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Efficacy and Safety of a 52-Week, Randomized, Double-Blind Trial of Ruxolitinib Cream for the Treatment of Vitiligo

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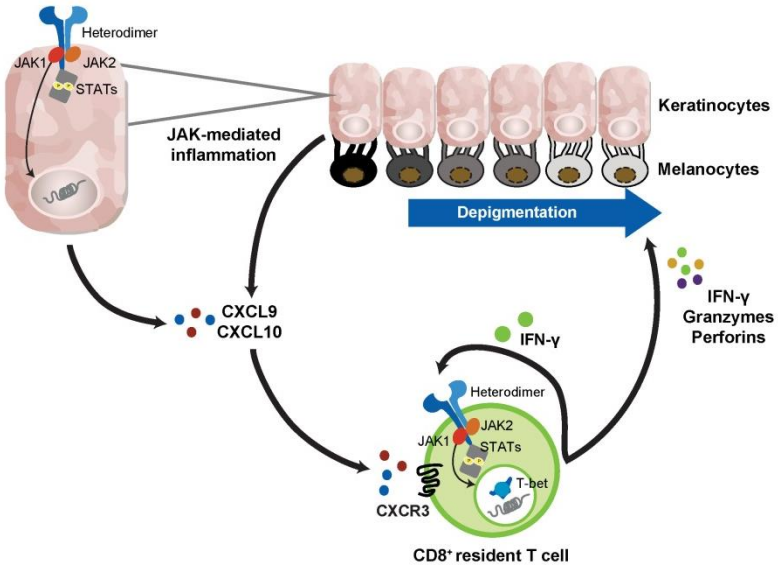
Presenting Author Disclosures

- Investigator for Aclaris Therapeutics, Immune Tolerance Network, Incyte Corporation, and Pfizer
- Consultant for Incyte Corporation and Pfizer
- Board member who also holds stock options for Clarify Medical

JAK-Targeted Therapy for Vitiligo

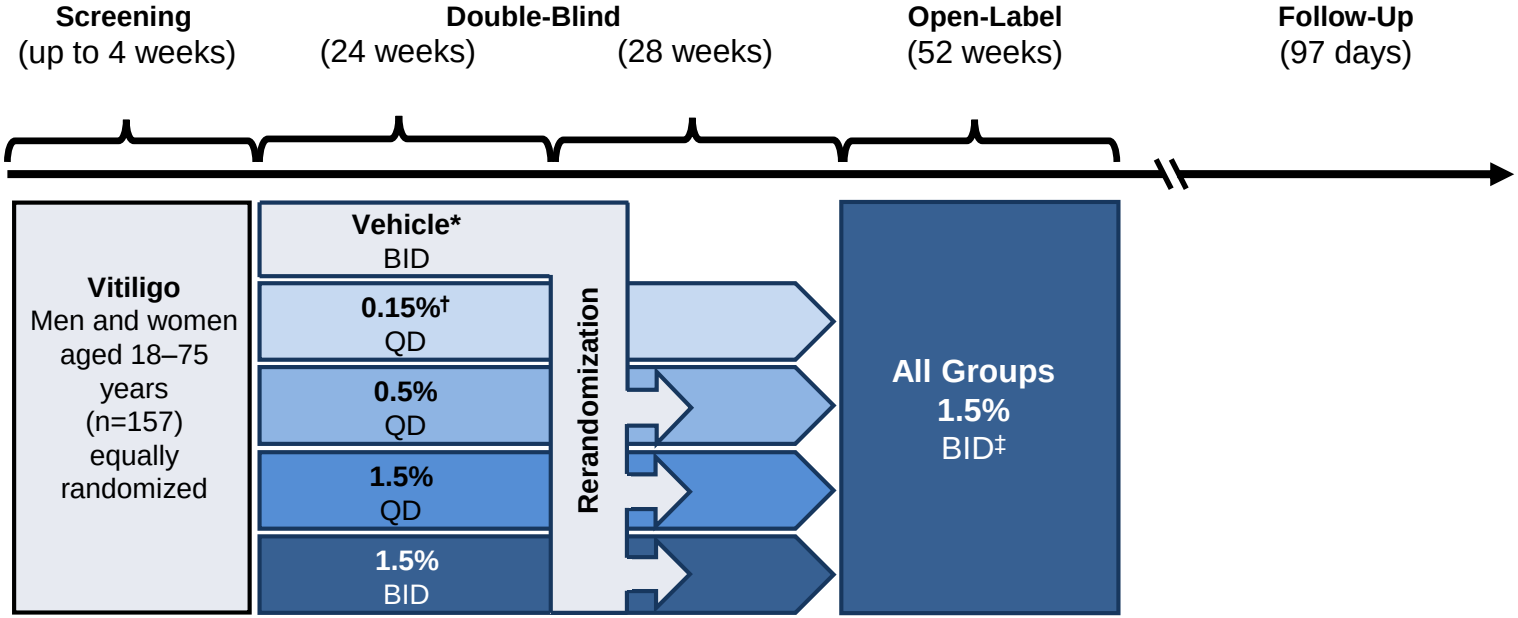
- Vitiligo is a chronic autoimmune disease that targets melanocytes, resulting in patches of skin depigmentation[1] and reduced quality of life[2]
- Disease pathogenesis is driven by signaling through JAK1/JAK2[3]
- A cream formulation of ruxolitinib, a JAK1/JAK2 inhibitor,[4] is under investigation for the treatment of vitiligo
- Ruxolitinib cream provided significant repigmentation of facial vitiligo lesions after 24 weeks of double-blind, vehicle-controlled treatment (NCT03099304)[5]
- **Objective:** To further investigate the therapeutic potential of ruxolitinib cream in patients with vitiligo after 52 weeks of double-blind treatment



