Abstract #2931
Presented at the 30th European Academy of Dermatology and Venereology (EADV) Congress
September 29−October 2, 2021; Virtual

Efficacy and Safety of Ruxolitinib Cream for the Treatment of Vitiligo: 24-Week Results From 2 Randomized, Double-Blind Phase 3 Studies

David Rosmarin, MD,[1] Amit G. Pandya, MD,[2,3] Pearl Grimes, MD,[4] John E. Harris, MD, PhD,[5] Seemal R. Desai, MD,[3,6] Mark Lebwohl, MD,[7] Mireille Ruer-Mulard, MD,[8] Thierry Passeron, MD, PhD,[9,10] Julien Seneschal, MD, PhD,[11] Albert Wolkerstorfer, MD, PhD,[12] Deanna Kornacki, PhD,[13] Kang Sun, PhD,[13] Kathleen Butler, MD,[13] Khaled Ezzedine, MD, PhD[14]

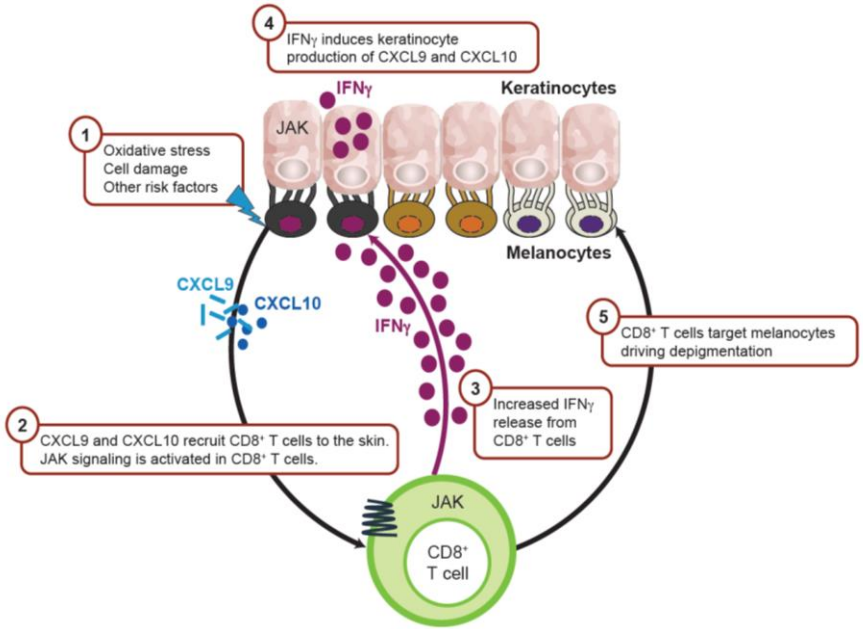
[1]Tufts Medical Center, Boston, MA, USA; [2]Palo Alto Foundation Medical Group, Mountain View, CA, USA; [3]University of Texas Southwestern Medical Center, Dallas, TX, USA; [4]The Vitiligo & Pigmentation Institute of Southern California, Los Angeles, CA, USA; [5]University of Massachusetts Medical School, Worcester, MA, USA; [6]Innovative Dermatology, Plano, TX, USA; [7]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [8]Office of Mireille Ruer-Mulard, MD, Martiques, France; [9]Centre Hospitalier Universitaire de Nice, Université Côte d'Azur, Nice, France; [10]INSERM U1065, C3M, Université Côte d'Azur, Nice, France; [11]Department of Dermatology and Pediatric Dermatology, National Reference Center for Rare Skin Disorders, Hôpital Saint-André, INSERM, BMGIC, U1035, F-33000, Bordeaux, France; [12]Amsterdam University Medical Center, Amsterdam, Netherlands; [13]Incyte Corporation, Wilmington, DE, USA; [14]Henri Mondor University Hospital and Université Paris-Est Créteil Val de Marne, Paris, France

Presenting Author Disclosures

- Received honoraria as consultant for AbbVie, Abcuro, AltruBio, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Concert, Dermavant Sciences, Dermira, Incyte Corporation, Janssen, Kyowa Kirin, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, Sanofi, Sun Pharmaceuticals, UCB, and VielaBio
- Received research support from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Dermira, Galderma, Incyte Corporation, Janssen, Lilly, Merck, Novartis, Pfizer, and Regeneron Pharmaceuticals
- Served as a paid speaker for AbbVie, Amgen, Celgene, Janssen, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, and Sanofi

JAK-Targeted Therapy for Vitiligo

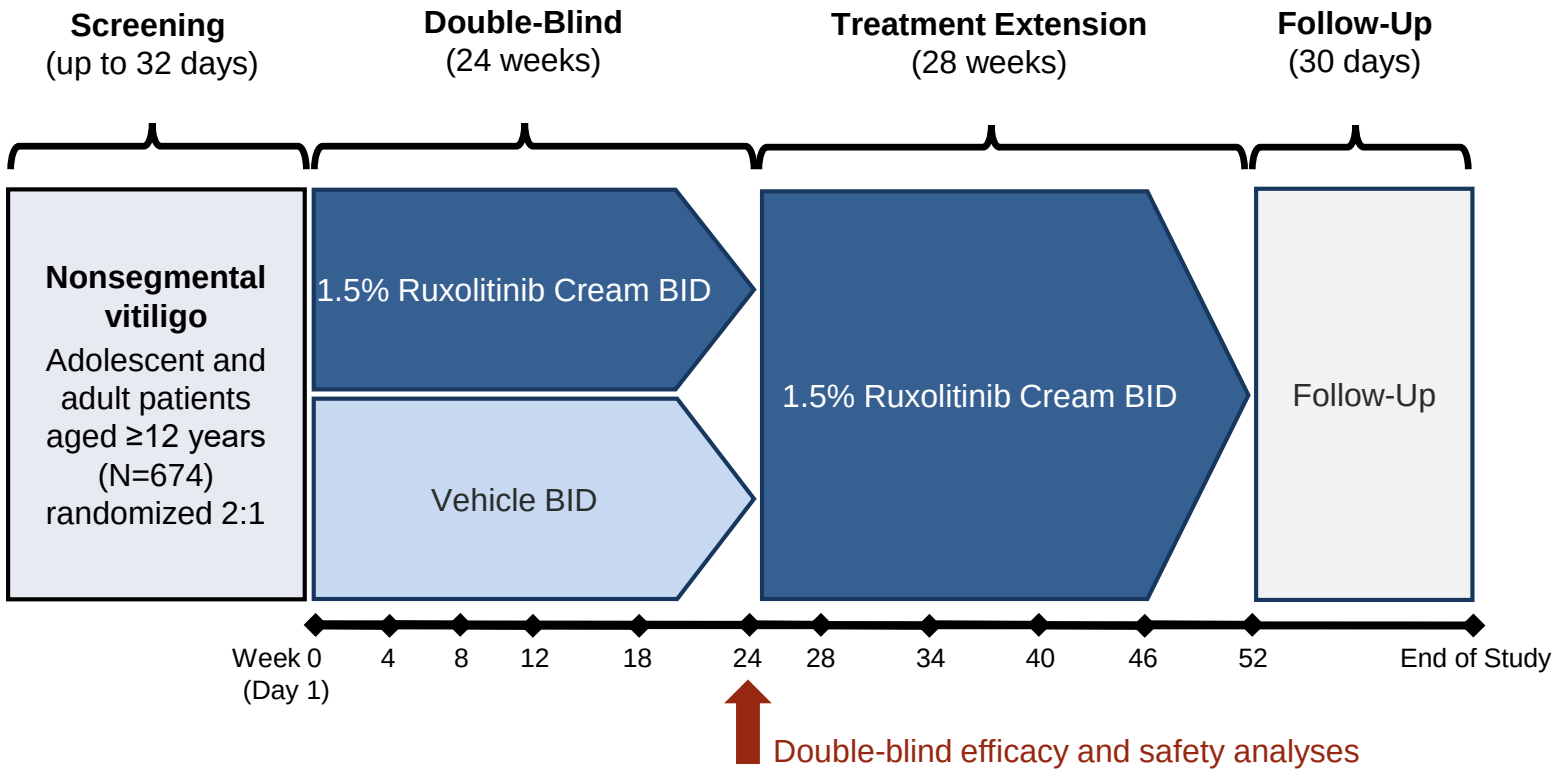
- Vitiligo is a chronic autoimmune disease that targets melanocytes, causing skin depigmentation[1]
- Disease pathogenesis is largely regulated by interferon-γ activation of the JAK signaling pathway[2]
- A cream formulation of ruxolitinib, a JAK1/JAK2 inhibitor, is under investigation for the treatment of vitiligo[3]
- Ruxolitinib cream demonstrated substantial repigmentation in a 52-week phase 2, dose-ranging, randomized study in adult patients with vitiligo (NCT03099304)[3]
- **Objective:** To evaluate the efficacy and safety of ruxolitinib cream in adolescent and adult patients with vitiligo in 2 ongoing 52-week, randomized, double-blind, phase 3 studies



