CO130

Subgroup Analysis of Quality-of-Life Outcomes in Patients Achieving F-VASI75: Pooled Results From 2 Randomized Phase 3 Studies of Ruxolitinib Cream for the Treatment of Vitiligo

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Introduction

- Vitiligo is a chronic autoimmune disease that targets melanocytes, resulting in patches of skin depigmentation,[1] and is associated with reduced quality of life (QoL)[2,3]
- Disease pathogenesis is largely regulated by interferon-γ activation of the Janus kinase (JAK) signaling pathway[4]
- A cream formulation of ruxolitinib, a JAK1/JAK2 inhibitor,[5] demonstrated substantial and clinically meaningful repigmentation over 52 weeks in a phase 2, dose-ranging, randomized study in adult patients with vitiligo (NCT03099304)[6]
- In 2 randomized, double-blind, phase 3 Topical Ruxolitinib Evaluation in Vitiligo studies (TRuE-V1 [NCT04052425] and TRuE-V2 [NCT04057573]), ruxolitinib cream was statistically superior to vehicle at Week 24 in the primary and all key secondary efficacy endpoints[7]

Objective

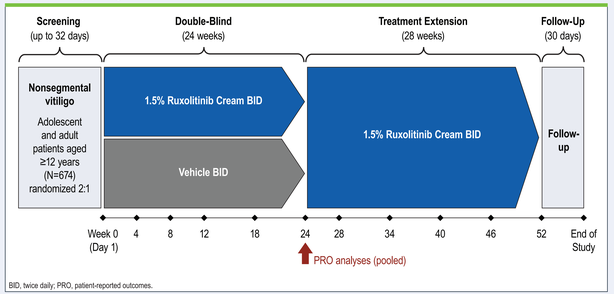
- To evaluate pooled patient-reported outcomes data from the TRuE-V1 and TRuE-V2 studies based on ≥75% and ≥90% improvement on the facial Vitiligo Area Scoring Index from baseline (F-VASI75 and F-VASI90, respectively) at Week 24

Methods

Patients and Study Design

- 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 F-VASI, and scores ≥3 on total VASI (T-VASI)
- Key exclusion criteria were the presence of complete leukotrichia within any facial lesions, dermatologic disease confounding vitiligo assessment, previous use of JAK inhibitor therapy, and use of the following therapies for vitiligo before baseline: any biological or experimental therapy within 12 weeks (or 5 half-lives), phototherapy within 8 weeks, immunomodulating treatments within 4 weeks, or topical treatments within 1 week
- Patients were stratified by geographic region (North America and Europe) and Fitzpatrick skin type (I–II and III–VI) and were randomized 2:1 to apply 1.5% ruxolitinib cream twice daily (BID) or vehicle BID for 24 weeks (**Figure 1**)
  - After completion of the Week 24 visit, all patients could apply 1.5% ruxolitinib cream BID for an additional 28 weeks in the open-label treatment extension

Figure 1. Study Design



BID, twice daily; PRO, patient-reported outcomes.

Assessments

- Efficacy outcomes included F-VASI75 (primary endpoint) and F-VASI90 (key secondary endpoint) at Week 24
- QoL was assessed by F-VASI75 and F-VASI90 response at Week 24 using the following measures:
  - Mean change from baseline in the 10-item Dermatology Life Quality Index (DLQI; for patients aged ≥16 years; range, 0–30); higher scores indicate more impairment of QoL[8]
  - Mean change from baseline in the 15-item Vitiligo-specific Quality of Life (VitiQoL; range, 0–90); higher scores indicate worse QoL[9]

Statistical Analyses

- All analyses were conducted using pooled data from both studies
- Analysis subgroups were achievement of F-VASI75 and F-VASI90 at Week 24 (yes/no for both analyses)
- Subgroups were analyzed using mixed-effect model repeat measurement

Results

Patients

- TRuE-V1/TRuE-V2 randomized 674 patients (ruxolitinib cream, n=450; vehicle, n=224; **Table 1**)
  - Mean (SD) age was 39.6 (15.1) years; mean disease duration was 14.8 (11.6) years
  - Mean (SD) facial and total BSA at baseline was 1.02% (0.64) and 7.39% (2.03), respectively

