including patients who received vehicle and 0.15% ruxolitinib cream QD through Week 24.
‡ Patients who received any dose of ruxolitinib cream since Day 1.

- Fifteen of 19 patients (78.9%) who received combination therapy experienced improvement in F-VASI and 18 of 19 patients (94.7%) experienced T-VASI improvement
  - Mean percent improvements in F-VASI and T-VASI with combination therapy were 50.2% and 29.5%, respectively (**Figure 3**)
- Among the 12 patients receiving combination therapy who did not achieve F-VASI50 at Week 24, F-VASI scores were improved in 10 patients (83.3%) and T-VASI scores were improved in 11 patients (91.7%)
  - Mean percent improvements in F-VASI and T-VASI with combination therapy were 47.8% and 31.1%, respectively

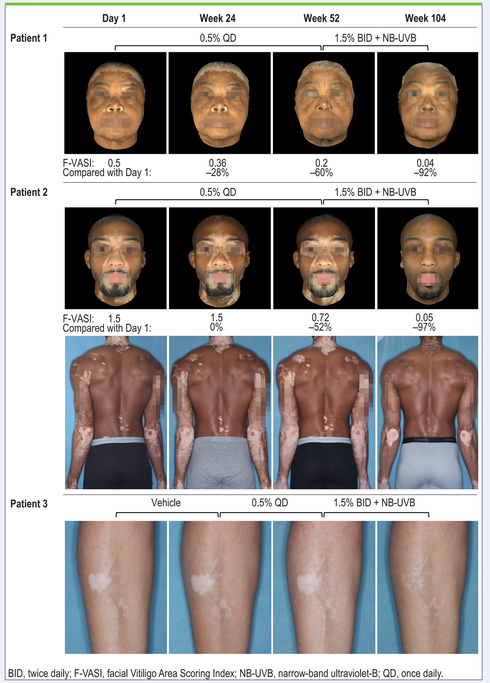
Figure 3. Mean Percentage Change in F-VASI and T-VASI Scores With Combination 1.5% Ruxolitinib Cream BID and NB-UVB Phototherapy*†



BID, twice daily; F-VASI, facial Vitiligo Area Scoring Index; NB-UVB, narrow-band ultraviolet-B; SEM, standard error of the mean; T-VASI, total Vitiligo Area Scoring Index.
* Patients could start combination phototherapy at any time after the Week-52 study visit.
† No patients experienced worsening (increased scores) of F-VASI or T-VASI.

- Representative clinical images of 3 patients who used combination 1.5% ruxolitinib cream BID and NB-UVB phototherapy during open-label treatment are shown in **Figure 4**

Figure 4. Representative Clinical Images Showing Facial and Total Body Vitiligo Lesions of Patients Treated With Combination 1.5% Ruxolitinib Cream BID and NB-UVB Phototherapy During the Open-Label Period



BID, twice daily; F-VASI, facial Vitiligo Area Scoring Index; NB-UVB, narrow-band ultraviolet-B; QD, once daily.

Safety

- Only 4 patients (21.1%) experienced AEs (all grade 1 or 2 in severity) after receiving add-on NB-UVB (**Table 3**)
- No AEs were related to treatment
- No phototherapy burns were reported
- No AEs related to skin malignancies or laboratory abnormalities were reported

Table 3. Patient-Level AEs Reported After Receiving Concomitant NB-UVB Phototherapy

Patient	NB-UVB Frequency	AE*
1	Twice weekly	Anxiety, blurred vision, abnormal coordinating, insomnia, migraine, muscular weakness, muscle twitching, myalgia, sleep disorder, upper respiratory infection
2	Thrice weekly	Abdominal wall abscess, hyperglycemia, tooth infection
3	Twice weekly	Sinus congestion
4	Every other day	Application site dermatitis, salpingectomy

AE, adverse event; NB-UVB, narrow-band ultraviolet-B.
* No AEs were related to treatment.

Conclusions

- **The addition of phototherapy to ruxolitinib cream in patients with vitiligo was well tolerated; the frequency of AEs was low, and none were related to treatment**
- **The addition of NB-UVB to ruxolitinib cream resulted in further substantial improvement in repigmentation, including in patients who did not achieve F-VASI50 at Week 24**
- **The findings of this analysis in 19 patients who received combination therapy with 1.5% ruxolitinib cream BID and NB-UVB phototherapy need to be confirmed in larger studies**

Disclosures

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. 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. 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. IH has served as an advisory board member for AbbVie; a consultant for Incyte Corporation, Pfizer, and UCB; a principal investigator for AbbVie, Allergan, Bayer, Clinuvel Pharmaceuticals, Estée Lauder, Ferndale Laboratories, Galderma Laboratories LP, GE Healthcare, Incyte Corporation, Janssen, Janssen Biotech, Johnson & Johnson, Lenicura, LEO Pharma, Pfizer, and Unigen; a subinvestigator for Amgen, Bristol Myers Squibb, Foamix Pharmaceuticals, and Janssen; president of the HS Foundation; and co-chair of the Global Vitiligo Foundation. KB, FIK, and SW 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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