Supplementary Appendix

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This appendix has been provided by the authors to give readers additional information about the work.

SUPPLEMENTARY APPENDIX

Two Phase 3 Randomized Controlled Trials of Ruxolitinib Cream for Vitiligo

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* Locations shown are for the 94 centers that randomized patients across North America and Europe.

† Original principal investigator was replaced.

SUPPLEMENTARY METHODS

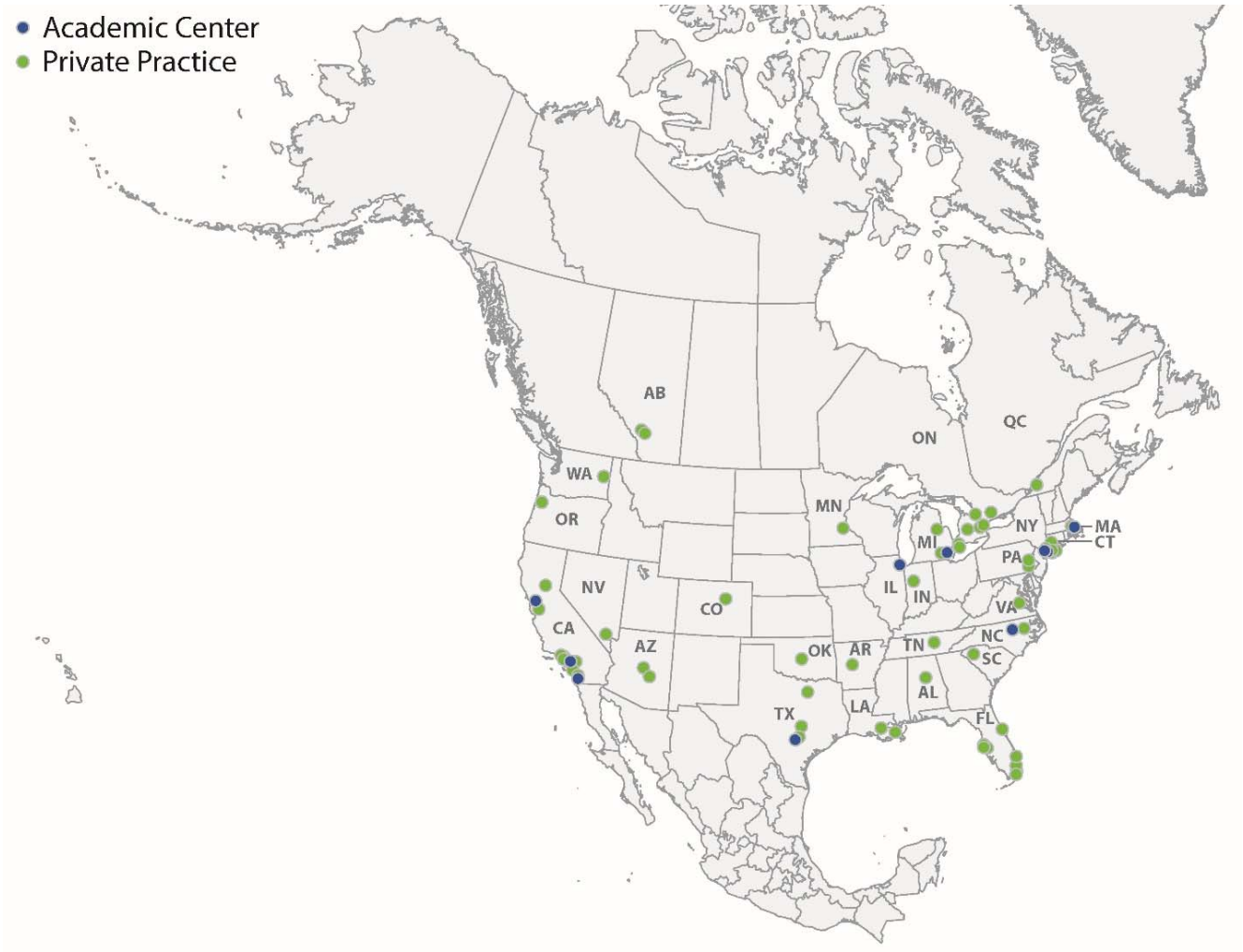
Total body Vitiligo Area Scoring Index (VASI) included facial and non-facial areas. For physician assessment, the body was divided into 6 separate and mutually exclusive sites that included the head/neck (including scalp), trunk (including genitalia), upper extremities (including axillae), hands, lower extremities (including buttocks), and feet. For facial VASI, the face included the area on the forehead to the original hairline, the cheeks to the jawline vertically and laterally from the corner of the mouth to the tragus, nose, and eyelids; the lips, scalp, ears, and neck were not included. Boundaries and exclusions for determination of body surface area (BSA) and VASI were similar. VASI scores include a component of BSA and a score for depigmentation within a lesion. The BSA score used in VASI was the same as the BSA standalone assessment. The VASI score integrates the BSA with the depigmentation score, thus taking into account the integrity of the entire lesion, whereas the BSA represents the lesion margins only.

Color-matching was assessed by patients on a 5-point scale (excellent, very good, good, poor, and very poor) by comparing skin color of repigmented facial lesions versus normal unaffected facial areas.

