

Efficacy and Safety of Ruxolitinib Cream Monotherapy for the Treatment of Vitiligo: Results From Two 52-Week Phase 3 Studies

David Rosmarin, MD,¹ Thierry Passeron, MD, PhD,^{2,3} Amit G. Pandya, MD,^{4,5} Pearl Grimes, MD,⁶ John E. Harris, MD, PhD,⁷ Seemal R. Desai, MD,^{5,8} Mark Lebwohl, MD,⁹ Mireille Ruer-Mulard, MD,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, PhD¹⁴

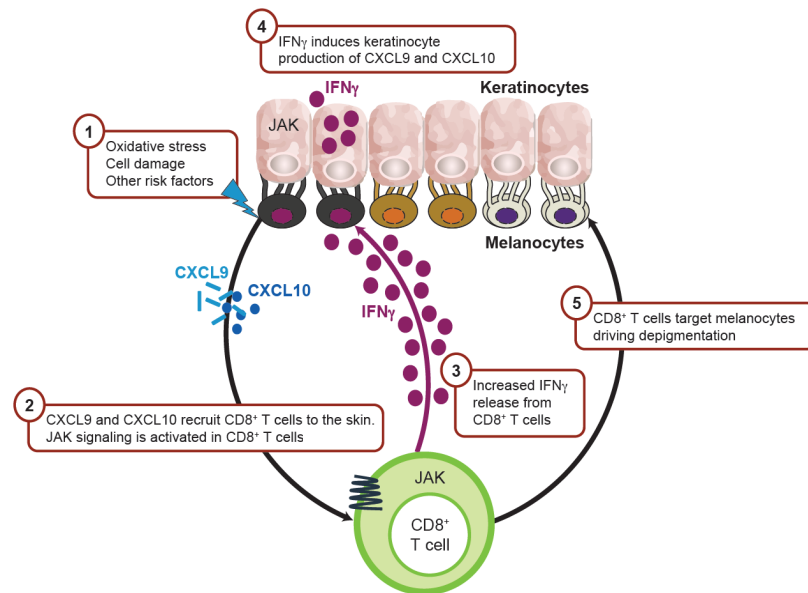
¹Tufts Medical Center, Boston, MA, USA; ²Centre Hospitalier Universitaire de Nice, Université Côte d'Azur, Nice, France; ³INSERM U1065, C3M, Université Côte d'Azur, Nice, France; ⁴Palo Alto Foundation Medical Group, Sunnyvale, CA, USA; ⁵University of Texas Southwestern Medical Center, Dallas, TX, USA;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

Presenting Author Disclosures

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JAK-Targeted Therapy for Vitiligo

- Vitiligo is a chronic autoimmune disease that targets melanocytes, causing skin depigmentation¹
- Disease pathogenesis is largely regulated by interferon- γ activation of the JAK signaling pathway²
- Ruxolitinib (JAK1/JAK2 inhibitor) cream demonstrated substantial repigmentation in a 52-week, phase 2, dose-ranging, randomized study in adult patients with vitiligo³
- In 2 randomized phase 3 studies in adolescent and adult patients (TRuE-V1/TRuE-V2), ruxolitinib cream was statistically superior to vehicle at Week 24 in the primary and all key secondary endpoints⁴
- **Objective:** To evaluate the efficacy and safety of ruxolitinib cream up to Week 52 in TRuE-V1/TRuE-V2