CXCL9/10, chemokine C-X-C motif ligand 9/10; IFNγ, interferon gamma; JAK, Janus kinase.

1. Rodrigues M, et al. *J Am Acad Dermatol*. 2017;77:1-13; 2. Rashighi M and Harris JE. *Ann Transl Med*. 2015;3(21):343; 3. Rosmarin D, et al. *Lancet*. 2020;396(10244):110-120; 4. Howell MD, et al. *Front Immunol.* 2019;10:2342.

TRuE-V1 and TRuE-V2 Study Design



BID, twice daily; TRuE-V1/2, Topical Ruxolitinib Evaluation in Vitiligo studies 1 and 2.

Study Endpoints

- **Primary Endpoint**
  - Proportion of patients achieving ≥75% improvement from baseline in F-VASI (F-VASI75) at Week 24
- **Key Secondary Endpoints**
  - Proportion of patients achieving ≥50% and ≥90% improvement from baseline in F-VASI score (F-VASI50 and F-VASI90, respectively) at Week 24
  - Proportion of patients achieving ≥50% improvement from baseline in T-VASI (T-VASI50) at Week 24
  - Proportion of patients achieving a VNS rating of “a lot less noticeable” or “no longer noticeable” at Week 24
  - Percentage change from baseline in F-BSA at Week 24
- Safety and tolerability were also assessed

F-BSA, facial body surface area; F-VASI, facial Vitiligo Area Scoring Index; T-VASI, total Vitiligo Area Scoring Index; VNS, Vitiligo Noticeability Scale.

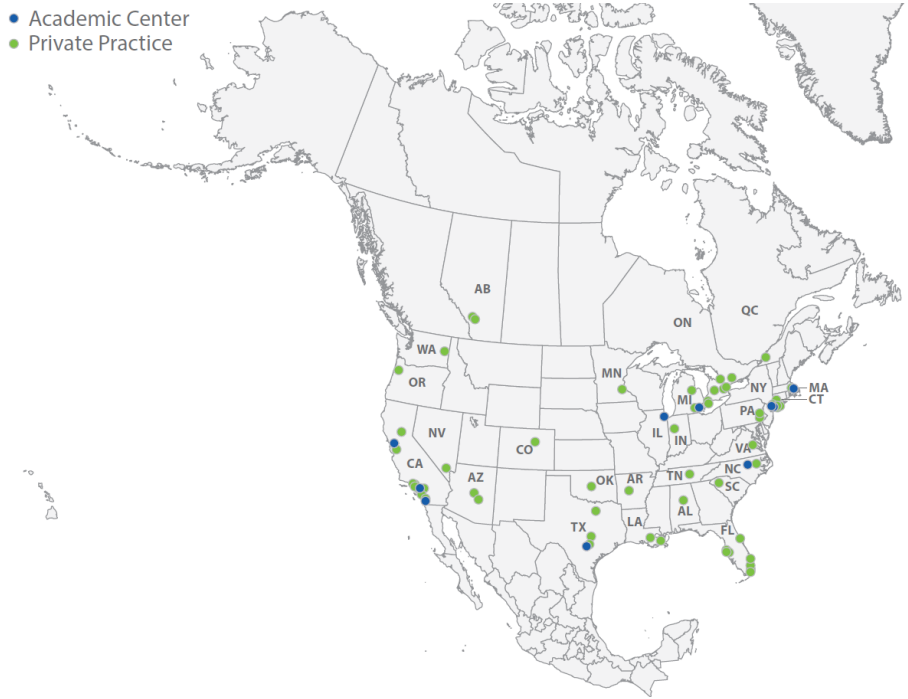
Eligibility Criteria

- **Key Inclusion Criteria**
  - Patients aged ≥12 years with nonsegmental vitiligo
  - Depigmented areas including the following
    - ≥0.5% of total BSA on the face and ≥3% of total BSA on nonfacial areas
    - Score ≥0.5 on F-VASI and ≥3 on T-VASI
- **Key Exclusion Criteria**
  - Presence of complete leukotrichia within any lesions on the face
  - Dermatologic disease confounding vitiligo assessment
  - Previous use of JAK inhibitor therapy
  - 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
    - Topical treatments within 1 week

BSA, body surface area.