SUPPLEMENTARY FIGURES

Figure S1. Geographic Distribution of Study Sites.*

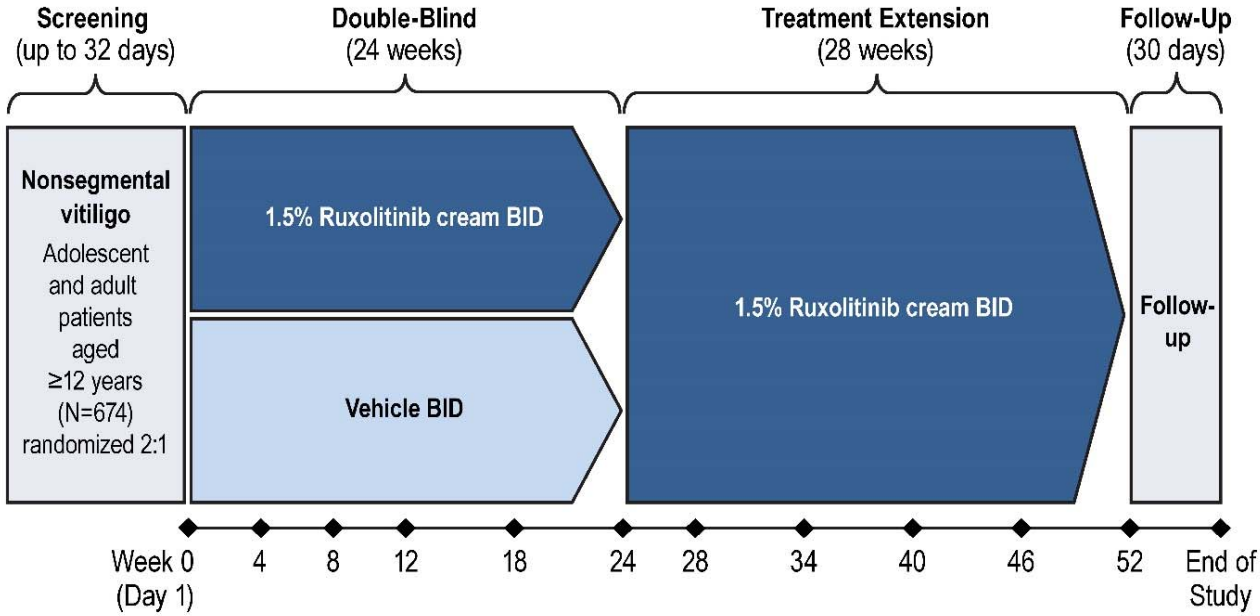
A. North America



B. Europe

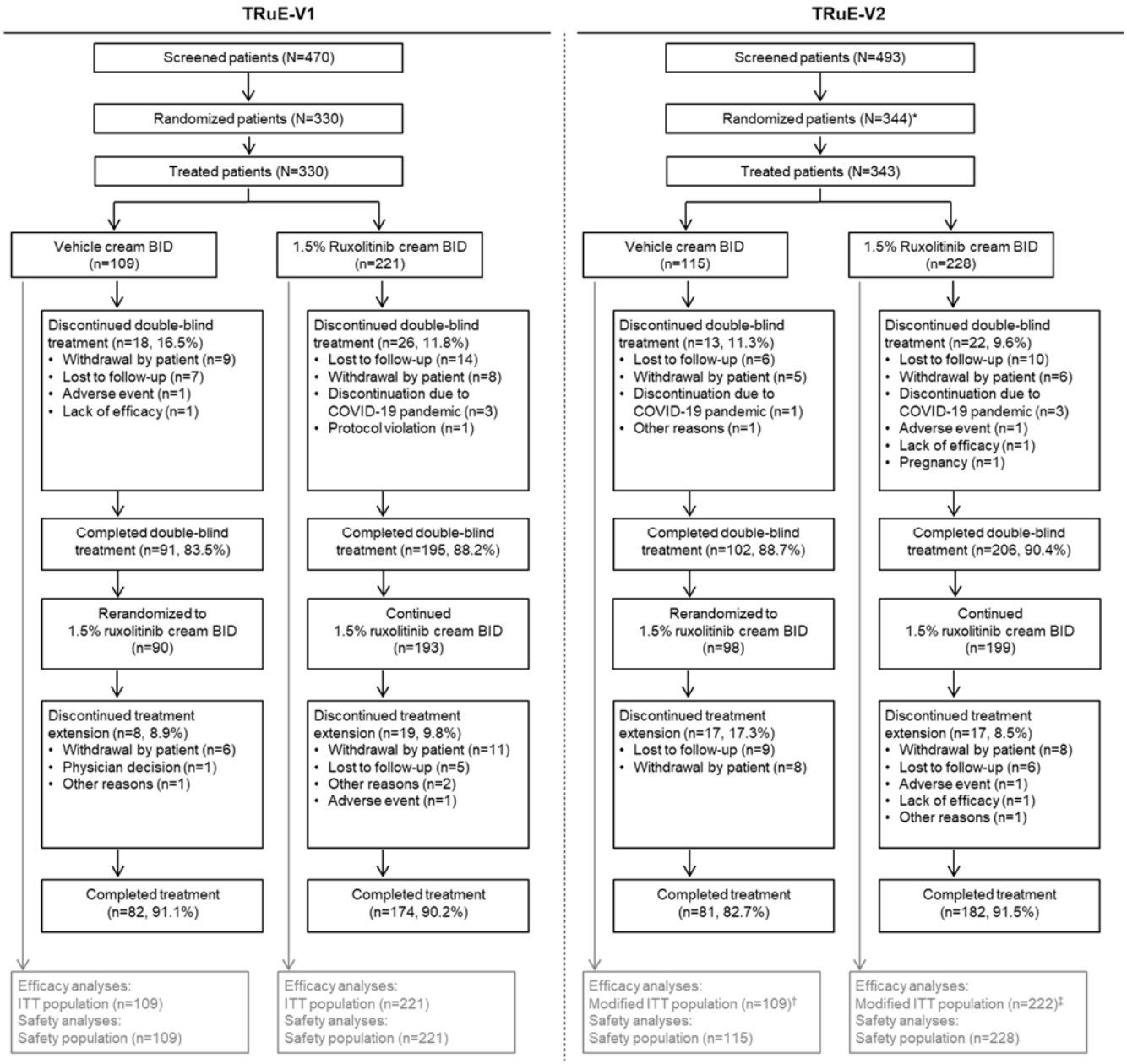
* Study sites shown are for the 101 centers that screened patients across North America and Europe. Seven centers that screened but did not randomize patients were located in Bulgaria (Stara Zagora), Canada (Calgary, AB; Windsor, ON), and the United States (Brighton, MI; Danbury, CT; Oceanside, CA; San Diego, CA).

Figure S2. Study Design.



BID, twice daily.

Figure S3. Patient Disposition.



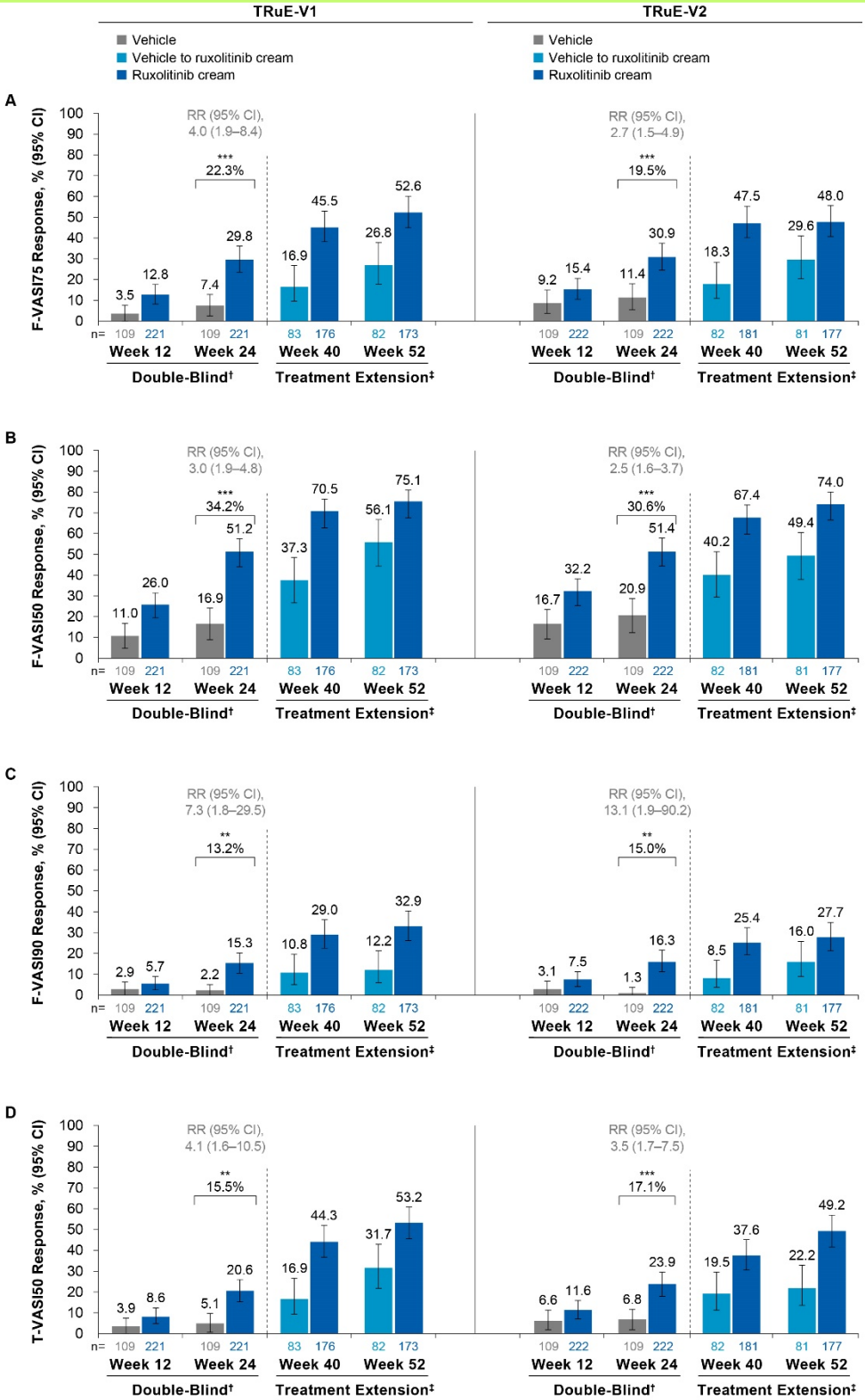
BID, twice daily; COVID-19, coronavirus disease 2019; ITT, intent to treat; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

* One randomized patient did not apply ≥1 dose of ruxolitinib cream and was excluded from the safety population.

† Six patients from one study site were excluded from the intent-to-treat population because of compliance issues.

‡ Seven patients from one study site were excluded from the intent-to-treat population because of compliance issues.

Figure S4. Efficacy of Ruxolitinib Cream Application on (A) the Primary Endpoint F-VASI75 Response, and Key Secondary Endpoints (B) F-VASI50 Response, (C) F-VASI90 Response, and (D) T-VASI50 Response (Modified ITT Population; Primary and Key Secondary Endpoints).



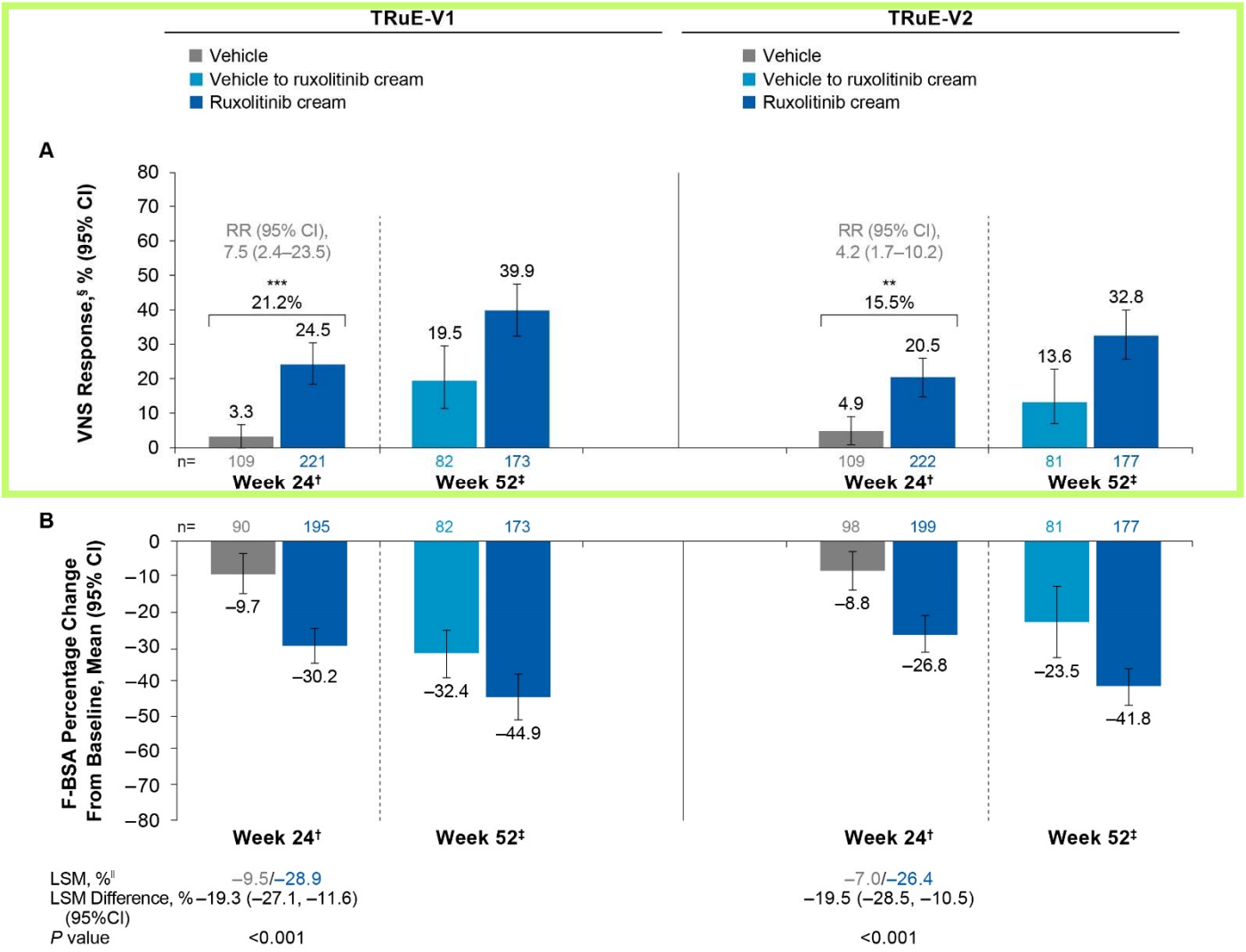
F-VASI, facial Vitiligo Area Scoring Index; F-VASI50/75/90, ≥50%/≥75%/≥90% improvement in F-VASI from baseline; ITT, intent to treat; RR, relative risk; T-VASI50, ≥50% improvement in total Vitiligo Area Scoring Index from baseline; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