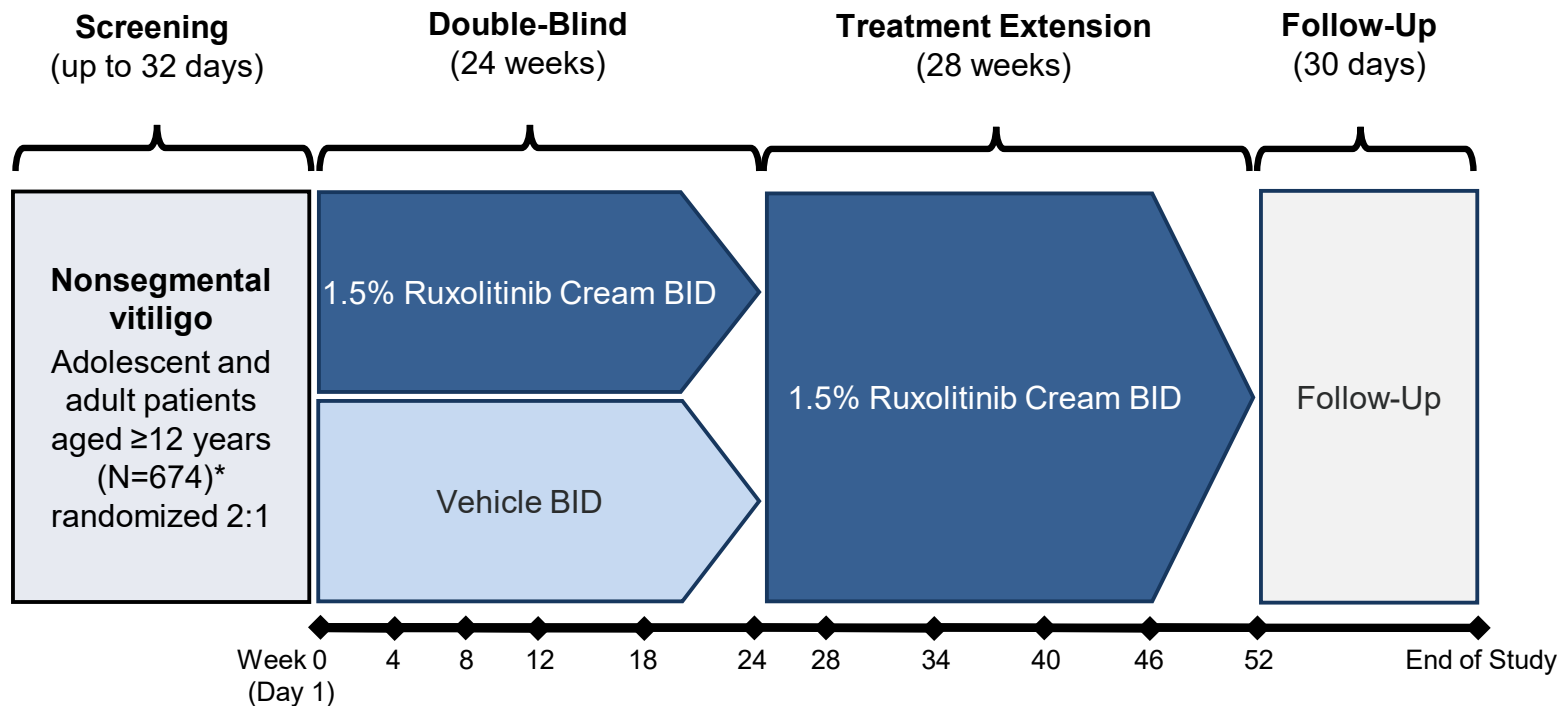


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CXCL9/10, chemokine C-X-C motif ligand 9/10; IFN γ , interferon gamma; JAK, Janus kinase; TRuE-V1/2, Topical Ruxolitinib Evaluation in Vitiligo studies 1 and 2.

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. Rosmarin D, et al. Efficacy and safety of ruxolitinib cream for the treatment of vitiligo: 24-week results from 2 randomized double-blind phase 3 studies. Presented at: European Academy of Dermatology and Venereology Congress; September 29–October 2, 2021; 5. Howell MD, et al. *Front Immunol*. 2019;10:2342.

TRuE-V1 and TRuE-V2 Study Design



BID, twice daily.

* 1 randomized patient who did not apply ≥1 dose of ruxolitinib cream was excluded from safety analyses. 13 patients from 1 study site were excluded from efficacy analyses for compliance issues.

Study Endpoints

- Efficacy endpoints
 - Proportion of patients achieving $\geq 75\%$ improvement from baseline in F-VASI (F-VASI75)
 - Proportion of patients achieving $\geq 50\%$ and $\geq 90\%$ improvement from baseline in F-VASI (F-VASI50 and F-VASI90, respectively)
 - Proportion of patients achieving $\geq 50\%$ improvement from baseline in T-VASI (T-VASI50)
 - Proportion of patients achieving a VNS rating of “a lot less noticeable” or “no longer noticeable”
- Safety and tolerability were also assessed

Eligibility Criteria

- **Key Inclusion Criteria**

- Patients aged ≥ 12 years with nonsegmental vitiligo
- Depigmented areas $\leq 10\%$ total BSA (facial and nonfacial) including the following
 - $\geq 0.5\%$ of total BSA on the face and $\geq 3\%$ 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