Geographic Distribution of Study Sites

North America



Europe

Patient Demographics

- Baseline demographics and clinical characteristics were similar for TRuE-V1 and TRuE-V2

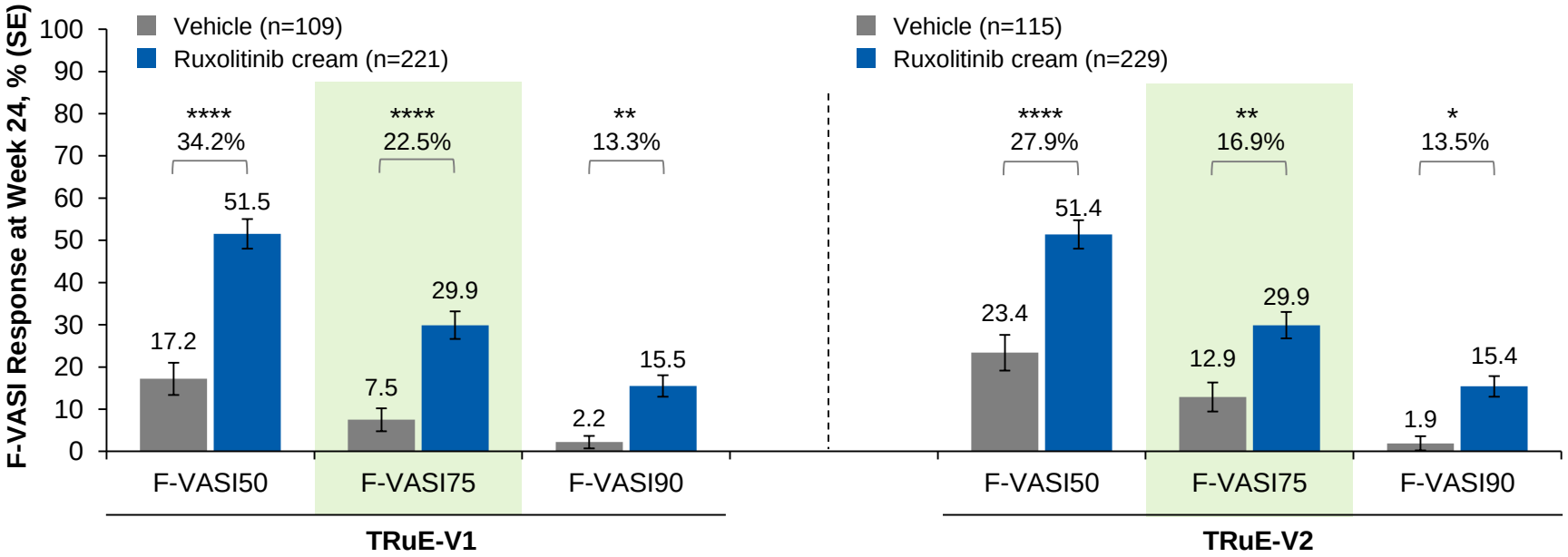
Characteristic	TRuE-V1 (N=330)	TRuE-V2 (N=344)
Age, mean (SD), y	40.2 (15.9)	39.0 (14.3)
Female, n (%)	186 (56.4)	172 (50.0)
White, n (%)	276 (83.6)	276 (80.2)
Skin phototype, n (%)		
I	13 (3.9)	3 (0.9)
II	114 (34.5)	89 (25.9)
III	132 (40.0)	135 (39.2)
IV	49 (14.8)	80 (23.3)
V	18 (5.5)	27 (7.8)
VI	4 (1.2)	10 (2.9)
Baseline F-VASI, mean (SD)	0.95 (0.59)	0.88 (0.52)
Baseline T-VASI, mean (SD)	6.47 (1.99)	6.89 (2.11)

Characteristic	TRuE-V1 (N=330)	TRuE-V2 (N=344)
F-BSA,* mean (SD), %	1.09 (0.70)	0.96 (0.57)
T-BSA, mean (SD), %	7.26 (2.02)	7.51 (2.03)
Duration of disease, median (range), y	11.1 (0–60.5)	13.0 (0–59.5)
Diagnosed in childhood, n (%)	106 (32.1)	139 (40.4)
Disease stability,† n (%)		
Stable	245 (74.2)	254 (73.8)
Progressive	85 (25.8)	90 (26.2)
Other autoimmune disorders, n (%)	71 (21.5)	55 (16.0)
Previous therapy,‡ n (%)	192 (58.2)	219 (63.7)
Topical calcineurin inhibitors	103 (31.2)	111 (32.3)
Topical corticosteroids	95 (28.8)	94 (27.3)
Phototherapy§	92 (27.9)	123 (35.8)

NB-UVB, narrow-band ultraviolet-B; PUVA, psoralen ultraviolet-A; T-BSA, total body surface area.
* Percentage of T-BSA; † Determination of disease stability was based on investigator judgment. ‡ Patients could have used multiple previous lines of therapy. § Phototherapy includes NB-UVB phototherapy, excimer laser, and PUVA photochemotherapy.

F-VASI Responses at Week 24

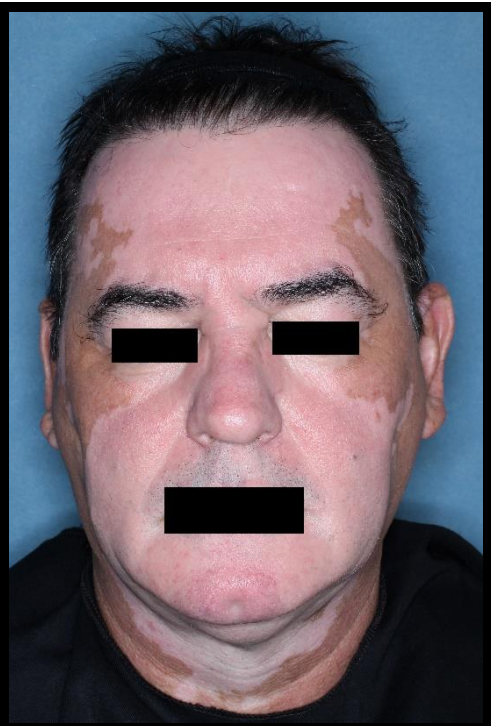
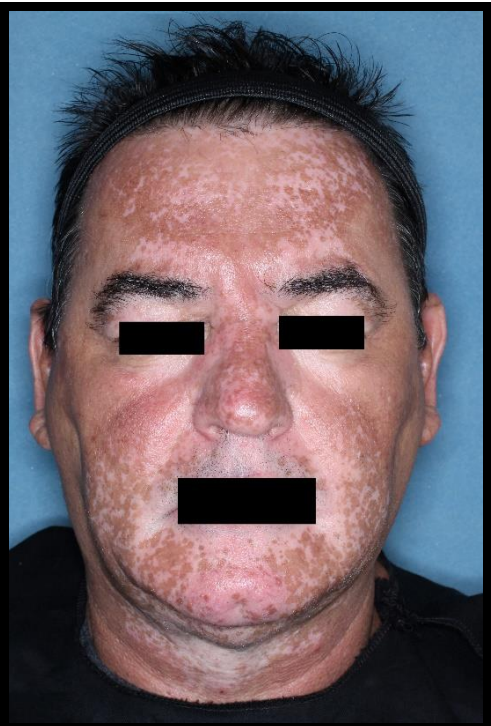
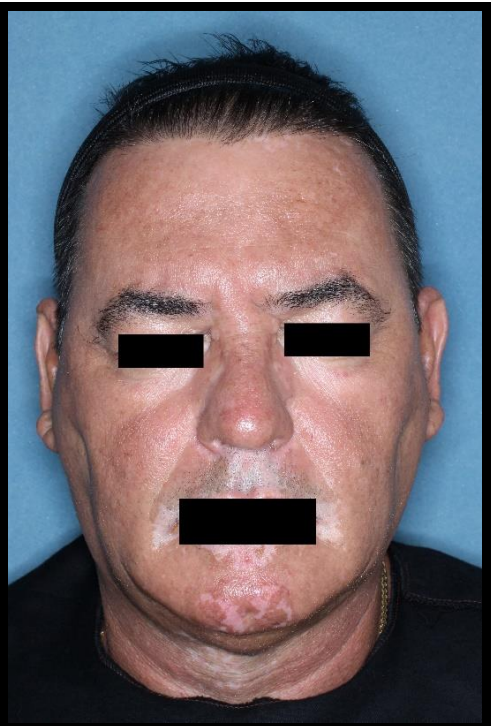
- At Week 24, F-VASI75 was achieved by a significantly greater proportion of patients applying ruxolitinib cream vs vehicle (primary endpoint)
  - Significant results were also observed for F-VASI50 and F-VASI90 at Week 24