** $P<0.01$, *** $P<0.001$ for response rate difference for ruxolitinib cream vs vehicle.

† During the double-blind period (up to Week 24), multiple imputation was applied to account for missing values.

‡ During the open-label treatment extension (after Week 24), responses were reported as observed.

Figure S5. Efficacy of Ruxolitinib Cream Application on Key Secondary Endpoints (A) VNS Response and (B) Percentage Change From Baseline in F-BSA (Modified ITT Population; Key Secondary Endpoints).



ANCOVA, analysis of covariance; F-BSA, facial body surface area; ITT, intent to treat; LSM, least squares mean; RR, relative risk; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies; VNS, Vitiligo Noticeability Scale.

** *P*<0.01, *** *P*<0.001 for response rate difference for ruxolitinib cream vs vehicle.

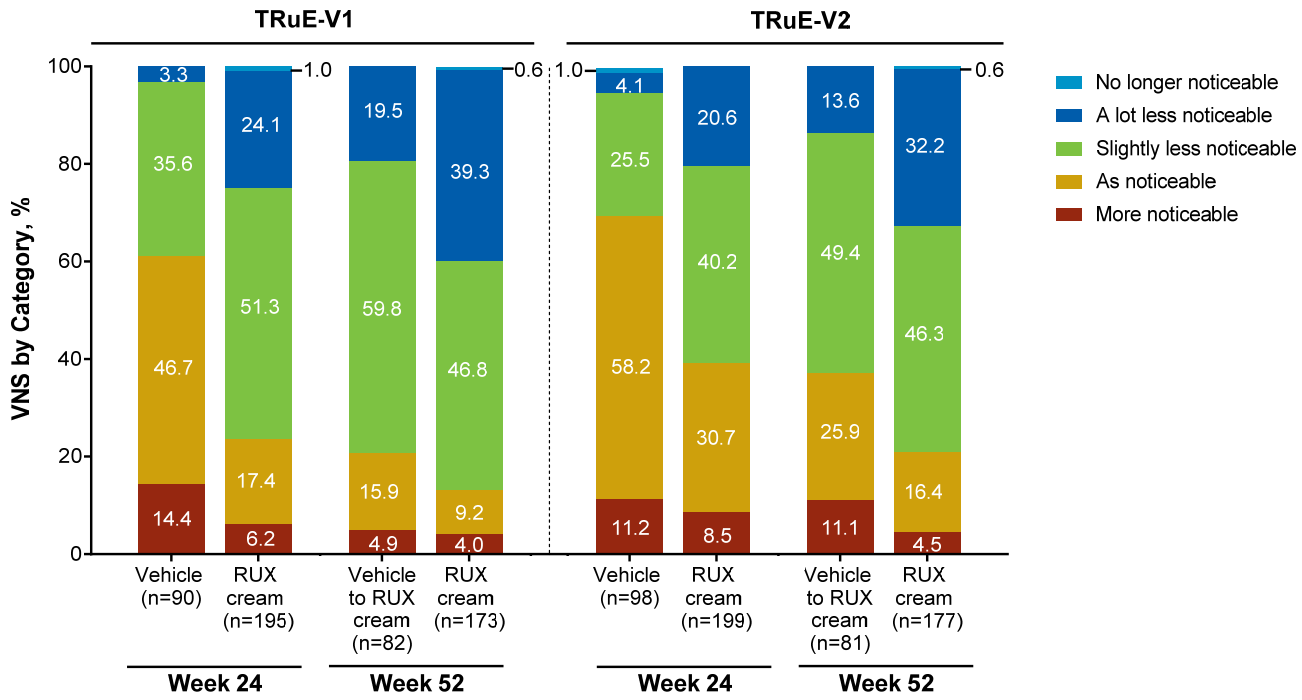
† During the double-blind period (up to Week 24), multiple imputation was applied to account for missing values.

‡ During the open-label treatment extension (after Week 24), responses were reported as observed.

§ VNS response was defined as achieving a rating of “a lot less noticeable” or “no longer noticeable.”

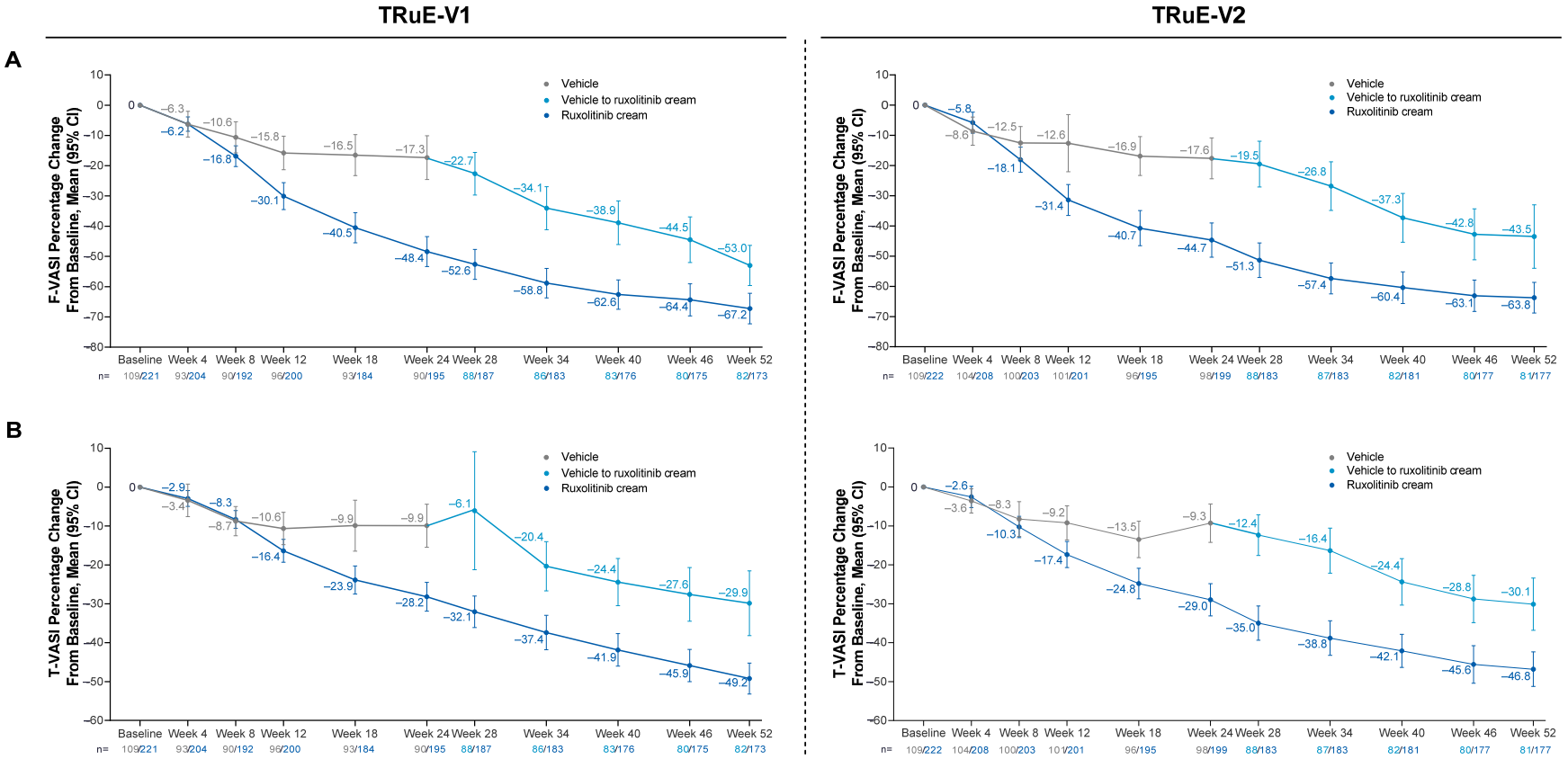
‖ At Week 24, an ANCOVA model was applied to determine LSM, LSM difference, and *P* value.