Patient Demographics and Clinical Characteristics

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

Characteristic	TRuE-V1 (N=330)	TRuE-V2 (N=343)
Age, mean (SD), y	40.2 (15.9)	38.9 (14.3)
Female, n (%)	186 (56.4)	172 (50.1)
White, n (%)	276 (83.6)	275 (80.2)
Skin phototype, n (%)		
I	13 (3.9)	3 (0.9)
II	114 (34.5)	89 (25.9)
III	132 (40.0)	134 (39.1)
IV	49 (14.8)	80 (23.3)
V	18 (5.5)	27 (7.9)
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)	6.90 (2.10)

Characteristic	TRuE-V1 (N=330)	TRuE-V2 (N=343)
F-BSA,* mean (SD), %	1.09 (0.70)	0.96 (0.57)
T-BSA, mean (SD), %	7.26 (2.02)	7.52 (2.02)
Duration of disease, median (range), y	11.1 (0–60.5)	13.0 (0–59.5)
Diagnosed in childhood, n (%)	106 (32.1)	139 (40.5)
Disease stability, [†] n (%)		
Stable	245 (74.2)	254 (74.1)
Progressive	85 (25.8)	89 (25.9)
Other autoimmune disorders, n (%)	71 (21.5)	55 (16.0)
Previous therapy, [‡] n (%)	192 (58.2)	219 (63.8)
Topical calcineurin inhibitors	103 (31.2)	111 (32.4)
Topical corticosteroids	95 (28.8)	94 (27.4)
Phototherapy [§]	92 (27.9)	123 (35.9)

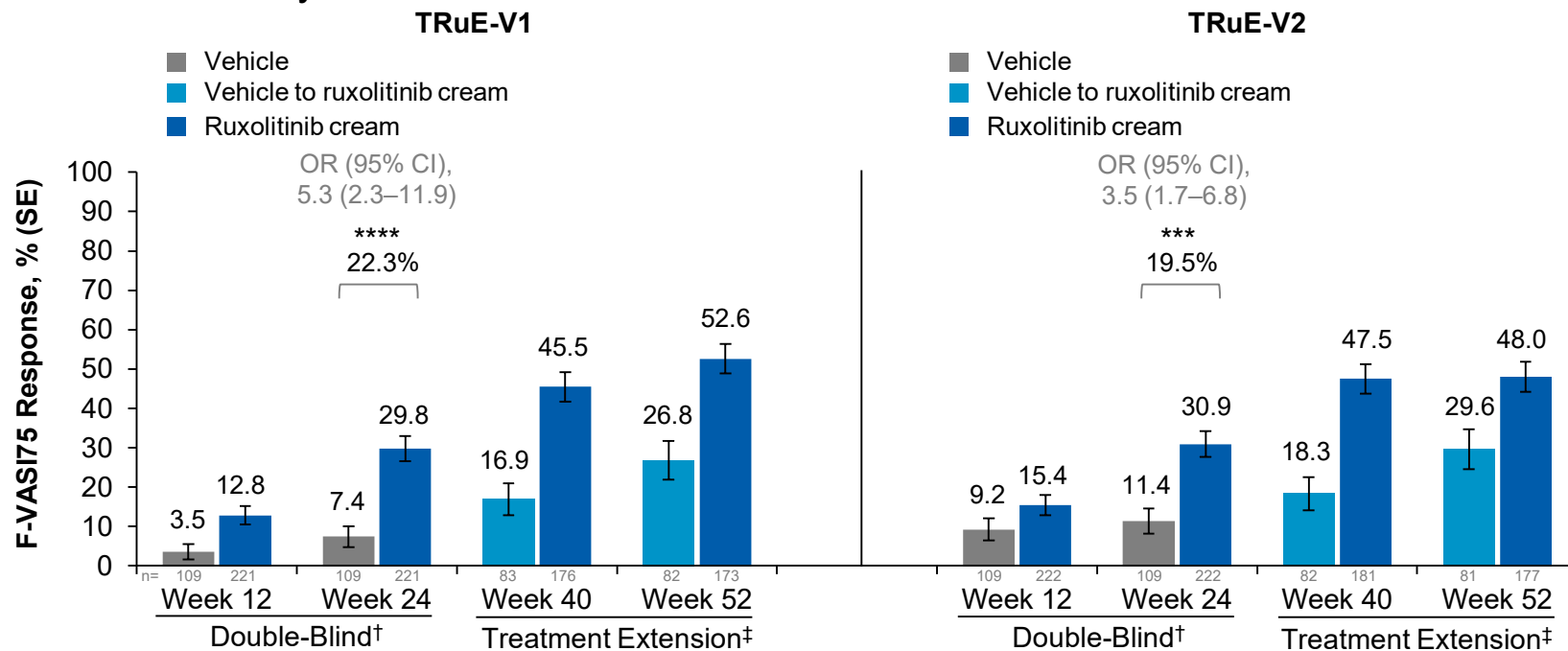
F-BSA, facial body surface area; NB-UVB, narrow-band ultraviolet-B; PUVA, psoralen ultraviolet-A; T-BSA, total body surface area.