* *P*<0.05, ** *P*<0.01, **** *P*<0.0001 for response rate difference for ruxolitinib cream vs vehicle.

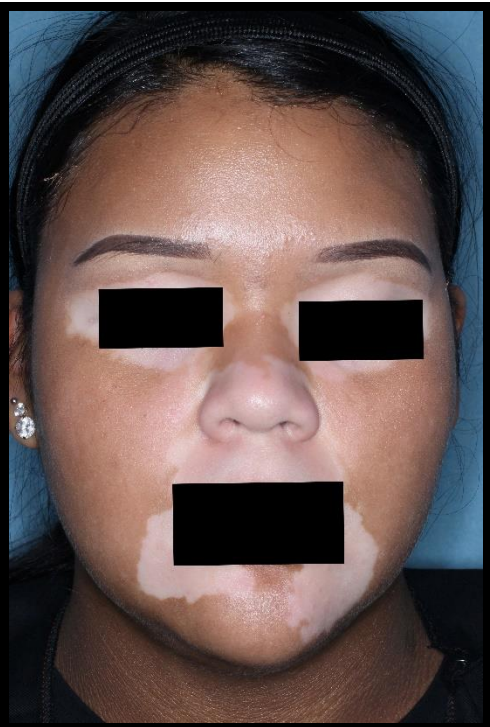
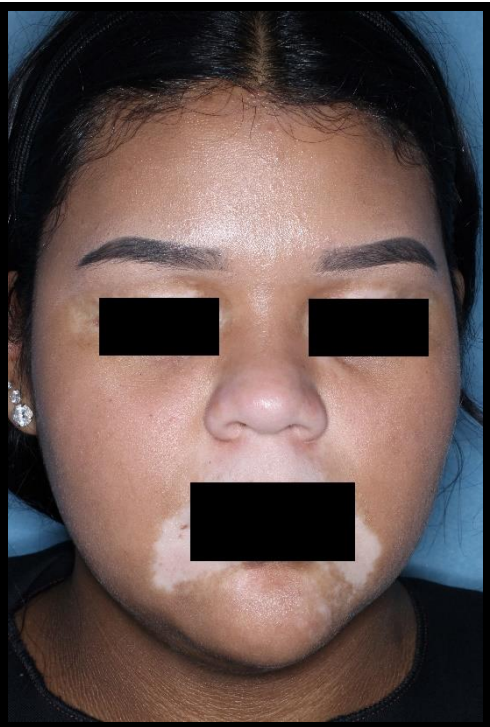
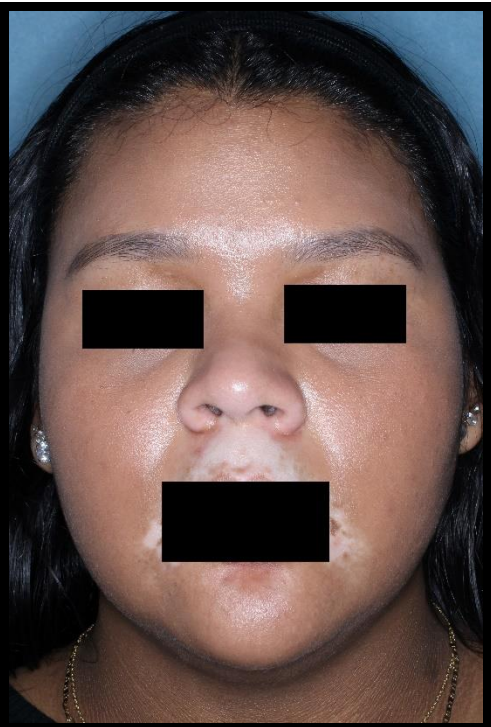
Clinical Images Showing F-VASI Response