Figure S6. Proportion of Patients in Each VNS Category (Secondary Endpoint).



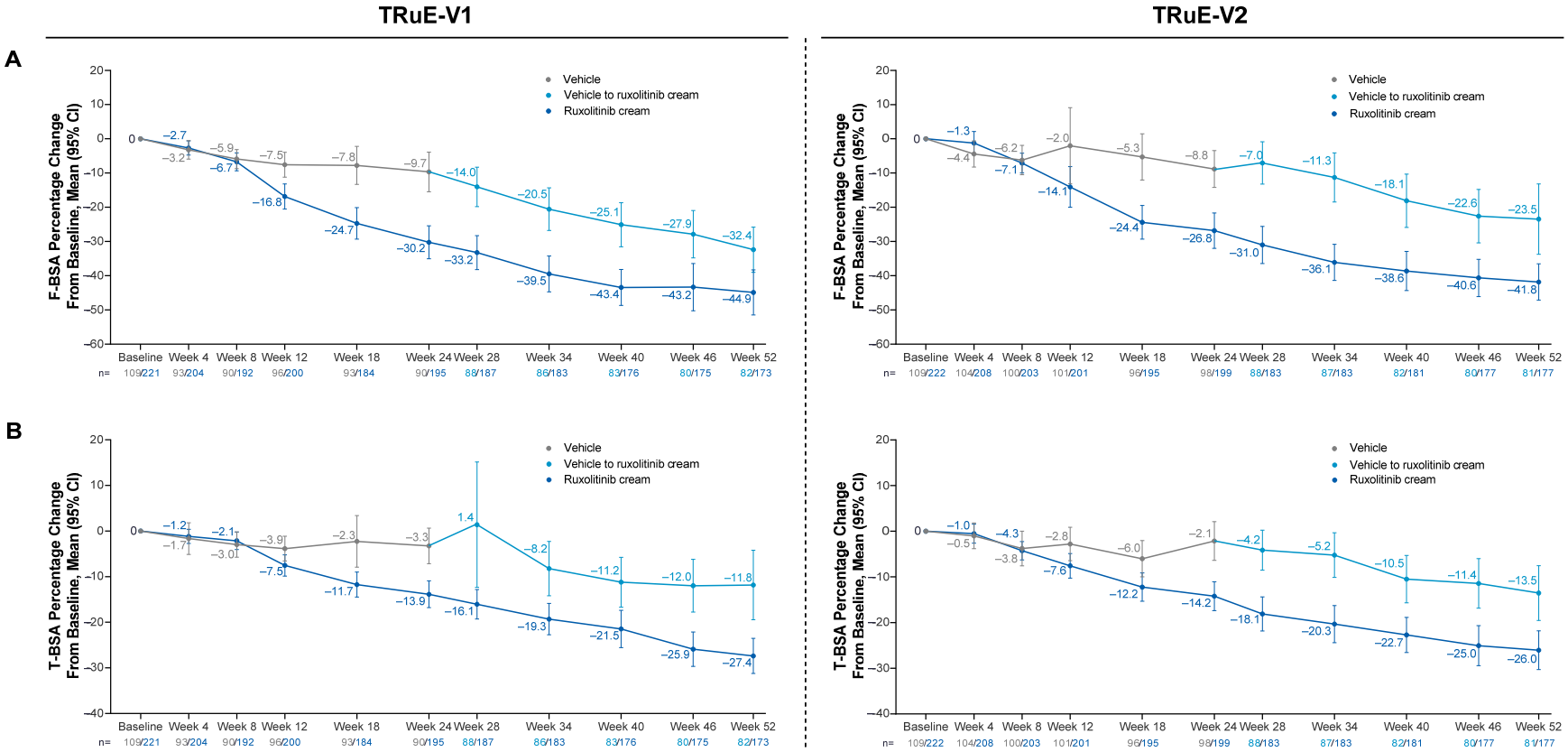
TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies; RUX, ruxolitinib; VNS, Vitiligo Noticeability Scale.

Figure S7. Percentage Change From Baseline* in (A) F-VASI and (B) T-VASI During the Double-Blind and Open-Label Treatment Extension Periods (Secondary Endpoints).



F-VASI, facial Vitiligo Area Scoring Index; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies; T-VASI, total Vitiligo Area Scoring Index.
* Mean percentage change from baseline reported as observed.
For secondary outcomes, confidence intervals were not adjusted for multiplicity, and inferences drawn from the intervals may not be reproducible.

Figure S8. Percentage Change From Baseline* in (A) Facial BSA and (B) Total BSA During the Double-Blind and Open-Label Treatment Extension Periods (Secondary Endpoints).



BSA, body surface area; F-BSA, facial BSA; T-BSA, total BSA; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

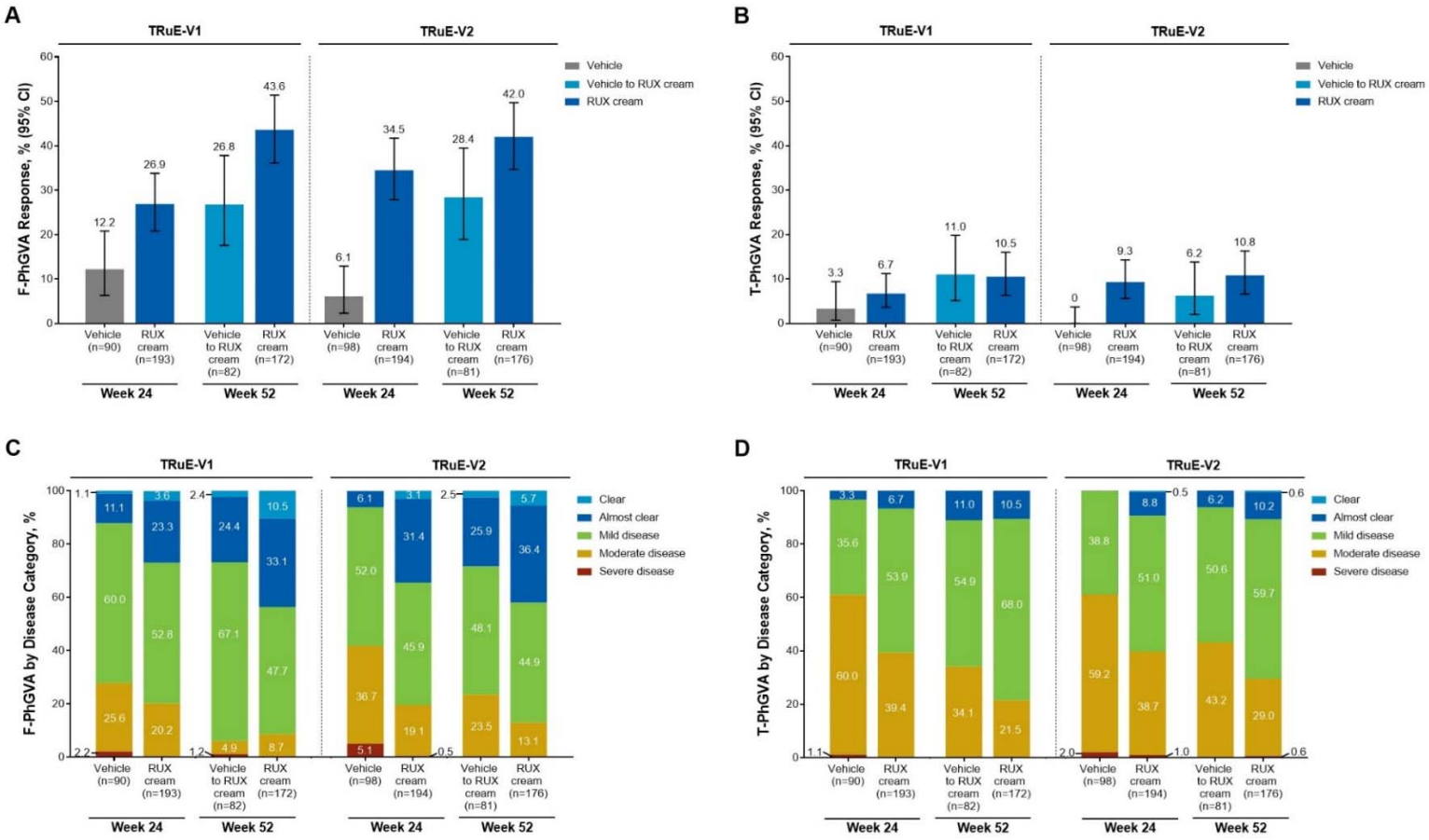
* Mean percentage change from baseline reported as observed.

For secondary outcomes, confidence intervals were not adjusted for multiplicity, and inferences drawn from the intervals may not be reproducible.

Figure S9. Representative Clinical Images of Patients Who Applied Ruxolitinib Cream During the Double-Blind and Open-Label Treatment Extension Periods.

F-VASI, facial Vitiligo Area Scoring Index; T-VASI, total Vitiligo Area Scoring Index.