CD, cluster of differentiation; CXCL, chemokine ligand; CXCR, chemokine receptor; IFN, interferon; JAK, Janus kinase; STAT, signal transducer and activator of transcription; T-bet, T-box–containing protein.

1. Taïeb A and Picardo M. *N Engl J Med*. 2009;360(2):160-169; 2. Morrison B, et al. *Br J Dermatol*. 2017;177(6):e338-e339; 3. Rashighi M and Harris JE. *Ann Transl Med*. 2015;3(21):343; 4. Quintas-Cardama A, et al. *Blood*. 2010;115(15):3109-3117; 5. Rosmarin D, et al. Efficacy and safety of ruxolitinib cream for the treatment of vitiligo: results of a 24-week, randomized, double-blind, dose-ranging, vehicle-controlled study. Presented at: World Congress of Dermatology 2019.

Study Design



***** 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 concurrent NB-UVB phototherapy.

BID, twice daily; F-VASI, facial Vitiligo Area Scoring Index; NB-UVB, narrow-band ultraviolet light B; QD, once daily.

Study Endpoints

- **Primary Endpoint**
  - Proportion of patients treated with ruxolitinib cream who achieved a ≥50% improvement from baseline in F-VASI (F-VASI50) at Week 24 compared with patients treated with vehicle

- **Secondary Endpoints**
  - Proportion of patients achieving ≥50% improvement from baseline in T-VASI (T-VASI50) at Week 52
  - Proportion of patients who achieved a F-PhGVA of clear (no signs of vitiligo) or almost clear (only specks of depigmentation present) at Week 24
  - Safety and tolerability

F-PhGVA, facial Physician Global Vitiligo Assessment; T-VASI, total Vitiligo Area Scoring Index.

Eligibility Criteria

- **Key Inclusion Criteria**
  - Patients aged 18–75 years with clinical diagnosis of vitiligo
  - Depigmented areas including both of the following
    - ≥0.5% of total BSA on the face
    - ≥3% of total BSA on nonfacial areas
- **Key Exclusion Criteria**
  - Dermatologic disease confounding vitiligo assessment
  - Use of any biological or experimental therapy for vitiligo within 12 weeks of screening
  - Use of phototherapy within 8 weeks of screening
  - Use of immunomodulating treatments within 4 weeks of screening
  - Previous JAK inhibitor therapy

BSA, body surface area.