* 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-VASI75 Responses

- Approximately half of patients who applied ruxolitinib cream from Day 1 achieved F-VASI75 by Week 52

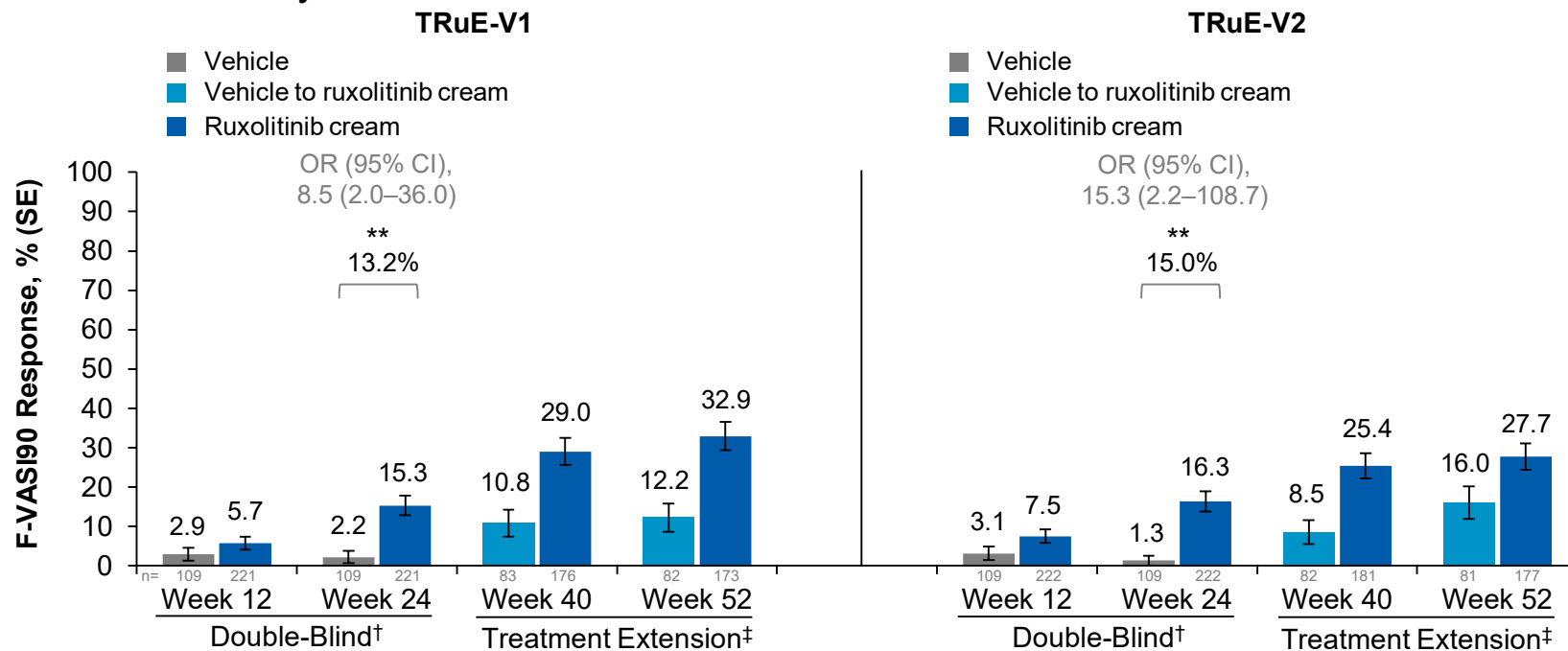


OR, odds ratio. *** $P < 0.001$, **** $P < 0.0001$ for response rate difference for ruxolitinib cream vs vehicle.