1.5% Ruxolitinib Cream BID

Baseline	Week 12	Week 24
		
F-VASI: 1.62	F-VASI: 0.45	F-VASI: 0.14

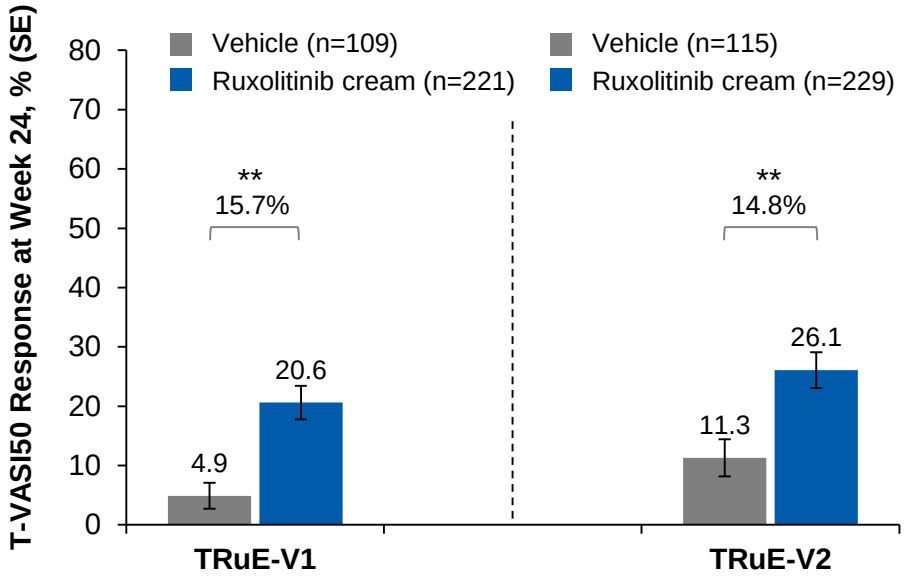
Clinical Images Showing F-VASI Response

1.5% Ruxolitinib Cream BID

Baseline	Week 12	Week 24
		
F-VASI: 1.00	F-VASI: 0.30	F-VASI: 0.10

T-VASI50 Response at Week 24

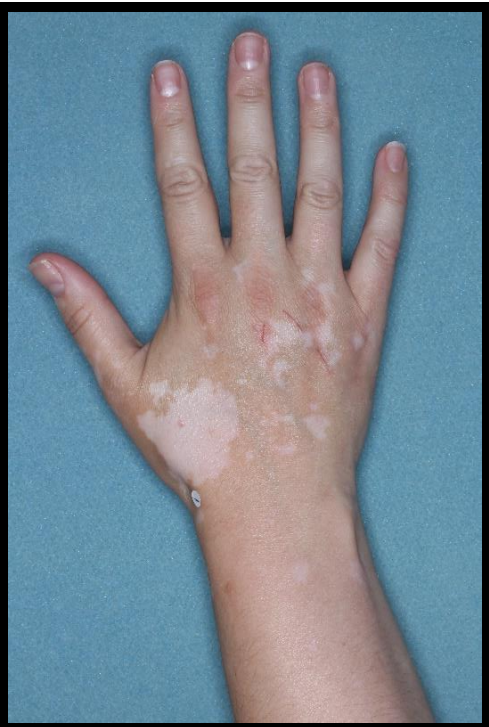
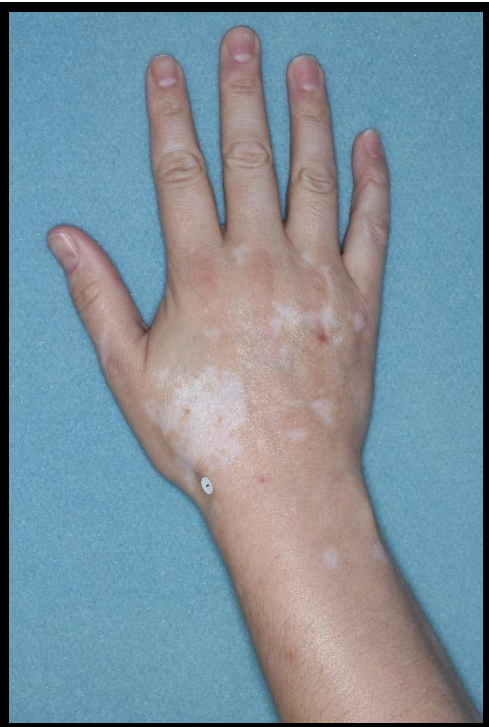
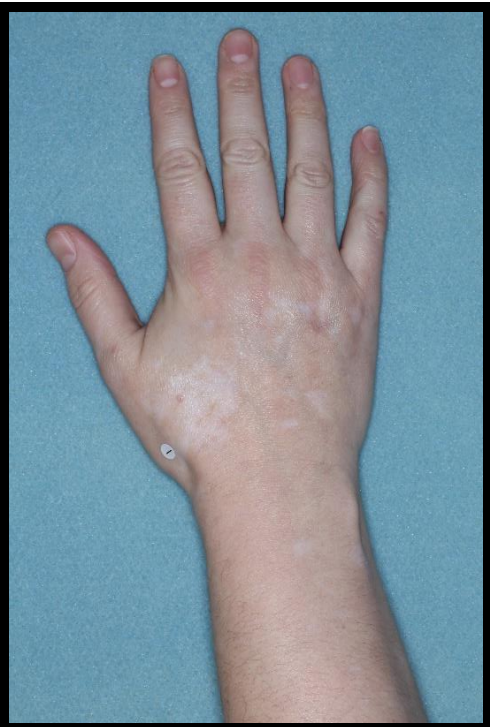
- T-VASI50 at Week 24 was achieved by a significantly greater proportion of patients applying ruxolitinib cream vs vehicle



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

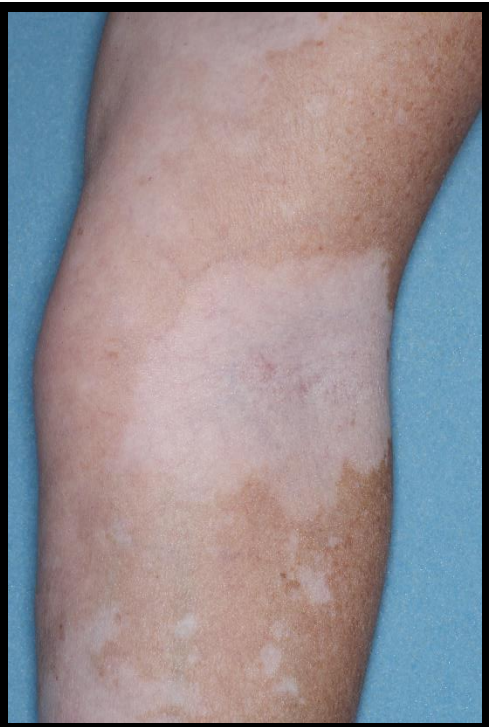
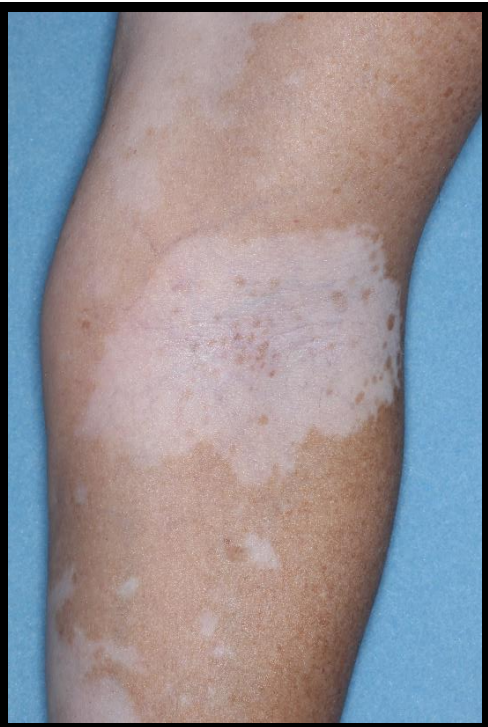
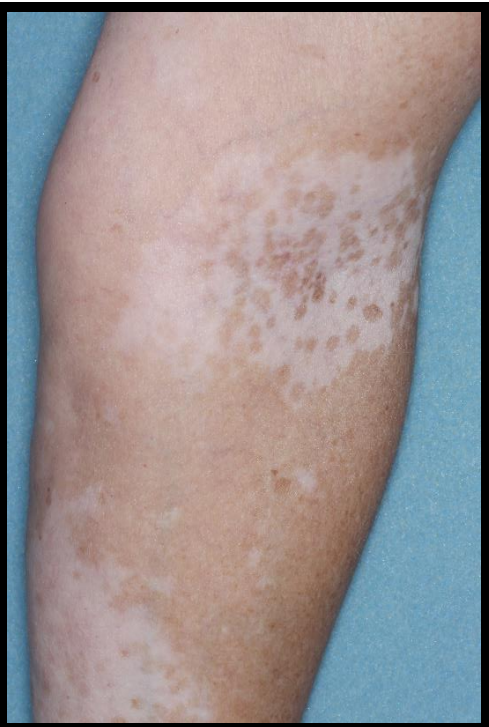
Clinical Images Showing T-VASI Response