Figure S10. Proportion of Patients* Achieving (A) F-PhGVA and (B) T-PhGVA Response† and in Each (C) F-PhGVA and (D) T-PhGVA Category (Exploratory Endpoints).



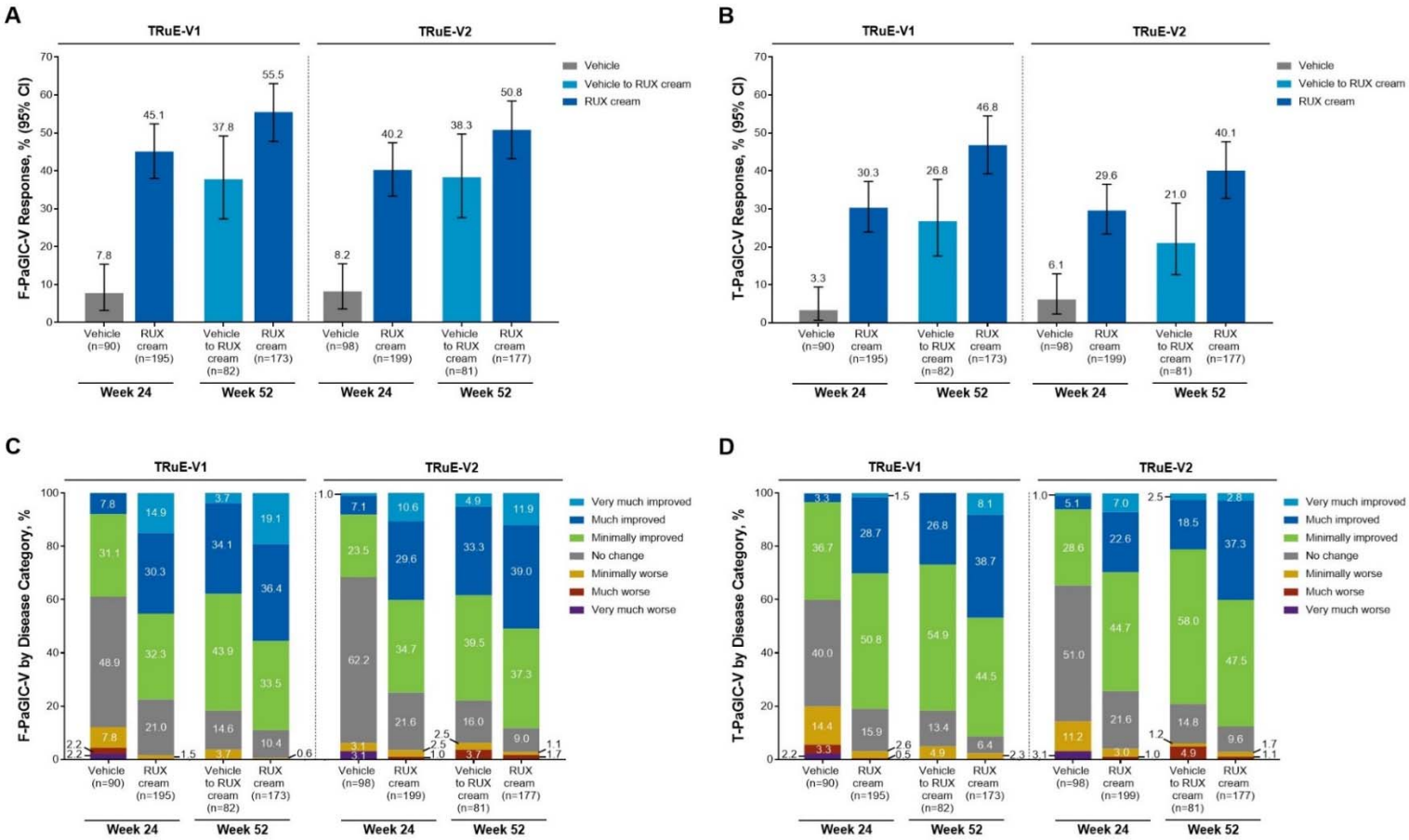
F-PhGVA, facial Physician's Global Vitiligo Assessment; RUX, ruxolitinib; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies; T-PhGVA, total Physician's Global Vitiligo Assessment.

* Proportion of patients reported as observed.

† F-PhGVA and T-PhGVA responses were defined as achieving a rating of clear or almost clear.

For exploratory outcomes, confidence intervals were not adjusted for multiplicity, and inferences drawn from the intervals may not be reproducible.

Figure S11. Proportion of Patients* Achieving (A) F-PaGIC-V and (B) T-PaGIC-V Response† and in Each (C) F-PaGIC-V and (D) T-PaGIC-V Category (Exploratory Endpoints).



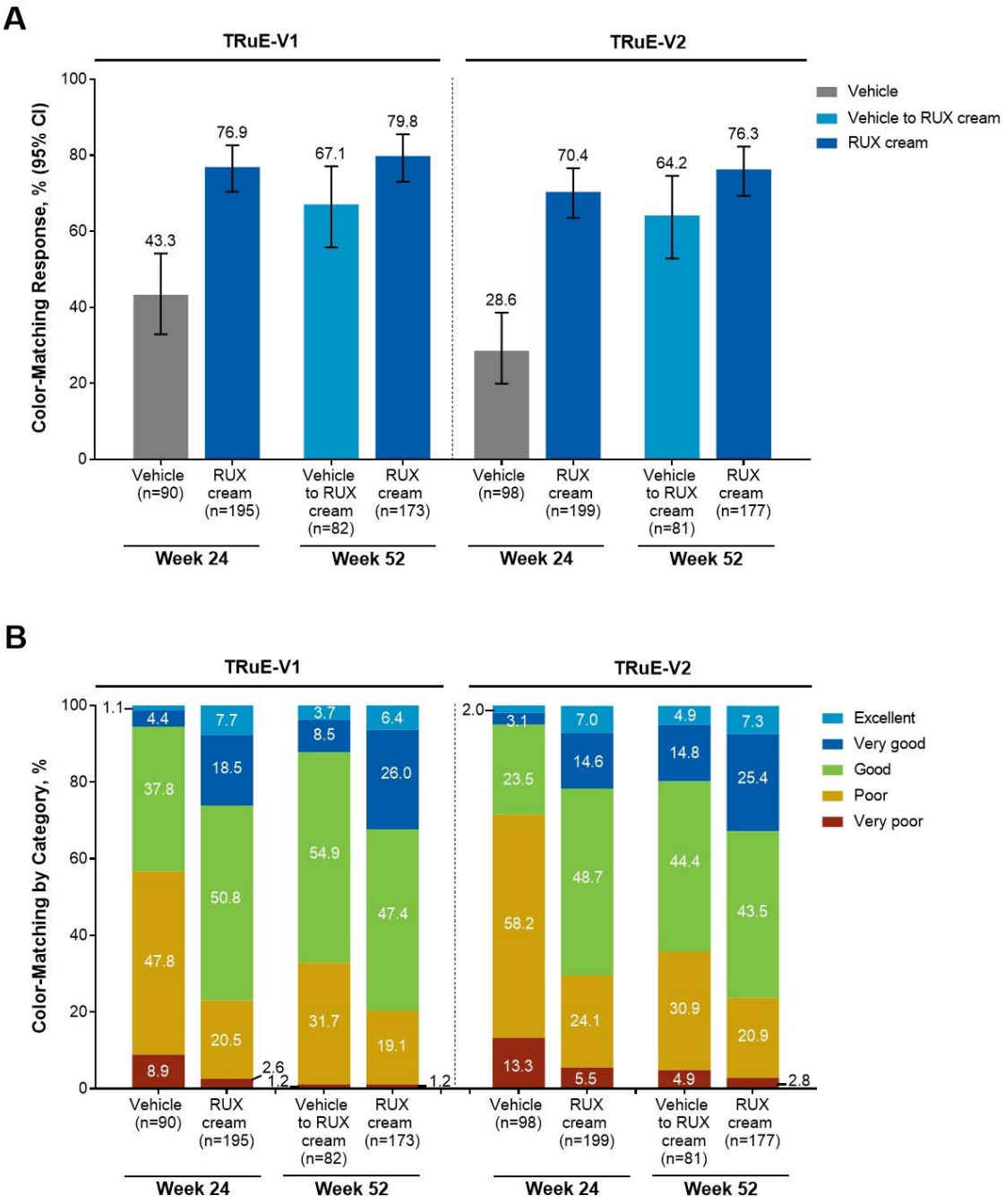
F-PaGIC-V, facial Patient's Global Impression of Change–Vitiligo; RUX, ruxolitinib; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies; T-PaGIC-V, total Patient's Global Impression of Change–Vitiligo.

* Proportion of patients reported as observed.

† F-PaGIC-V and T-PaGIC-V responses were defined as achieving a rating of very much or much improved.

For exploratory outcomes, confidence intervals were not adjusted for multiplicity, and inferences drawn from the intervals may not be reproducible.

Figure S12. Proportion of Patients* (A) Achieving Color-Matching Response† and (B) in Each Color-Matching Category (Exploratory Endpoint).