† During the double-blind period (up to Week 24), multiple imputation was applied to account for missing values. ‡ During the open-label extension (after Week 24), responses were reported as observed.

F-VASI90 Responses

- Approximately 30% of patients who applied ruxolitinib cream from Day 1 achieved F-VASI90 by Week 52

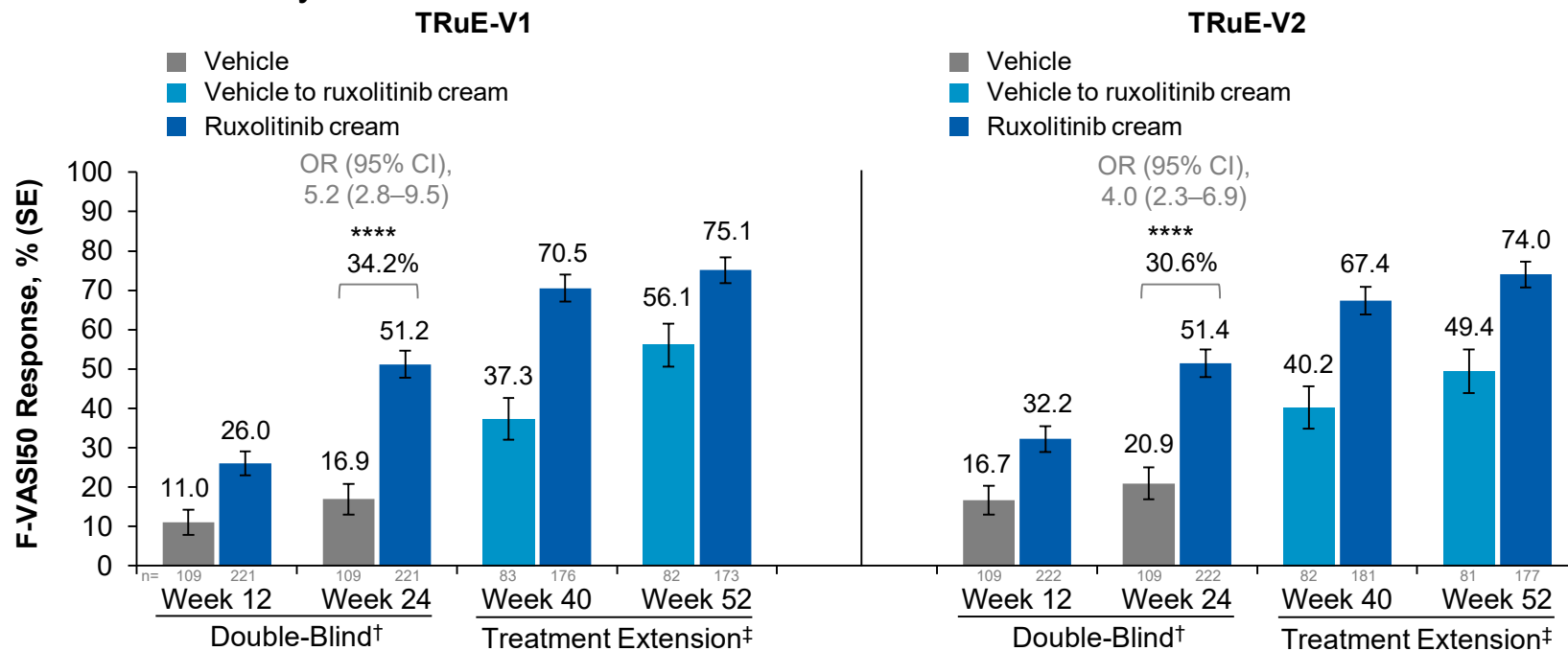


** $P < 0.01$ for response rate difference for ruxolitinib cream vs vehicle.

† During the double-blind period (up to Week 24), multiple imputation was applied to account for missing values. ‡ During the open-label extension (after Week 24), responses were reported as observed.

F-VASI50 Responses

- Approximately 75% of patients who applied ruxolitinib cream from Day 1 achieved F-VASI50 by Week 52



**** $P < 0.0001$ 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 extension (after Week 24), responses were reported as observed.