1.5% Ruxolitinib Cream BID

Baseline	Week 12	Week 24
		
T-VASI: 3.99	T-VASI: 2.35	T-VASI: 2.35

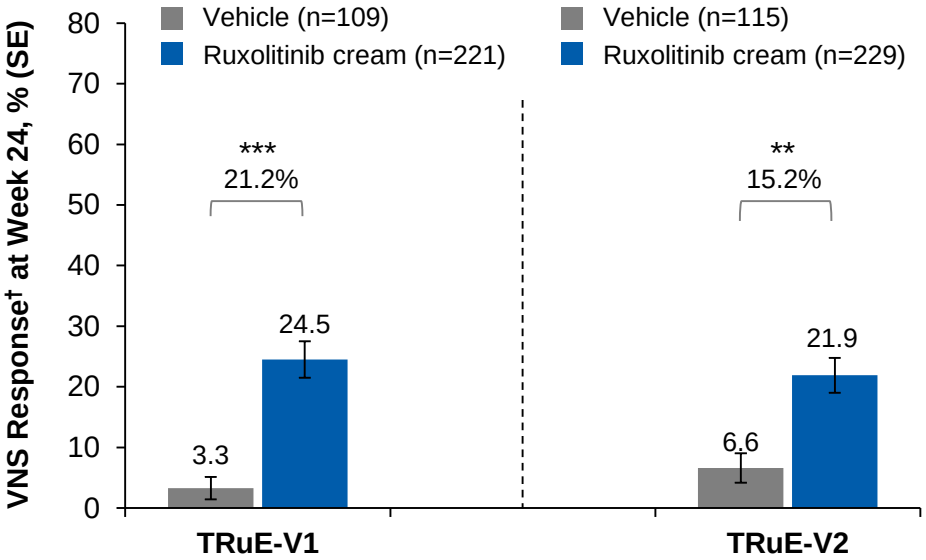
Clinical Images Showing T-VASI Response

1.5% Ruxolitinib Cream BID

Baseline	Week 12	Week 24
		
T-VASI: 9.40	T-VASI: 7.65	T-VASI: 4.65

VNS Response at Week 24

- At Week 24, the proportion of patients achieving a VNS response was significantly higher with application of ruxolitinib cream vs vehicle

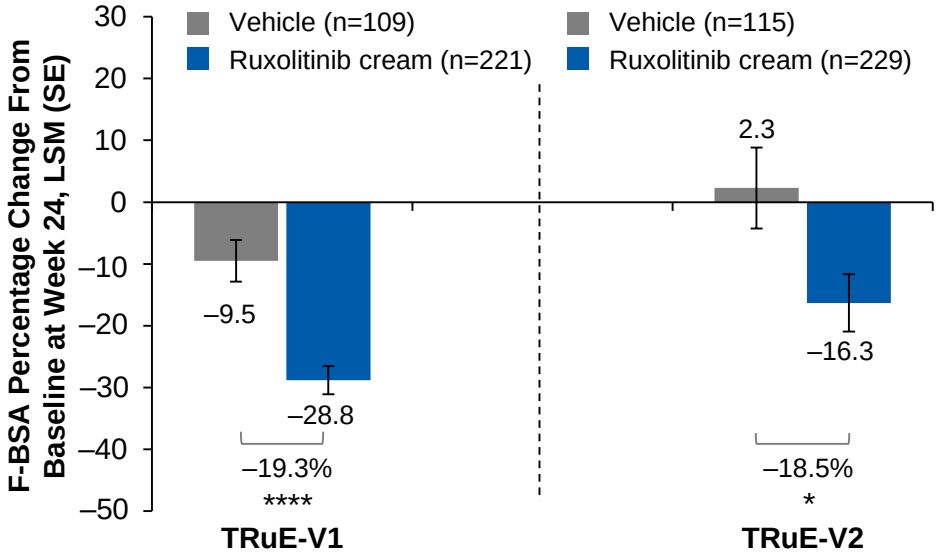


** *P*<0.01, *** *P*<0.001 for response rate difference for ruxolitinib cream vs vehicle.

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

Percentage Change in F-BSA at Week 24

- Least squares mean percentage change from baseline in F-BSA was significantly greater among patients who applied ruxolitinib cream vs vehicle



LSM, least squares mean.
* *P*<0.05, **** *P*<0.0001 for response rate difference for ruxolitinib cream vs vehicle.