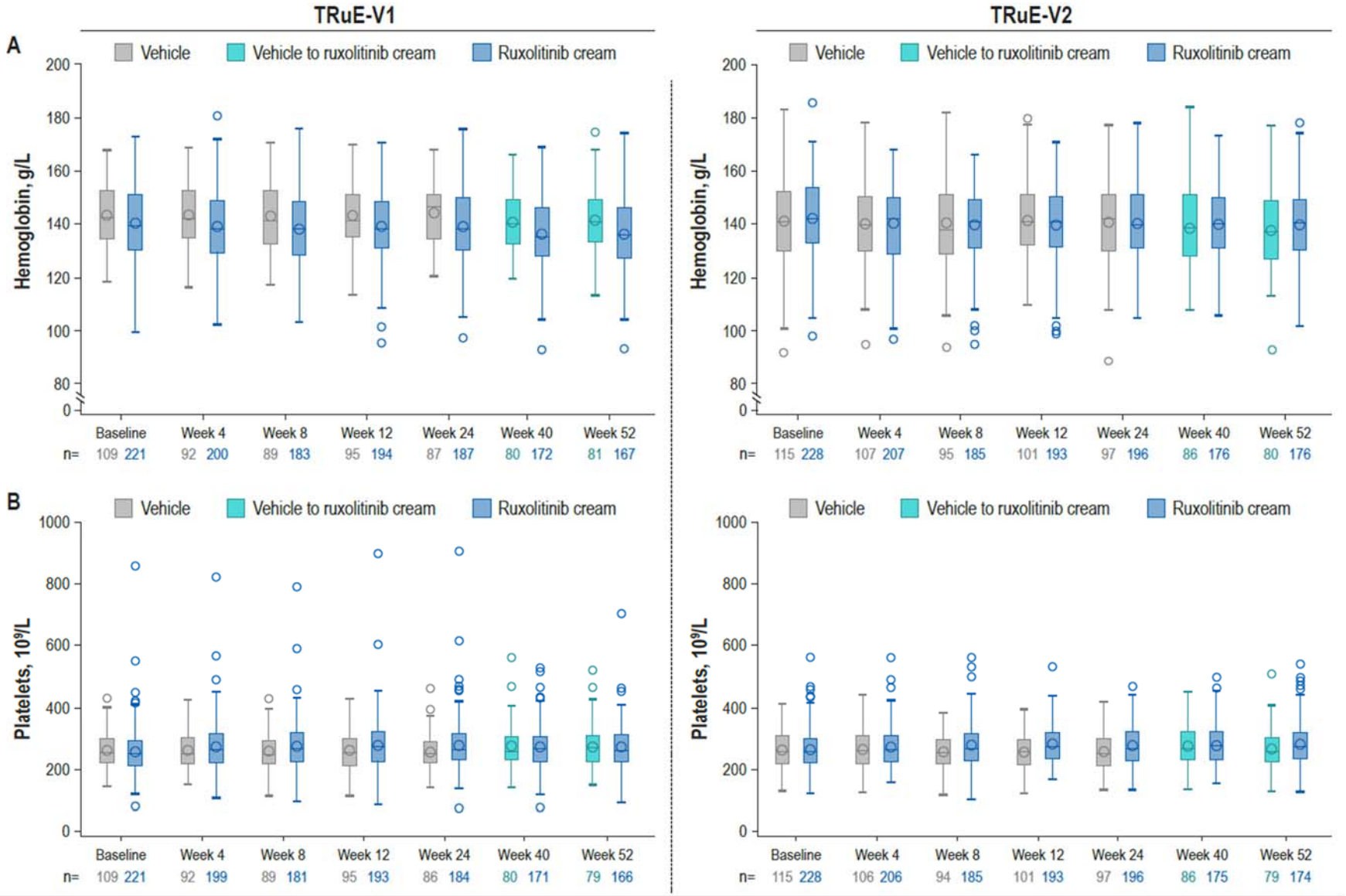
RUX, ruxolitinib; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

* Proportion of patients reported as observed.

† Color-matching response was defined as achieving a rating of good, very good, or excellent.

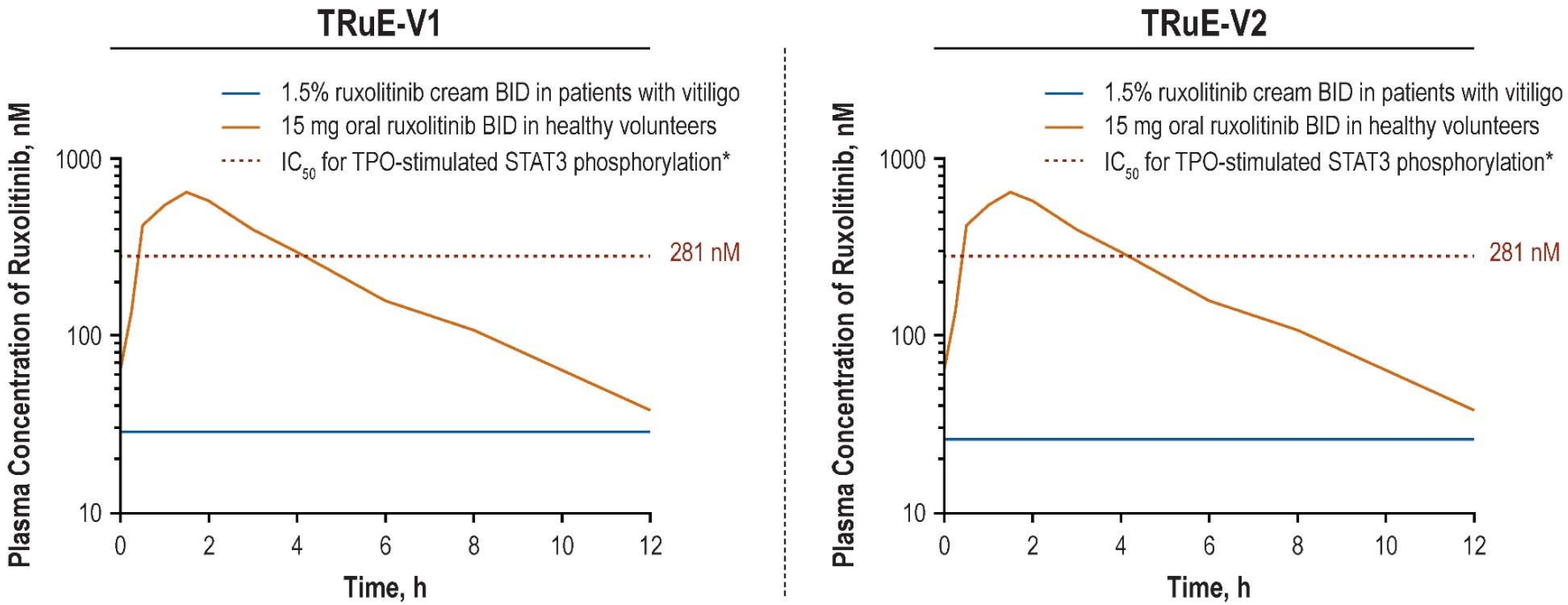
For exploratory outcomes, confidence intervals were not adjusted for multiplicity, and inferences drawn from the intervals may not be reproducible.

Figure S13. Laboratory Values for (A) Hemoglobin and (B) Platelets.



TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

Figure S14. Comparison of Ruxolitinib Plasma Concentration-Time Curves After Oral Administration in Healthy Participants and Topical Administration in Patients With Vitiligo† From TRuE-V1 and TRuE-V2 Studies.



BID, twice daily; IC_{50}, half-maximal inhibitory concentration; JAK, Janus kinase; STAT3, signal transducer and activator of transcription 3; TPO, thrombopoietin; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

* The whole-blood IC_{50} for ruxolitinib-mediated inhibition of TPO-stimulated STAT3 phosphorylation (281 nM), which is driven by JAK2, was used as a proxy parameter to evaluate JAK-related myelosuppression in the bone marrow (Quintas-Cardama A, et al. Blood. 2010;115[15]:3109-3117).

† Geometric mean steady-state plasma concentrations (average of Weeks 4 and 24) for topical administration of ruxolitinib (solid blue lines), 28.4 nM for TRuE-V1 and 26.4 nM for TRuE-V2.

SUPPLEMENTARY TABLES

Table S1. Representativeness of Patients in the TRuE-V1 and TRuE-V2 Clinical Trials

Category	Example
Disease, problem, or condition under investigation	Vitiligo
Special considerations related to:	
Sex and gender	Vitiligo prevalence may be slightly higher in females vs males[1,2]; this may be related, in part, to female patients seeking healthcare more frequently than their male counterparts.[1,3]
Age	Vitiligo signs can appear at any age, but onset often occurs during adolescence and early adulthood.[1] In most patients, vitiligo onset occurs at ≤30 years of age.[2-5]
Race or ethnic group	Vitiligo is most prevalent among White patients in the United States (~75%) and Europe (~90%).[4,6]
Geography	Global prevalence is approximately 0.5%–2.0% and varies geographically; among United States and European populations, prevalence ranges from 0.1%–1.5% and 0%–3.1%, respectively.[4,6-8]
Other considerations	Most patients with vitiligo have an affected BSA ≤10%.[9,10] The most common Fitzpatrick skin type among patients with vitiligo in the United States and Europe is type III (~40%), followed by types IV (~30%) and II (~20%).[4,6]
Overall representativeness of these trials	The TRuE-V1/TRuE-V2 studies conducted in the United States and Europe included a slight majority of female patients (56%/50%). Biologic sex (male/female) was reported for all patients per their medical history. In line with vitiligo onset generally occurring by 30 years of age, the studies included 11%/11% adolescent patients and 55%/57% patients who were ≤40 years old (mean age, 40.2/38.9 years). As expected based on the scientific literature, randomized patients were mostly White (84%/80%), although the proportion of Black patients was relatively small (5%/5%). Consistent with vitiligo population prevalence studies, the majority of patients enrolled in TRuE-V1/TRuE-V2 had Fitzpatrick skin type III (40%/39%); however, there were fewer patients with type IV (15%/23%) and more patients with type II (35%/26%) compared with previous reports.