Clinical Images Showing F-VASI Response

1.5% Ruxolitinib Cream BID

Baseline



F-VASI: 1.62

Week 24



F-VASI: 0.14

Week 52



F-VASI: 0.12

Clinical Images Showing F-VASI Response

1.5% Ruxolitinib Cream BID

Baseline



F-VASI: 1.00

Week 24



F-VASI: 0.10

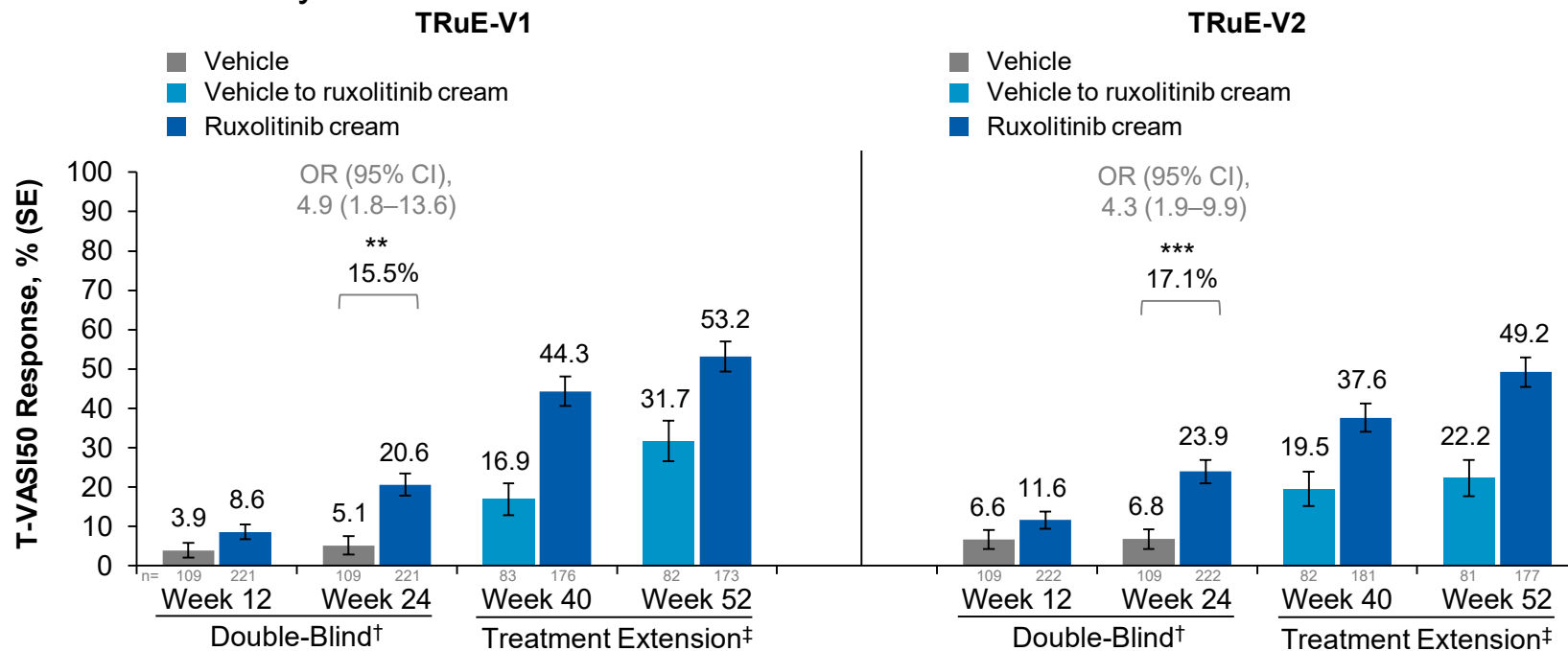
Week 52



F-VASI: 0.01

T-VASI50 Responses

- Approximately half of patients who applied ruxolitinib cream from Day 1 achieved T-VASI50 by Week 52



** $P < 0.01$, *** $P < 0.001$ 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 extension (after Week 24), responses were reported as observed.