Safety

TEAEs Through Week 24

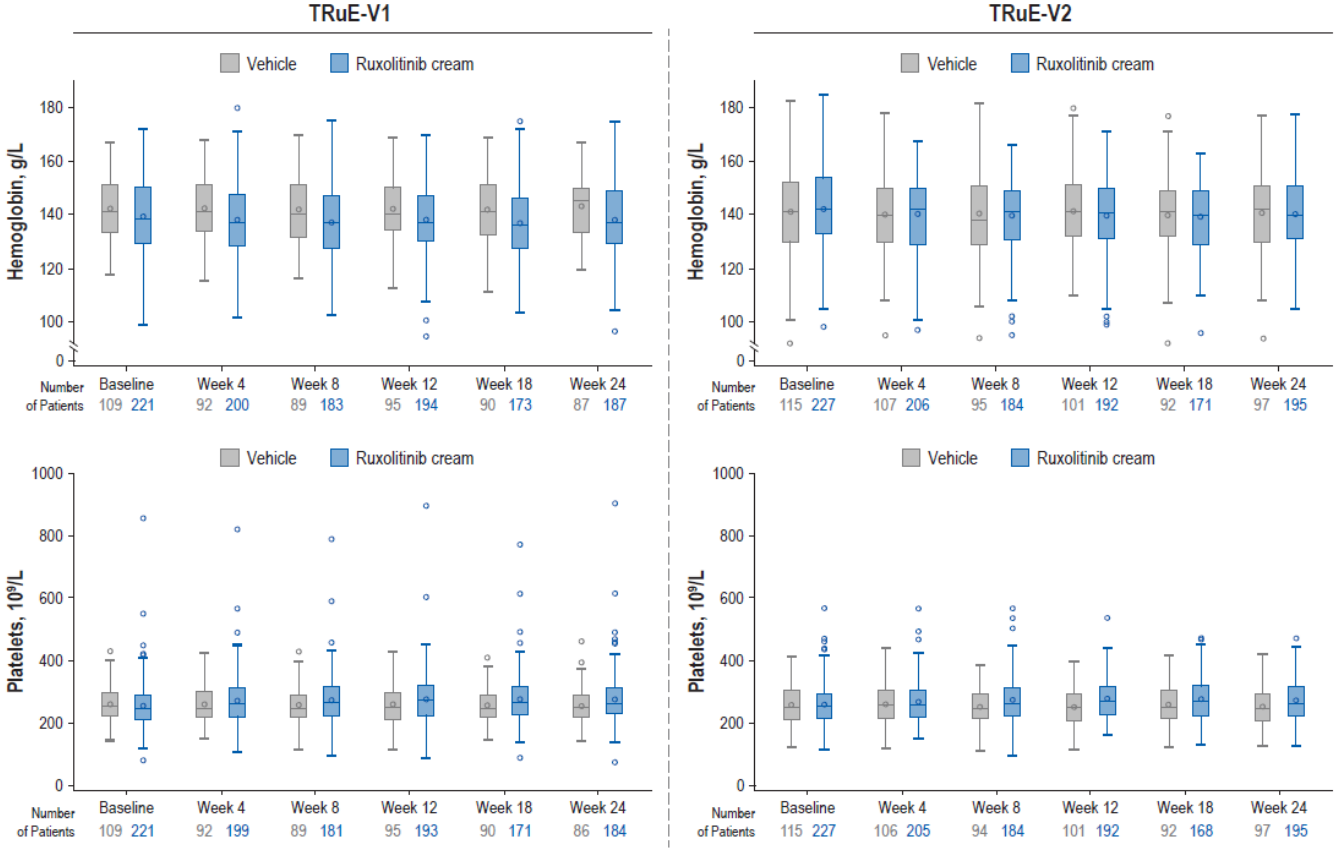
- Ruxolitinib cream was well tolerated
- There were no clinically significant application site reactions or serious treatment-related adverse events
- Ruxolitinib plasma C_{ss} was similar in TRuE-V1/TRuE-V2 (mean, 55.8/58.0 nM) and was well below the IC_{50} for JAK2-mediated changes in the bone marrow (281 nM)[1]

	TRuE-V1		TRuE-V2	
Characteristic, n (%)	Vehicle (n=109)	Ruxolitinib Cream (n=221)	Vehicle (n=115)	Ruxolitinib Cream (n=228)*
Patients with TEAE	41 (37.6)	101 (45.7)	38 (33.0)	113 (49.6)
Most common TEAEs†				
Application site acne	0	13 (5.9)	2 (1.7)	13 (5.7)
Application site pruritus	4 (3.7)	11 (5.0)	2 (1.7)	12 (5.3)
Nasopharyngitis	4 (3.7)	9 (4.1)	1 (0.9)	10 (4.4)
Headache	2 (1.8)	6 (2.7)	4 (3.5)	11 (4.8)
Upper respiratory tract infection	5 (4.6)	6 (2.7)	0	7 (3.1)
COVID-19	4 (3.7)	3 (1.4)	2 (1.7)	10 (4.4)
Patients with treatment-related TEAE	10 (9.2)	38 (17.2)	7 (6.1)	28 (12.3)
Most common treatment-related TEAEs†				
Application site acne	0	12 (5.4)	2 (1.7)	10 (4.4)
Application site pruritus	4 (3.7)	11 (5.0)	2 (1.7)	10 (4.4)
Patients with serious TEAE‡	1 (0.9)	6 (2.7)	0	2 (0.9)
Patients with TEAE leading to discontinuation	1 (0.9)	1 (0.5)	0	1 (0.4)

C_{ss}, steady-state concentration; IC_{50}, half-maximal inhibitory concentration; TEAE, treatment-emergent adverse event.
* 1 randomized patient who did not apply ≥1 dose of ruxolitinib cream was excluded from the safety population.
† Occurring in ≥4% of patients in any treatment group.
‡ No serious TEAEs were considered related to treatment.
1. Quintas-Cardama A, et al. *Blood*. 2010;115(15):3109-3117.

