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Correlation of the Vitiligo Area Scoring Index With Patient- and Physician-Reported Measures of Clinical Improvement in a Randomized, Double-Blind Phase 2 Study

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Background

- The Vitiligo Area Scoring Index (VASI) is a sensitive, quantitative, and validated clinical tool that was developed to measure vitiligo treatment response[1]
- The instrument is based on a composite estimate of the overall area of vitiligo patches (ie, skin depigmentation) and the degree of macular repigmentation within these patches over time[1]
  - VASI is measured using hand units to determine vitiligo involvement, where 1 hand unit represents approximately 1% of the total body surface area (BSA)
- A phase 2, dose-ranging, randomized study used the facial and total VASI (F-VASI and T-VASI, respectively) to demonstrate significant repigmentation with ruxolitinib cream, a Janus kinase (JAK) 1/JAK2 inhibitor, over 52 weeks[2]

Objective

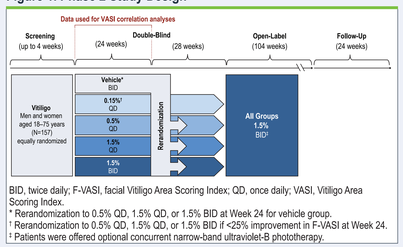
- To evaluate the correlation between F-VASI and T-VASI scores with measures of clinical improvement based on a randomized, double-blind phase 2 study in patients with vitiligo

Methods

Phase 2 Study Design

- This phase 2 study (NCT03099304) enrolled adult patients (aged 18–75 years) with vitiligo that included depigmentation ≥0.5% of BSA on the face and ≥3% of BSA on nonfacial areas
- 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**)
- Eligibility criteria and the complete study design have been reported previously[2]

Figure 1. Phase 2 Study Design

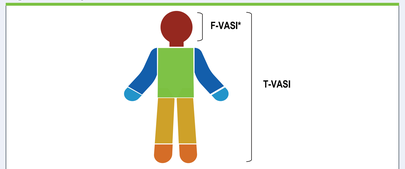


BID, twice daily; F-VASI, facial Vitiligo Area Scoring Index; QD, once daily; VASI, Vitiligo Area Scoring Index.
* Rerandomization to 0.5% QD, 1.5% QD, or 1.5% BID at Week 24 for vehicle group.
† Rerandomization to 0.5% QD, 1.5% QD, or 1.5% BID if <25% improvement in F-VASI at Week 24.
‡ Patients were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

Determination of VASI Scores

- Hand units for VASI measurement were based on patient hand sizes
- The body was divided into 6 separate and mutually exclusive sites (**Figure 2**); these are head/neck, hands, upper extremities (excluding hands), trunk, lower extremities (excluding feet), and feet
- The degree of depigmentation for each site was determined and estimated to the nearest percentage as follows:
  - 100%: no pigment is present
  - 90%: specks of pigment are present
  - 75%: depigmented area exceeds the pigmented area
  - 50%: depigmented and pigmented areas are equal
  - 25%: pigmented area exceeds the depigmented area
  - 10%: only specks of depigmentation are present
  - 0%: no depigmentation is present

Figure 2. Body Sites for Determination of F-VASI and T-VASI Scores



F-VASI, facial Vitiligo Area Scoring Index; T-VASI, total Vitiligo Area Scoring Index.
* For F-VASI, the face area includes the nose but does not include the surface area of the lips, scalp, eyelids, ears, or neck.

- F-VASI and T-VASI scores were derived by multiplying the area of depigmentation in hand units (approximately 1% BSA per hand unit) for each region by the extent of depigmentation within each hand unit (ie, 0%, 10%, 25%, 50%, 75%, 90%, or 100%) for each site (**Figure 2**) and summing these values for all regions

$$\text{VASI} = \sum_{\text{all body sites}} [\text{hand units}] \times [\text{residual depigmentation}]$$

- For F-VASI, possible scores range from 0 to 3
  - For F-VASI, the face was defined as including the forehead (to original hairline), the cheeks to the jawline vertically and laterally from the corner of the mouth to the tragus, and the nose; the surface area of the lips, scalp, eyelids, ears, and neck were excluded
- For T-VASI, possible scores range from 0 to 100