Clinical Images Showing T-VASI Response

1.5% Ruxolitinib Cream BID

Baseline



T-VASI: 3.99

Week 24



T-VASI: 2.35

Week 52



T-VASI: 1.40

Clinical Images Showing T-VASI Response

1.5% Ruxolitinib Cream BID

Baseline



T-VASI: 9.60

Week 24



T-VASI: 4.65

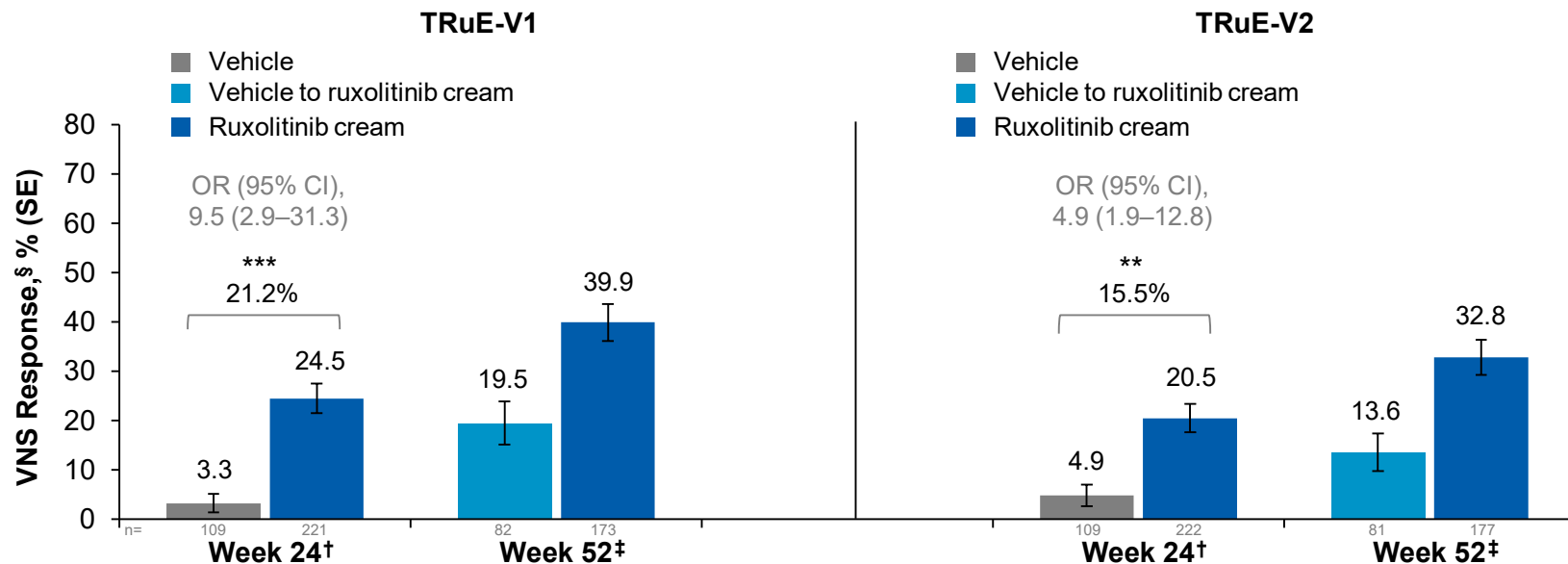
Week 52



T-VASI: 0.76

VNS Responses

- The proportion of patients achieving a VNS response by Week 52 among patients who applied ruxolitinib cream from Day 1 was 39.9% and 32.8% in TRuE-V1 and TRuE-V2, respectively



** $P < 0.01$, *** $P < 0.001$ 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.”

Safety (52 Weeks)

Patients Who Applied Ruxolitinib Cream Throughout the Study

- Ruxolitinib cream was well tolerated
- There were no clinically significant application site reactions or serious treatment-related AEs

Characteristic, n (%)	TRuE-V1	TRuE-V2
	Ruxolitinib Cream (n=221)	Ruxolitinib Cream (n=228)
Patients with a 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)
Patients with a treatment-related AE	41 (18.6)	35 (15.4)
Most common treatment-related AEs*		
Application site acne	13 (5.9)	12 (5.3)
Application site pruritus	11 (5.0)	10 (4.4)
Patients with a serious TEAE [†]	7 (3.2)	4 (1.8)
Patients with a TEAE leading to discontinuation	1 (0.5)	2 (0.9)