BSA, body surface area; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

Table S2. Other Secondary Endpoints (Double-Blind and Open-Label Treatment Extension Periods; Modified ITT Population)

	TRuE-V1				TRuE-V2			
	Vehicle (up to Week 24) / 1.5% Ruxolitinib Cream (after Week 24)		1.5% Ruxolitinib Cream		Vehicle (up to Week 24) / 1.5% Ruxolitinib Cream (after Week 24)		1.5% Ruxolitinib Cream	
Other Secondary Endpoints	n	Outcome (Variability)	n	Outcome (Variability)	n	Outcome (Variability)	n	Outcome (Variability)
Proportion of patients achieving F-VASI25/50/75/90 during the treatment period								
F-VASI25, % (95% CI)								
Week 12*	109	26.5 (17.8, 35.3)	221	46.3 (39.5, 53.0)	109	29.5 (20.8, 38.3)	222	51.5 (44.6, 58.4)
Week 24*	109	30.0 (20.8, 39.2)	221	69.8 (63.5, 76.2)	109	32.0 (23.0, 41.0)	222	63.9 (57.2, 70.6)
Week 52†	82	74.4 (63.6, 83.4)	173	89.6 (84.1, 93.7)	81	71.6 (60.5, 81.1)	177	82.5 (76.1, 87.8)
F-VASI50, % (95% CI)								
Week 12*	109	11.0 (4.8, 17.2)	221	26.0 (20.0, 32.0)	109	16.7 (9.5, 23.9)	222	32.2 (25.7, 38.7)
Week 24*	109	16.9 (9.3, 24.6)	221	51.2 (44.4, 58.0)	109	20.9 (12.9, 28.9)	222	51.4 (44.6, 58.3)
Week 52†	82	56.1 (44.7, 67.0)	173	75.1 (68.0, 81.4)	81	49.4 (38.1, 60.7)	177	74.0 (66.9, 80.3)
F-VASI75, % (95% CI)								
Week 12*	109	3.5 (0, 7.4)	221	12.8 (8.1, 17.4)	109	9.2 (3.6, 14.8)	222	15.4 (10.5, 20.4)
Week 24*	109	7.4 (2.2, 12.6)	221	29.8 (23.5, 36.1)	109	11.4 (5.2, 17.7)	222	30.9 (24.5, 37.3)
Week 52†	82	26.8 (17.6, 37.8)	173	52.6 (44.9, 60.2)	81	29.6 (20.0, 40.8)	177	48.0 (40.5, 55.6)
F-VASI90, % (95% CI)								
Week 12*	109	2.9 (0, 6.1)	221	5.7 (2.5, 8.9)	109	3.1 (0, 6.6)	222	7.5 (4.0, 11.0)
Week 24*	109	2.2 (0, 5.1)	221	15.3 (10.4, 20.2)	109	1.3 (0, 3.8)	222	16.3 (11.2, 21.5)
Week 52†	82	12.2 (6.0, 21.3)	173	32.9 (26.0, 40.5)	81	16.0 (8.8, 25.9)	177	27.7 (21.2, 34.9)
Percentage change from baseline in F-VASI during the treatment period								
F-VASI, mean (95% CI)								
Percent change at Week 24	90	–17.3 (–24.6, –10.1)	195	–48.4 (–53.4, –43.4)	98	–17.6 (–24.4, –10.9)	199	–44.7 (–50.3, –39.0)
Percent change at Week 52	82	–53.0 (–59.6, –46.4)	173	–67.2 (–72.3, –62.2)	81	–43.5 (–54.0, –33.0)	177	–63.8 (–68.8, –58.7)
Percentage change from baseline in F-BSA during the treatment period								

F-BSA, mean (95% CI)								
Percent change at Week 24	90	–9.7 (–15.4, –3.9)	195	–30.2 (–35.0, –25.4)	98	–8.8 (–14.2, –3.4)	199	–26.8 (–32.0, –21.7)
Percent change at Week 52	82	–32.4 (–39.0, –25.8)	173	–44.9 (–51.5, –38.3)	81	–23.5 (–33.7, –13.2)	177	–41.8 (–47.1, –36.5)
Percentage change from baseline in T-VASI during the treatment period								
T-VASI, mean (95% CI)								
Percent change at Week 24	90	–9.9 (–15.4, –4.4)	195	–28.2 (–31.9, –24.5)	98	–9.3 (–14.2, –4.3)	199	–29.0 (–33.1, –24.8)
Percent change at Week 52	82	–29.9 (–38.2, –21.5)	173	–49.2 (–53.2, –45.3)	81	–30.1 (–36.8, –23.4)	177	–46.8 (–51.2, –42.4)
Percentage change from baseline in T-BSA during the treatment period								
T-BSA, mean (95% CI)								
Percent change at Week 24	90	–3.3 (–7.2, –0.6)	195	–13.9 (–16.8, –10.9)	98	–2.1 (–6.4, 2.1)	199	–14.2 (–17.4, –11.1)
Percent change at Week 52	82	–11.8 (–19.5, –4.2)	173	–27.4 (–31.2, –23.5)	81	–13.5 (–19.5, –7.5)	177	–26.0 (–30.3, –21.8)
Proportion of patients achieving T-VASI25/50/75/90 during the treatment period								
T-VASI25, % (95% CI)								
Week 12*	109	17.2 (9.7, 24.6)	221	26.8 (20.8, 32.9)	109	15.6 (8.6, 22.6)	222	28.5 (22.2, 34.8)
Week 24*	109	23.8 (15.2, 32.5)	221	48.8 (41.9, 55.6)	109	21.2 (12.9, 29.4)	222	50.2 (43.3, 57.1)
Week 52†	82	56.1 (44.7, 67.0)	173	77.5 (70.5, 83.5)	81	53.1 (41.7, 64.3)	177	76.8 (69.9, 82.8)
T-VASI50, % (95% CI)								
Week 12*	109	3.9 (0.1, 7.6)	221	8.6 (4.8, 12.3)	109	6.6 (1.9, 11.3)	222	11.6 (7.3, 15.9)
Week 24*	109	5.1 (0.6, 9.7)	221	20.6 (15.2, 26.0)	109	6.8 (1.9, 11.7)	222	23.9 (18.1, 29.8)
Week 52†	82	31.7 (21.9, 42.9)	173	53.2 (45.5, 60.8)	81	22.2 (13.7, 32.8)	177	49.2 (41.6, 56.8)
T-VASI75, % (95% CI)								
Week 12*	109	1.8 (0, 4.4)	221	1.4 (0, 2.9)	109	0.9 (0, 2.7)	222	1.8 (0.1, 3.6)
Week 24*	109	1.8 (0, 4.4)	221	4.1 (1.5, 6.7)	109	1.8 (0, 4.4)	222	8.0 (4.4, 11.6)
Week 52†	82	9.8 (4.3, 18.3)	173	20.2 (14.5, 27.0)	81	8.6 (3.5, 17.0)	177	20.9 (15.2, 27.6)
T-VASI90, % (95% CI)								
Week 12*	109	0 (NE)	221	0.9 (0, 2.2)	109	0 (NE)	222	0 (NE)
Week 24*	109	0 (NE)	221	0.5 (0, 1.3)	109	0 (NE)	222	1.0 (0, 2.3)
Week 52†	82	2.4 (0.3, 8.5)	173	3.5 (1.3, 7.4)	81	1.2 (0, 6.7)	177	6.8 (3.6, 11.5)

Proportion of patients in each category of VNS during the treatment period								
Week 24, n (%)								
More noticeable	90	13 (14.4)	195	12 (6.2)	98	11 (11.2)	199	17 (8.5)
As noticeable	90	42 (46.7)	195	34 (17.4)	98	57 (58.2)	199	61 (30.7)
Slightly less noticeable	90	32 (35.6)	195	100 (51.3)	98	25 (25.5)	199	80 (40.2)
A lot less noticeable	90	3 (3.3)	195	47 (24.1)	98	4 (4.1)	199	41 (20.6)
No longer noticeable	90	0	195	2 (1.0)	98	1 (1.0)	199	0
Week 52, n (%)								
More noticeable	82	4 (4.9)	173	7 (4.0)	81	9 (11.1)	177	8 (4.5)
As noticeable	82	13 (15.9)	173	16 (9.2)	81	21 (25.9)	177	29 (16.4)
Slightly less noticeable	82	49 (59.8)	173	81 (46.8)	81	40 (49.4)	177	82 (46.3)
A lot less noticeable	82	16 (19.5)	173	68 (39.3)	81	11 (13.6)	177	57 (32.2)
No longer noticeable	82	0	173	1 (0.6)	81	0	177	1 (0.6)
Change from baseline in DLQI or CDLQI during the treatment period								
DLQI, mean (95% CI)								
Change at Week 24	87	–0.8 (–1.5, –0.1)	178	–1.2 (–1.7, –0.6)	94	–0.7 (–1.5, 0.1)	182	–1.2 (–1.8, –0.6)
Change at Week 52	79	–1.4 (–2.2, –0.6)	157	–1.4 (–2.1, –0.8)	78	–1.2 (–2.1, –0.2)	161	–0.8 (–1.5, –0.2)
CDLQI,‡ mean (95% CI)								
Change at Week 24	3	0 (0, 0)	16	–0.3 (–1.4, 0.9)	3	–2.3 (–23.5, 18.8)	17	0 (–0.9, 0.9)
Change at Week 52	3	0 (–2.5, 2.5)	15	–1.0 (–2.4, 0.4)	3	–1.0 (–12.4, 10.4)	16	1.2 (–1.3, 3.7)

CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; F-BSA, facial body surface area; F-VASI, facial Vitiligo Area Scoring Index; F-VASI25/50/75/90, ≥25%/≥50%/≥75%/≥90% improvement in F-VASI from baseline; ITT, intent to treat; NE, not evaluable; T-BSA, total body surface area; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies; T-VASI, total Vitiligo Area Scoring Index; T-VASI25/50/75/90, ≥25%/≥50%/≥75%/≥90% improvement in T-VASI from baseline; VNS, Vitiligo Noticeability Scale.