Measures for VASI Correlation

- Vitiligo severity was assessed by physicians using the 5-point Physician's Global Vitiligo Assessment (PhGVA) scale with scoring as follows:
  - 0: clear; no signs of vitiligo
  - 1: almost clear; only specks of depigmentation present
  - 2: mild disease; pigmented and depigmented areas are equal
  - 3: moderate disease; more or complete depigmentation (may include <30% hair whitening)
  - 4: severe disease; complete depigmentation plus >30% hair whitening
- Vitiligo severity was also assessed by patients, comparing their impression of their disease from the baseline visit using the 7-point Patient Global Impression of Change–Vitiligo (PaGIC-V) scale, with scoring as follows:
  - 1: very much improved
  - 2: much improved
  - 3: minimally improved
  - 4: no change
  - 5: minimally worse
  - 6: much worse
  - 7: very much worse

Results

Test-Retest Reliability

- Among stable patients (ie, no change from baseline in PaGIC-V [score of 4]), VASI scores showed excellent test-retest reliability at Weeks 12 and 24, indicating stability of the VASI instrument over time (**Table 1**)

Table 1. Intraclass Correlation Coefficients Between Time Points Within Stable Patients as Defined by the PaGIC-V at Weeks 12 and 24

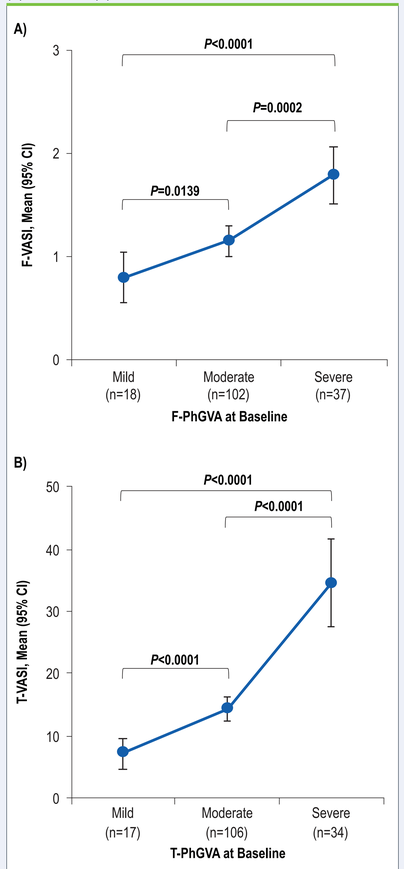
Cohort	n	F-VASI ICC	T-VASI ICC
1 (Week 12)	53	0.97	0.99
2 (Week 24)	35	0.95	0.99

F-VASI, facial Vitiligo Area Scoring Index; ICC, intraclass correlation coefficient; PaGIC-V, Patient Global Impression of Change–Vitiligo; T-VASI, total Vitiligo Area Scoring Index.

Construct Validity

- Convergent validity was assessed by evaluating the relationship between the VASI and PhGVA; there was a significant positive relationship between the 2 instruments ($P<0.0001$; **Figure 3**)
- Known-group validity was evaluated using PhGVA as an indicator of overall vitiligo severity
- Significant differences in VASI were detected among PhGVA categories (mild, moderate, severe) at baseline, which showed known-group validity (pairwise, all $P<0.015$; **Figure 3**)

Figure 3. Known Group Validity Based on the Correlation of (A) F-VASI and (B) T-VASI With PhGVA at Baseline