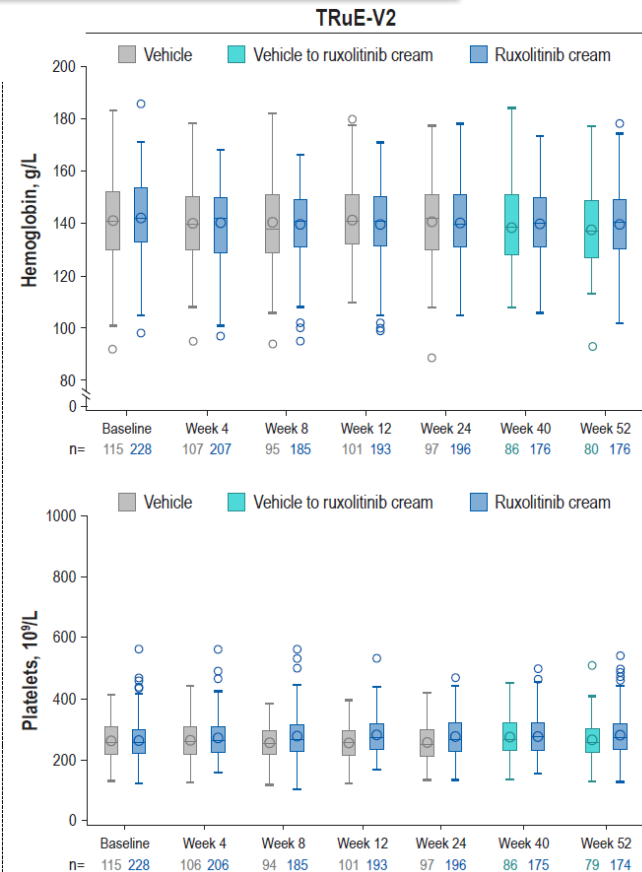
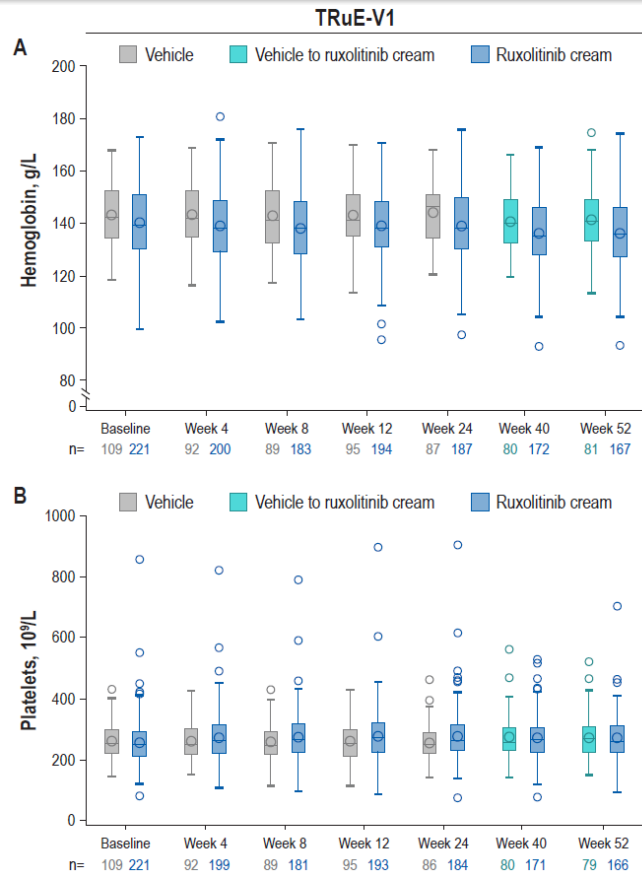
AE, adverse event; COVID-19, coronavirus disease 2019; TEAE, treatment-emergent adverse event.

* Occurring in $\geq 4\%$ of patients in any treatment group. [†] No serious TEAEs were considered related to treatment.

Safety (52 Weeks)

Hematopoietic Assessments

- Hematopoietic TEAEs were infrequent (<3%)
 - All were mild or moderate
 - None were considered related to treatment
- There were no clinically significant changes in hemoglobin or platelet levels



Conclusions

- Adolescent and adult patients with nonsegmental vitiligo achieved substantial facial and total body repigmentation at Week 24, with a higher proportion of patients responding at Week 52
- Half of patients who applied ruxolitinib cream from Day 1 achieved F-VASI75 and T-VASI50 responses by Week 52
- Efficacy at Week 52 in crossover patients (after 28 weeks of ruxolitinib cream) was consistent with Week 24 data in patients who applied ruxolitinib cream from Day 1
- Ruxolitinib cream was well tolerated, and no serious treatment-related AEs were reported