Table 1. Patient Demographics and Baseline Clinical Characteristics

Characteristic	Vehicle (n=224)	Ruxolitinib Cream (n=450)	Total (N=674)
Age, mean (SD), y	39.7 (14.5)	39.5 (15.4)	39.6 (15.1)
Female, n (%)	110 (49.1)	248 (55.1)	358 (53.1)
White, n (%)	189 (84.4)	363 (80.7)	552 (81.9)
Fitzpatrick skin type, n (%)			
I	4 (1.8)	12 (2.7)	16 (2.4)
II	72 (32.1)	131 (29.1)	203 (30.1)
III	88 (39.3)	179 (39.8)	267 (39.6)
IV	40 (17.9)	89 (19.8)	129 (19.1)
V	17 (7.6)	28 (6.2)	45 (6.7)
VI	3 (1.3)	11 (2.4)	14 (2.1)
Geographic region, n (%)			
North America	156 (69.6)	308 (68.4)	464 (68.8)
Europe	68 (30.4)	142 (31.6)	210 (31.2)
Baseline F-VASI, mean (SD)	0.92 (0.56)	0.92 (0.55)	0.92 (0.56)
Baseline T-VASI, mean (SD)	6.73 (2.09)	6.66 (2.05)	6.69 (2.06)
Facial BSA,* mean (SD), %	1.03 (0.65)	1.02 (0.63)	1.02 (0.64)
Total BSA, mean (SD), %	7.46 (2.03)	7.36 (2.02)	7.39 (2.03)
Duration of disease, mean (SD), y	14.6 (11.0)	14.9 (11.9)	14.8 (11.6)
Diagnosed in childhood, n (%)	77 (34.4)	168 (37.3)	245 (36.4)
Disease stability,† n (%)			
Stable	168 (75.0)	331 (73.6)	499 (74.0)
Progressive	56 (25.0)	119 (26.4)	175 (26.0)
DLQI, mean (SD)‡	5.0 (4.9)	4.5 (4.5)	4.7 (4.6)
VitiQoL, mean (SD)§	39.4 (23.9)	36.5 (23.2)	37.5 (23.5)
Other autoimmune disorders, n (%)	36 (16.1)	90 (20.0)	126 (18.7)
Prior therapy,¶ n (%)	137 (61.2)	274 (60.9)	411 (61.0)

BSA, body surface area; DLQI, Dermatology Life Quality Index; F-VASI, facial Vitiligo Area Scoring Index; T-VASI, total Vitiligo Area Scoring Index; VitiQoL, Vitiligo-specific Quality of Life.
* Percentage of total BSA.
† Determination of disease stability was based on investigator judgment.
‡ Data available for 632 patients (vehicle, n=216; ruxolitinib cream, n=416).
§ Data available for 672 patients (vehicle, n=223; ruxolitinib cream, n=449).
¶ Patients could have used multiple previous lines of therapy.

Efficacy

- At Week 24, F-VASI75 was achieved by 30.1% of patients who applied ruxolitinib cream vs 10.8% who applied vehicle (P<0.0001)
- F-VASI90 at Week 24 was achieved by 15.4% of patients who applied ruxolitinib cream vs 2.2% who applied vehicle (P=0.0001)

Quality of Life

- Baseline scores for DLQI and VitiQoL by clinical response (F-VASI75 and F-VASI90) at Week 24 are shown in **Table 2**

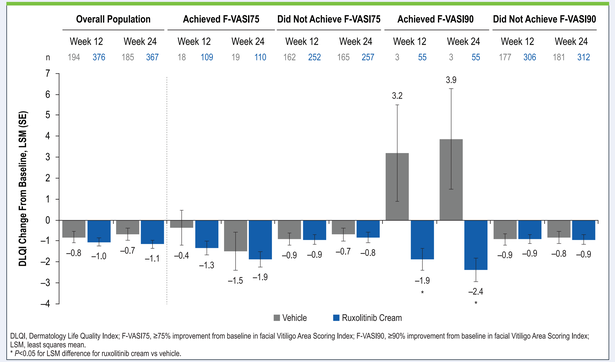
Table 2. Baseline Values for DLQI and VitiQoL by F-VASI75 and F-VASI90 Response at Week 24

	Vehicle (n=224)		Ruxolitinib Cream (n=450)	
	DLQI, mean (SD)*	VitiQoL, mean (SD)†	DLQI, mean (SD)*	VitiQoL, mean (SD)†
Achieved F-VASI75	5.2 (4.3) n=19	38.5 (24.6) n=19	5.3 (5.1) n=110	40.1 (25.0) n=122
Did not achieve F-VASI75	5.0 (4.8) n=165	40.7 (24.0) n=171	4.3 (4.3) n=257	35.7 (22.1) n=278
Achieved F-VASI90	9.7 (5.8) n=3	64.0 (22.5) n=3	6.1 (4.9) n=55	43.3 (23.9) n=64
Did not achieve F-VASI90	5.0 (4.7) n=181	40.1 (23.9) n=187	4.3 (4.4) n=312	35.9 (22.7) n=336