* During the double-blind period (up to Week 24), multiple imputation was applied to account for missing values in F-VASI25/50/75/90 and T-VASI25/50/75/90.

† During the open-label treatment extension (beyond Week 24), responses were reported as observed. For secondary outcomes, confidence intervals were not adjusted for multiplicity, and inferences drawn from the intervals may not be reproducible.

‡ The CDLQI was administered to patients <16 years old.

Table S3. TEAEs Among Patients Who Applied Ruxolitinib Throughout the Study (Baseline to Week 52; Safety Population)

	TRuE-V1	TRuE-V2
	1.5% Ruxolitinib Cream	1.5% Ruxolitinib Cream
n (%)	(n=221)	(n=228)
Patients with TEAE	121 (54.8)	142 (62.3)
Most common TEAEs*		
COVID-19	14 (6.3)	19 (8.3)
Application site acne	14 (6.3)	15 (6.6)
Nasopharyngitis	12 (5.4)	14 (6.1)
Application site pruritus	12 (5.4)	12 (5.3)
Headache	8 (3.6)	14 (6.1)
Upper respiratory tract infection	8 (3.6)	7 (3.1)
Sinusitis	7 (3.2)	6 (2.6)
Application site dermatitis	4 (1.8)	6 (2.6)
Application site rash	6 (2.7)	3 (1.3)
Urinary tract infection	6 (2.7)	3 (1.3)
Alanine aminotransferase increased	2 (0.9)	6 (2.6)
Hypertension	1 (0.5)	6 (2.6)
Pyrexia	1 (0.5)	5 (2.2)
Application site exfoliation	0	5 (2.2)
Cough	0	5 (2.2)
Patients with treatment-related TEAEs	41 (18.6)	35 (15.4)
Most common treatment-related TEAEs*		
Application site acne	13 (5.9)	12 (5.3)
Application site pruritus	11 (5.0)	10 (4.4)
Application site exfoliation	0	5 (2.2)
Patients with serious TEAE†	7 (3.2)	4 (1.8)
Patients with TEAE leading to discontinuation	1 (0.5)	2 (0.9)

COVID-19, coronavirus disease 2019; TEAE, treatment-emergent adverse event; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

* Occurring in >2% of patients in any treatment group.

† No serious TEAEs were considered related to treatment.

Table S4. Serious Treatment-Emergent Adverse Events in Patients Who Applied Ruxolitinib Cream in TRuE-V1 and TRuE-V2

AE	Age/ Sex	Day of treatment that AE occurred (period)	AE grade	Outcome (duration [d])	Considered related to treatment (Y/N)	Change in ruxolitinib cream treatment	Additional notes
TRuE-V1							
Anal fistula	32/M	58 (DB)	4	Resolved (4)	N	No change	Procedure or non-drug therapy performed
Appendicitis	34/M	169 (DB)	4	Resolved (3)	N	No change	Procedure or non-drug therapy performed
Concussion	27/M	151 (DB)	3	Resolved (4)	N	No change	Procedure or non-drug therapy performed
Hepatitis infectious mononucleosis	23/F	148 (DB)	3	Resolved (30)	N	Temporary interruption	Concomitant medications for AE administered
Hypersensitivity*	66/F	179 (TE)	3	Resolved (1)	N	Temporary interruption	Concomitant medications for AE administered
Kidney contusion	14/M	5 (DB)	2	Resolved (12)	N	No change	Procedure or non-drug therapy performed; concomitant medications for AE administered
Myocarditis	59/M	63 (DB)	2	Resolved (2)	N	No change	Concomitant medications for AE administered
Prostate cancer	66/M	323 (TE)[†]	3	Ongoing	N	No change	None
Subacute combined cord degeneration*	66/F	179 (TE)	3	Ongoing	N	No change	Concomitant medications for AE administered
TRuE-V2							
Appendiceal abscess	52/F	291 (TE)	4	Resolved (6)	N	No change	Procedure performed; concomitant medications for AE administered

AE	Age/ Sex	Day of treatment that AE occurred (period)	AE grade	Outcome (duration [d])	Considered related to treatment (Y/N)	Change in ruxolitinib cream treatment	Additional notes
Coronary artery stenosis	57/M	78 (DB)	3	Resolved (3)	N	Temporary interruption	Procedure or non-drug therapy performed; concomitant medications for AE administered
Joint dislocation	31/M	246 (TE)	3	Resolved (3)	N	No change	Procedure performed; concomitant medications for AE administered
Papillary thyroid cancer	31/F	174 (TE)	3	Ongoing	N	No change	Patient had an asymptomatic thyroid nodule for many years before cancer diagnosis; follow-up with endocrinologist and surgeon for further recommendation
Rhabdomyolysis	26/M	208 (TE)	3	Resolved (5)	N	No change	Patient had an excessive workout before the AE; CK level >22,000 IU/L on day of AE; hospitalization
Ureterolithiasis	27/M	120 (DB)	2	Resolved (2)	N	No change	Ureterorenoscopic lithotripsy; concomitant medications for AE administered

AE, adverse event; CK, creatine kinase; DB, double-blind; TE, treatment extension; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

* Hypersensitivity and subacute combined cord degeneration occurred in the same patient.

† Patient applied vehicle in the DB period. Ruxolitinib cream application began on approximately Day 169.

Table S5. Hematopoietic TEAEs During the Double-Blind and Open-Label Treatment Extension Periods

	TRuE-V1				TRuE-V2			
	Double-Blind*		Extension†		Double-Blind*		Extension†	
n (%)	Vehicle (n=109)	1.5% Ruxolitinib Cream (n=221)	Vehicle to 1.5% Ruxolitinib Cream (n=90)	1.5% Ruxolitinib Cream (n=193)	Vehicle (n=115)	1.5% Ruxolitinib Cream (n=228)	Vehicle to 1.5% Ruxolitinib Cream (n=98)	1.5% Ruxolitinib Cream (n=199)
Anemia	0	0	0	0	1 (0.9)	1 (0.4)	1 (1.0)	0
Hematocrit decreased	0	0	0	0	0	0	0	1 (0.5)
Hemoglobin decreased	0	1 (0.5)	0	0	0	1 (0.4)	0	0
Iron deficiency anemia	0	0	0	0	0	0	0	1 (0.5)
Mean cell volume decreased	0	0	0	0	0	0	0	1 (0.5)
Microcytic anemia	0	1 (0.5)	0	0	0	0	0	0
Monocyte count decreased	0	0	0	0	1 (0.9)	0	0	0
Neutropenia	0	0	0	0	0	0	2 (2.0)	1 (0.5)
Neutrophil count decreased	1 (0.9)	0	1 (1.1)	0	0	0	1 (1.0)	0
Pernicious anemia	0	0	0	1 (0.5)	0	0	0	0
Platelet count decreased	0	0	0	0	0	0	0	1 (0.5)
Platelet count increased	0	0	0	0	0	1 (0.4)	0	0
Thrombocytosis	0	0	0	1 (0.5)	0	0	0	0

TEAE, treatment-emergent adverse event; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

* TEAEs during the double-blind period (up to Week 24) are reported in the safety population.

† TEAEs during the open-label treatment extension period (up to Week 52) are reported in the treatment-extension evaluable population.

Table S6. Summary of Ruxolitinib Trough Plasma Concentrations at Weeks 4 and 24 of Double-Blind Treatment and Week 40 of the Open-Label Treatment Extension (Secondary Endpoint)

	TRuE-V1		TRuE-V2	
	n	**Concentration, nM**	**n**	**Concentration, nM**
Week 4				
Mean (SD)	206	57.1 (61.4)	208	61.0 (68.6)
Geometric mean (CV%)	206	26.7 (300)	208	26.6 (346)
Week 24				
Mean (SD)	191	56.3 (69.4)	189	54.5 (79.1)
Geometric mean (CV%)	191	19.6 (551)	189	17.0 (654)
Week 40				
1.5% ruxolitinib cream from Day 1				
Mean (SD)	173	55.5 (63.6)	184	57.0 (73.3)
Geometric mean (CV%)	173	22.8 (420)	184	18.6 (622)
Vehicle to 1.5% ruxolitinib cream at Week 24				
Mean (SD)	80	50.1 (55.8)	83	48.2 (57.0)
Geometric mean (CV%)	80	18.5 (538)	83	17.0 (605)

CV, coefficient of variation; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo studies.

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