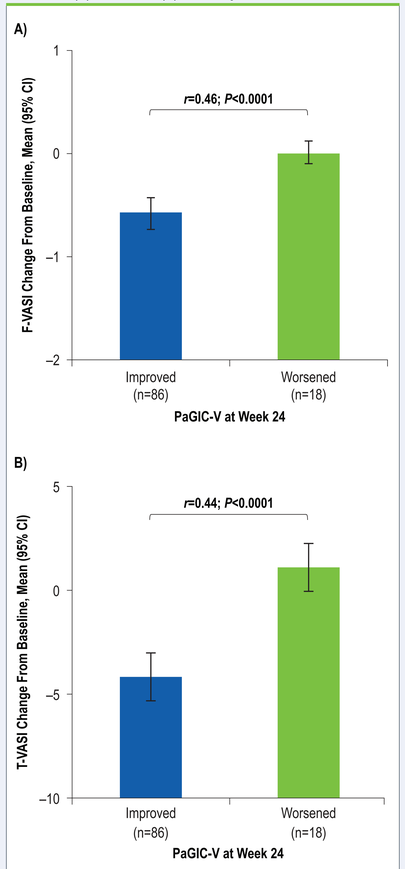


F-PhGVA, facial Physician's Global Vitiligo Assessment; F-VASI, facial Vitiligo Area Scoring Index; T-PhGVA, total Physician's Global Vitiligo Assessment; T-VASI, total Vitiligo Area Scoring Index.
P values based on 2-sample *t* test.

Ability to Detect Change

- The VASI was able to detect change in disease status during the treatment period
- VASI score changes were significantly different ($P<0.0001$) between patients who showed PaGIC-V improvement (scores of 1–3) or worsening (scores of 5–6) of vitiligo (**Figure 4**)
- VASI changes were significantly related to the PaGIC-V (Pearson's correlation coefficients, approximately 0.45)

Figure 4. Ability to Detect Change Based on the Change From Baseline in (A) F-VASI and (B) T-VASI by PaGIC-V at Week 24

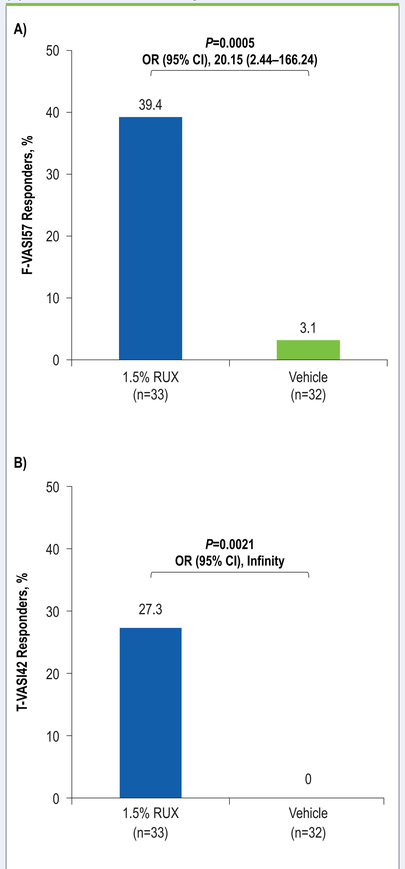


F-VASI, facial Vitiligo Area Scoring Index; PaGIC-V, Patient Global Impression of Change–Vitiligo; *r*, Pearson's correlation coefficient; T-VASI, total Vitiligo Area Scoring Index.
P values based on 2-sample *t* test.

Score Interpretability

- To assess interpretability, an anchor-based approach used PaGIC-V (score of 1 or 2) to define clinically meaningful change (CMC) on the VASI at Week 24
  - The mean percentage CMC was 57% for F-VASI and 42% for T-VASI
- Results of the phase 2 study indicated that a significantly higher percentage of patients treated with 1.5% ruxolitinib cream BID vs vehicle met or exceeded CMC thresholds on the VASI at Week 24 (**Figure 5**)

Figure 5. Clinically Meaningful Change of (A) F-VASI57 and (B) T-VASI42 in the Phase 2 Study



CMC, clinically meaningful change; F-VASI57, CMC of 57% for facial Vitiligo Area Scoring Index; OR, odds ratio; RUX, ruxolitinib cream; T-VASI42, CMC of 42% for total Vitiligo Area Scoring Index.
P values based on Fisher's exact test.

Conclusions

- **The VASI met or exceeded standards for reliability, validity, and ability to detect change in a large, randomized, vehicle-controlled study**
- **Analyses of treatment efficacy using the F-VASI and T-VASI reflect meaningful and relevant changes in patients with vitiligo**
- **Corresponding change and percentage change scores from baseline in the F-VASI and T-VASI are meaningful and interpretable, supporting use of the VASI instrument as a measure of primary efficacy in clinical studies**

Disclosures

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. 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. KB, FIK, ZZ, and KS are employees and shareholders of Incyte Corporation.

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