DLQI, Dermatology Life Quality Index; F-VASI75, ≥75% improvement from baseline in facial Vitiligo Area Scoring Index; F-VASI90, ≥90% improvement from baseline in facial Vitiligo Area Scoring Index; VitiQoL, Vitiligo-specific Quality of Life.
* DLQI score interpretation: 0–1, no effect; 2–5, small effect; 6–10, moderate effect; 11–20, very large effect; 21–30, extremely large effect.
† VitiQoL score interpretation: 0–5, no effect, 6–20, mild effect; 21–38, moderate effect; ≥39, severe effect.[10]

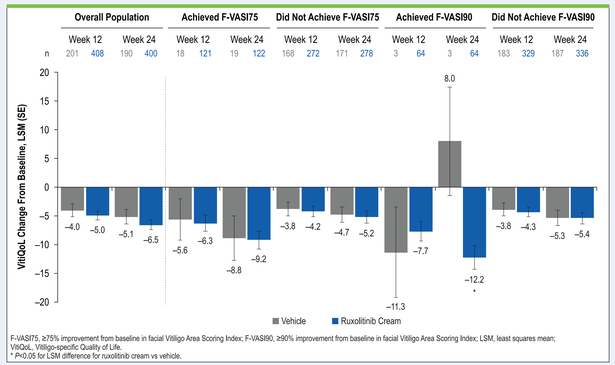
- Among patients who achieved or did not achieve an F-VASI75 response at Week 24, there were no significant differences (P>0.05) between patients who applied ruxolitinib cream vs vehicle in change from baseline in DLQI (**Figure 2**) or VitiQoL (**Figure 3**) total scores at Weeks 12 or 24
  - QoL appeared to improve from Weeks 12 to 24 among patients who applied ruxolitinib cream and achieved F-VASI75 at Week 24
- A significant difference between patients who applied ruxolitinib cream vs vehicle was observed among patients who achieved an F-VASI90 response at Week 24 for DLQI (**Figure 2**) and VitiQoL (**Figure 3**), although the number of patients in the vehicle group was low

Figure 2. Mean Change From Baseline in DLQI at Weeks 12 and 24 by F-VASI75 and F-VASI90 Response at Week 24



DLQI, Dermatology Life Quality Index; F-VASI75, ≥75% improvement from baseline in facial Vitiligo Area Scoring Index; F-VASI90, ≥90% improvement from baseline in facial Vitiligo Area Scoring Index; LSM, least squares mean.
* P<0.05 for LSM difference for ruxolitinib cream vs vehicle.

Figure 3. Mean Change From Baseline in VitiQoL at Weeks 12 and 24 by F-VASI75 and F-VASI90 Response at Week 24



F-VASI75, ≥75% improvement from baseline in facial Vitiligo Area Scoring Index; F-VASI90, ≥90% improvement from baseline in facial Vitiligo Area Scoring Index; LSM, least squares mean; VitiQoL, Vitiligo-specific Quality of Life.
* P<0.05 for LSM difference for ruxolitinib cream vs vehicle.

Safety

- Ruxolitinib cream was well tolerated in the TRuE-V studies
- Treatment-emergent adverse events (TEAEs) occurred in 47.7% of patients who applied ruxolitinib cream and 35.3% of patients who applied vehicle; TEAEs considered by investigators to be related to treatment occurred in 14.7% and 7.6% of patients, respectively.
  - No serious TEAEs were considered related to treatment

Conclusions

- **Application of ruxolitinib cream was not associated with improved QoL vs vehicle at Weeks 12 or 24 based on F-VASI75 response at Week 24, although there were trends for improvement between Weeks 12 and 24 in both DLQI and VitiQoL among patients applying ruxolitinib cream who achieved F-VASI75 at Week 24**
- **Significant improvement in QoL was observed for ruxolitinib cream vs vehicle at Week 24 among patients who achieved an F-VASI90 response, although sample sizes in the vehicle group were small**

Disclosures

Amit G. Pandya 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 Corporation, Pfizer, TWI, Viela Bio, and Villaris; and holds stock options for Tara Medical and Zerigo Health. Nanja van Geel is a consultant and/or investigator for AbbVie, Incyte Corporation, Pfizer, and Sun Pharma; and is chair of the Vitiligo Task Force for the European Academy of Dermatology and Venereology (EADV). Kristen Bibeau, Kathleen Butler, and Jessy Gao are employees and shareholders of Incyte Corporation. Khaled Ezzedine is a consultant for AbbVie, Incyte Corporation, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio.

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