CO108

Subgroup Analysis of Quality of Life and Treatment Satisfaction by Disease Duration and Use of Prior Treatment: 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 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

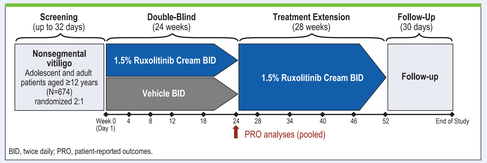
- To evaluate pooled patient-reported outcomes data from the TRuE-V1 and TRuE-V2 studies based on subgroup analyses by disease duration and use of prior treatment

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 facial Vitiligo Area Scoring Index (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

- QoL measures at Week 24
  - ≥3-point improvement from baseline (minimal clinically important difference)[8] in the 10-item Dermatology Life Quality Index (DLQI; for patients aged ≥16 years; range, 0–30); higher scores indicate more impairment of QoL[9]
    - Children's DLQI data were available in ≤5 patients in each subgroup and thus are not included in this analysis
  - Mean change from baseline in the 15-item Vitiligo-specific Quality of Life (VitiQoL; range, 0–90); higher scores indicate worse QoL[10]
  - Mean change from baseline in the 14-item Hospital Anxiety and Depression Scale (HADS; 7 items for each subscale; range, 0–21 for each subscale); higher scores indicate more anxiety or depression[11]
  - Mean change from baseline in the 5-item World Health Organization-Five Well-Being Index (WHO-5; range, 0–25); higher scores indicate better QoL[12]
- Least squares mean scores at Week 24 on the 9-item Treatment Satisfaction Questionnaire for Medication (TSQM-9; range, 0–100); higher scores indicate greater satisfaction[13]

Statistical Analyses

- All analyses were conducted using pooled data from both studies
- Analysis subgroups were disease duration (≤10 vs >10 years) and prior treatment (yes/no)
- ≥3-point improvement in DLQI was analyzed using exact logistic regression; change from baseline for HADS, VitiQoL, and WHO-5, as well as least squares mean TSQM-9 scores, 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, and 61.0% of patients had used prior therapy
  - 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)
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; F-VASI, facial Vitiligo Area Scoring Index; T-VASI, total Vitiligo Area Scoring Index.
* Percentage of total BSA.
† Determination of disease stability was based on investigator judgment.
‡ Patients could have used multiple previous lines of therapy.

- Baseline scores for DLQI, VitiQoL, HADS, and WHO-5 by disease duration and prior therapy subgroups are shown in **Table 2**

Table 2. Baseline Values for DLQI, VitiQoL, HADS, and WHO-5 by Disease Duration and Prior Therapy Subgroups

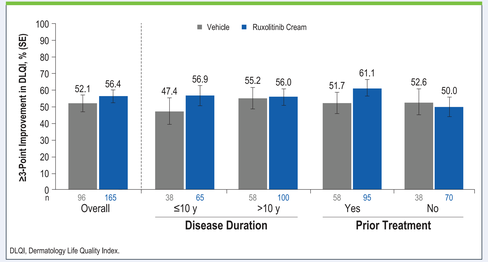
	Vehicle (n=224)					Ruxolitinib Cream (n=450)				
	DLQI, mean (SD)*	VitiQoL, mean (SD)†	HADS-D, mean (SD)‡	HADS-A, mean (SD)‡	WHO-5, mean (SD)§	DLQI, mean (SD)*	VitiQoL, mean (SD)†	HADS-D, mean (SD)‡	HADS-A, mean (SD)‡	WHO-5, mean (SD)§
Disease duration ≤10 y	5.3 (5.2) n=86	39.8 (24.9) n=92	3.5 (3.4) n=92	6.7 (4.1) n=92	16.4 (5.1) n=92	4.4 (4.3) n=166	34.4 (23.4) n=197	3.5 (3.4) n=197	6.4 (3.7) n=197	16.8 (5.1) n=197
Disease duration >10 y	4.9 (4.7) n=130	39.2 (23.3) n=131	3.8 (3.5) n=131	6.7 (3.6) n=131	16.6 (4.7) n=131	4.5 (4.5) n=250	38.2 (23.0) n=252	3.5 (2.9) n=252	6.9 (3.5) n=252	16.8 (4.1) n=253
Prior therapy	5.4 (5.2) n=130	41.0 (24.0) n=137	3.8 (3.5) n=137	7.0 (3.9) n=137	16.1 (5.1) n=137	4.6 (4.5) n=244	36.9 (23.3) n=273	3.5 (3.1) n=273	6.5 (3.6) n=273	16.9 (4.6) n=274
No prior therapy	4.5 (4.4) n=86	36.9 (23.7) n=86	3.5 (3.5) n=86	6.1 (3.5) n=86	17.2 (4.4) n=86	4.4 (4.4) n=172	35.8 (23.1) n=176	3.6 (3.2) n=176	7.0 (3.6) n=176	16.6 (4.5) n=176