Patient Demographics and Clinical Characteristics

- Distribution of baseline demographics and clinical characteristics were similar across treatment groups

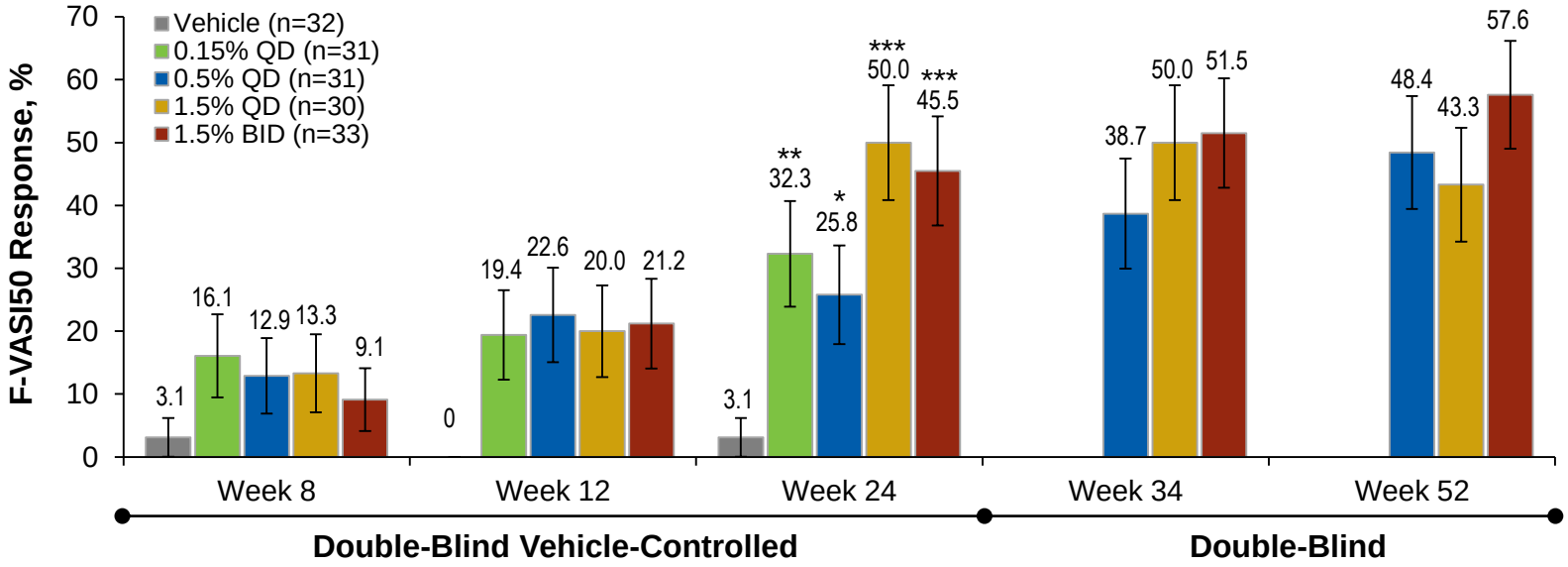
Demographics and Clinical Characteristics	Total (N=157)
Age, mean ± SD, years	48.3±12.9
Men, n (%)	73 (46.5)
White, n (%)	132 (84.1)
Skin type, n (%)	
I	6 (3.8)
II	50 (31.8)
III	50 (31.8)
IV	31 (19.7)
V	10 (6.4)
VI	10 (6.4)

Clinical Characteristics	Total (N=157)
Baseline F-VASI, mean ± SD	1.26±0.82
Baseline T-VASI, mean ± SD	18.0±15.5
Facial BSA,* mean ± SD, %	1.48±0.86
Total BSA, mean ± SD, %	22.1±18.4
Duration of disease, median (range), years	14.0 (0.3–67.9)
Diagnosed in childhood,† n (%)	35 (22.3)
Other autoimmune disorders,‡ n (%)	42 (26.8)
Prior therapy, n (%)	
Topical corticosteroids	72 (45.9)
Calcineurin inhibitors	70 (44.6)
Phototherapy	55 (35.0)

* Percentage of total BSA; † Data missing from 1 patient in the 1.5% BID group; ‡ Including patients (n [%]) with thyroid disorders (39 [24.8]), juvenile diabetes mellitus (2 [1.3]), and pernicious anemia (1 [0.6]).