Hemoglobin and Platelet Values During Treatment

- There were no clinically significant changes in hemoglobin or platelet levels

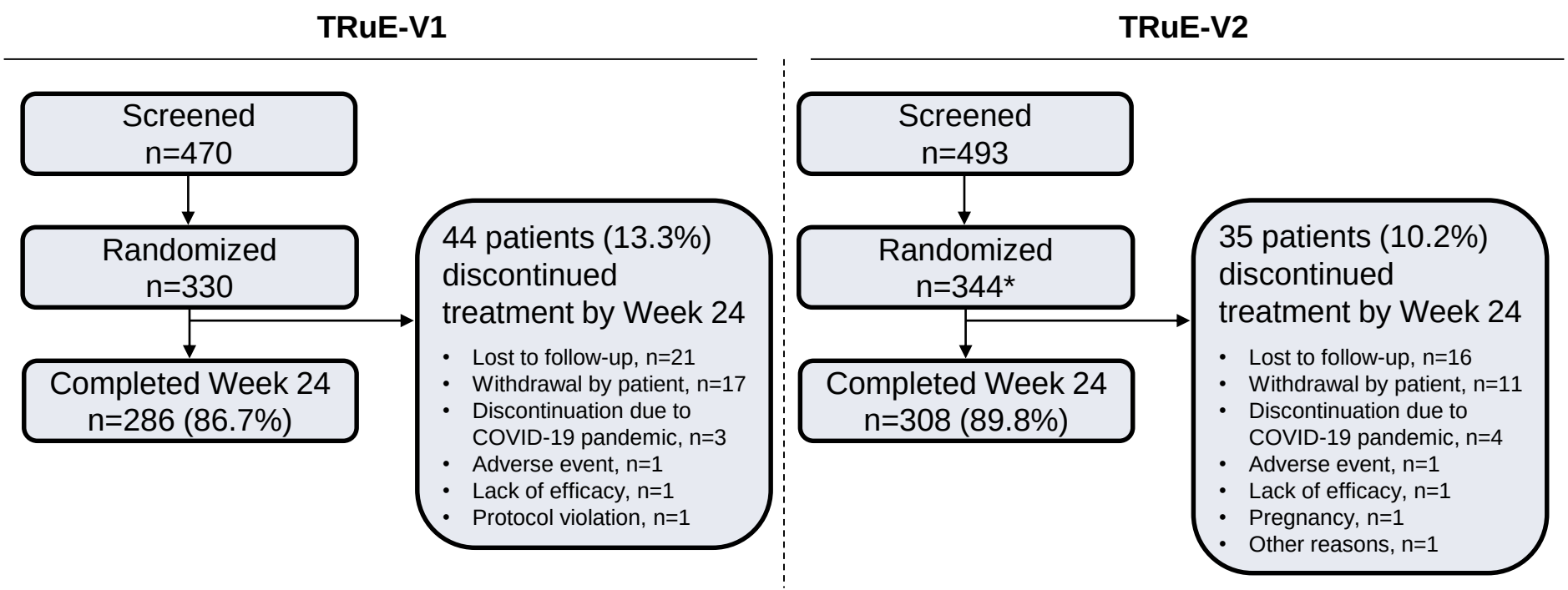


Conclusions

- Ruxolitinib cream demonstrated clinically meaningful superiority to vehicle for the primary and all key secondary endpoints in the two phase 3 TRuE-V studies, confirming phase 2 findings
- Adolescent and adult patients with nonsegmental vitiligo achieved substantial facial and total body repigmentation at 24 weeks
- Ruxolitinib cream was well tolerated, and no serious treatment-related AEs were reported

Backup Slides

Patient Disposition



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

Patient Demographics

- Baseline demographics were similar for both TRuE-V1 and TRuE-V2 as well as treatment assignment

Characteristic	TRuE-V1			TRuE-V2		
	Vehicle (n=109)	Ruxolitinib Cream (n=221)	Total (N=330)	Vehicle (n=115)	Ruxolitinib Cream (n=229)	Total (N=344)
Age, mean (SD), y	39.7 (16.7)	40.5 (15.4)	40.2 (15.9)	39.8 (12.1)	38.6 (15.3)	39.0 (14.3)
Female, n (%)	50 (45.9)	136 (61.5)	186 (56.4)	60 (52.2)	112 (48.9)	172 (50.0)
White, n (%)	96 (88.1)	180 (81.4)	276 (83.6)	93 (80.9)	183 (79.9)	276 (80.2)
Skin phototype, n (%)						
I	3 (2.8)	10 (4.5)	13 (3.9)	1 (0.9)	2 (0.9)	3 (0.9)
II	40 (36.7)	74 (33.5)	114 (34.5)	32 (27.8)	57 (24.9)	89 (25.9)
III	43 (39.4)	89 (40.3)	132 (40.0)	45 (39.1)	90 (39.3)	135 (39.2)
IV	15 (13.8)	34 (15.4)	49 (14.8)	25 (21.7)	55 (24.0)	80 (23.3)
V	7 (6.4)	11 (5.0)	18 (5.5)	10 (8.7)	17 (7.4)	27 (7.8)
VI	1 (0.9)	3 (1.4)	4 (1.2)	2 (1.7)	8 (3.5)	10 (2.9)

Clinical Characteristics

- Baseline clinical characteristics were similar for both TRuE-V1 and TRuE-V2 as well as treatment assignment

Characteristic	TRuE-V1			TRuE-V2		
	Vehicle (n=109)	Ruxolitinib Cream (n=221)	Total (N=330)	Vehicle (n=115)	Ruxolitinib Cream (n=229)	Total (N=344)
Baseline F-VASI, mean (SD)	1.00 (0.59)	0.93 (0.58)	0.95 (0.59)	0.83 (0.52)	0.90 (0.52)	0.88 (0.52)
Baseline T-VASI, mean (SD)	6.42 (1.92)	6.49 (2.02)	6.47 (1.99)	7.02 (2.20)	6.83 (2.06)	6.89 (2.11)
F-BSA,* mean (SD), %	1.15 (0.71)	1.05 (0.69)	1.09 (0.70)	0.92 (0.57)	0.98 (0.57)	0.96 (0.57)
T-BSA, mean (SD), %	7.22 (2.01)	7.28 (2.03)	7.26 (2.02)	7.68 (2.04)	7.43 (2.02)	7.51 (2.03)
Duration of disease, median (range), y	12.0 (0.1–47.5)	10.6 (0–60.5)	11.1 (0–60.5)	14.0 (0–59.5)	13.0 (0–50.3)	13.0 (0–59.5)
Diagnosed in childhood, n (%)	34 (31.2)	72 (32.6)	106 (32.1)	43 (37.4)	96 (41.9)	139 (40.4)
Disease stability,† n (%)						
Stable	80 (73.4)	165 (74.7)	245 (74.2)	88 (76.5)	166 (72.5)	254 (73.8)
Progressive	29 (26.6)	56 (25.3)	85 (25.8)	27 (23.5)	63 (27.5)	90 (26.2)

T-BSA, total body surface area.
* Percentage of T-BSA; † Determination of disease stability was based on investigator judgment.

Clinical Characteristics (cont'd)

- Thyroid disorders were the most common comorbid autoimmune disorders among patients
- Over half of patients across both studies used ≥1 previous lines of therapy

Characteristic	TRuE-V1			TRuE-V2		
	Vehicle (n=109)	Ruxolitinib Cream (n=221)	Total (N=330)	Vehicle (n=115)	Ruxolitinib Cream (n=229)	Total (N=344)
Other autoimmune disorders, n (%)	18 (16.5)	53 (24.0)	71 (21.5)	18 (15.7)	37 (16.2)	55 (16.0)
Thyroid disorders	17 (15.6)	50 (22.6)	67 (20.3)	15 (13.0)	35 (15.3)	50 (14.5)
Juvenile diabetes mellitus	1 (0.9)	0	1 (0.3)	0	0	0
Pernicious anemia	0	1 (0.5)	1 (0.3)	0	0	0
Other	1 (0.9)	5 (2.3)	6 (1.8)	6 (5.2)	5 (2.2)	11 (3.2)
Previous therapy,* n (%)	61 (56.0)	131 (59.3)	192 (58.2)	76 (66.1)	143 (62.4)	219 (63.7)
Topical calcineurin inhibitors	31 (28.4)	72 (32.6)	103 (31.2)	37 (32.2)	74 (32.3)	111 (32.3)
Topical corticosteroids	28 (25.7)	67 (30.3)	95 (28.8)	28 (24.3)	66 (28.8)	94 (27.3)
Phototherapy†	31 (28.4)	61 (27.6)	92 (27.9)	46 (40.0)	77 (33.6)	123 (35.8)

NB-UVB, narrow-band ultraviolet-B; PUVA, psoralen ultraviolet-A.
* Patients could have used multiple previous lines of therapy. † Phototherapy includes NB-UVB phototherapy, excimer laser, and PUVA photochemotherapy.