DLQI, Dermatology Life Quality Index; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale-Depression; VitiQoL, Vitiligo-specific Quality of Life; WHO-5, World Health Organization-Five Well-Being Index.
* 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.[14]
‡ HADS scores ≥8 indicate depression or anxiety.[11]
§ WHO-5 score <13 indicates poor well-being.[15]

Quality of Life

- There were no significant differences at Week 24 in the proportion of patients who achieved a ≥3-point improvement from baseline in DLQI (**Figure 2**) among patients who applied ruxolitinib cream vs vehicle

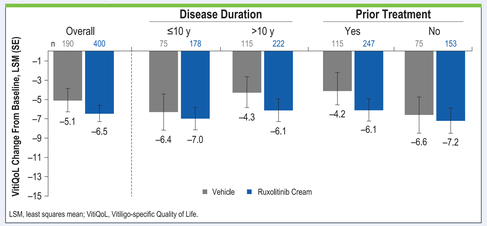
Figure 2. Patients With ≥3-Point Improvement From Baseline in DLQI at Week 24



DLQI, Dermatology Life Quality Index.

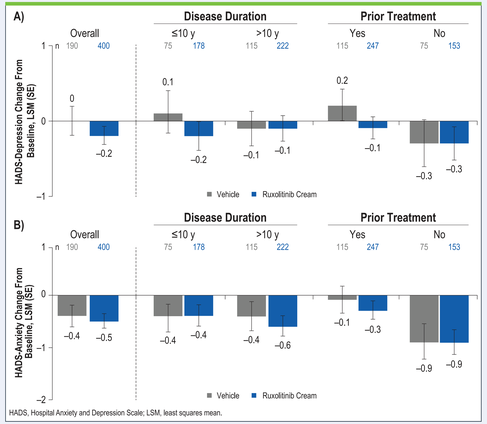
- No significant differences were observed at Week 24 in VitiQoL (**Figure 3**), HADS-depression (**Figure 4A**), HADS-anxiety (**Figure 4B**), or WHO-5 (**Figure 5**) among patients who applied ruxolitinib cream vs vehicle

Figure 3. Mean Change From Baseline in VitiQoL at Week 24



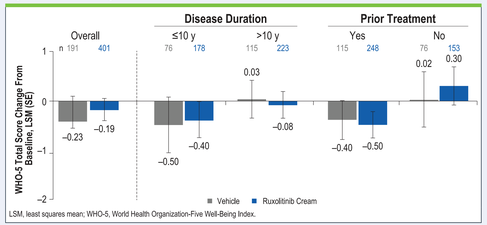
LSM, least squares mean; VitiQoL, Vitiligo-specific Quality of Life.

Figure 4. Mean Change From Baseline in (A) HADS-Depression and (B) HADS-Anxiety at Week 24



HADS, Hospital Anxiety and Depression Scale; LSM, least squares mean.

Figure 5. Mean Change From Baseline in WHO-5 Total Score at Week 24

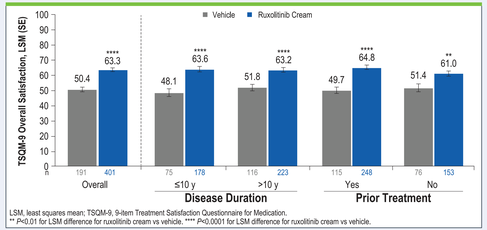


LSM, least squares mean; WHO-5, World Health Organization-Five Well-Being Index.

Treatment Satisfaction

- At Week 24, patients had significantly higher ($P<0.01$) treatment satisfaction with application of ruxolitinib cream vs vehicle per least squares mean TSQM-9 scores regardless of disease duration (≤10 years, 63.6 vs 48.1; >10 years, 63.2 vs 51.8) or use of prior treatment (yes, 64.8 vs 49.7; no, 61.0 vs 51.4; **Figure 6**)

Figure 6. TSQM-9 Overall Satisfaction at Week 24



LSM, least squares mean; TSQM-9, 9-item Treatment Satisfaction Questionnaire for Medication.
** P<0.01 for LSM difference for ruxolitinib cream vs vehicle, **** P<0.0001 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

- **Ruxolitinib cream was associated with significantly improved treatment satisfaction vs vehicle at Week 24 regardless of disease duration and use of prior treatment**
- **Effects on QoL as assessed by the DLQI, VitiQoL, WHO-5, HADS-depression, and HADS-anxiety were not apparent at Week 24**
  - **Although ruxolitinib cream monotherapy was statistically superior to vehicle at Week 24 in efficacy endpoints (as previously reported),[7] longer duration of therapy or combination therapy may be needed to observe differences in QoL**

Disclosures

Khaled Ezzedine is a consultant for AbbVie, Incyte Corporation, La Roche-Posay, Pfizer, Pierre Fabre, Sanofi, and Viela Bio. 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). Kathleen Butler, Kristen Bibeau, and Jessy Gao are employees and shareholders of Incyte Corporation. 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.

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