F-VASI50 Response

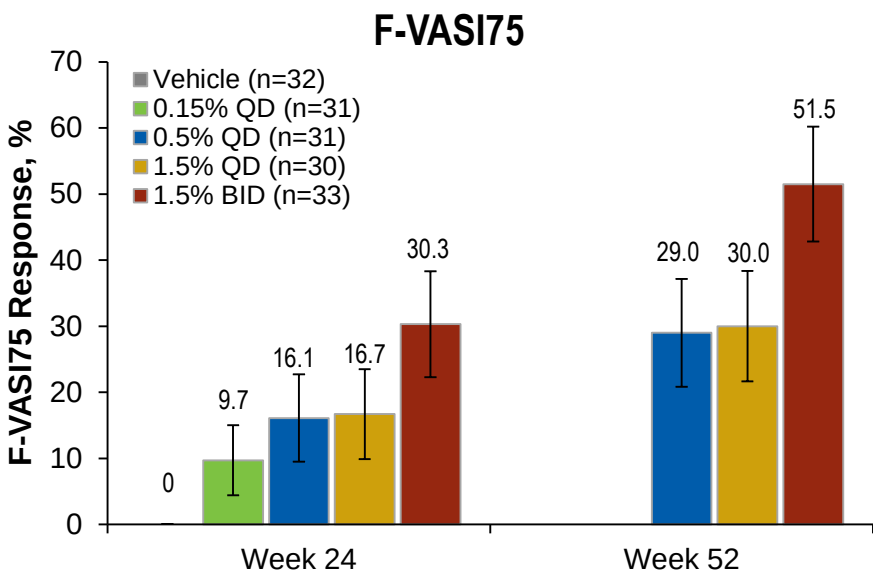
- At Week 24, F-VASI50 was achieved by a significantly greater proportion of patients receiving ruxolitinib cream (25.8%–50.0% across doses) vs vehicle (3.1%)
- At Week 52, the proportion of patients achieving an F-VASI50 response was highest in the 1.5% BID group

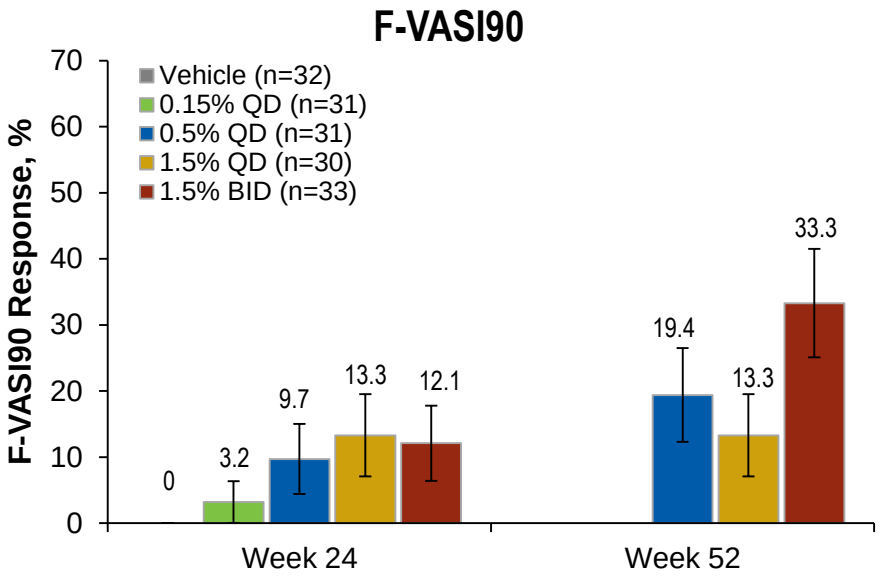


Error bars indicate standard error.
* *P*<0.05 vs vehicle at Week 24; ** *P*<0.01 vs vehicle at Week 24; *** *P*<0.001 vs vehicle at Week 24.

F-VASI75 and F-VASI90 Responses

- At Week 52, the proportions of patients achieving F-VASI75 and F-VASI90 responses were highest in the 1.5% BID group

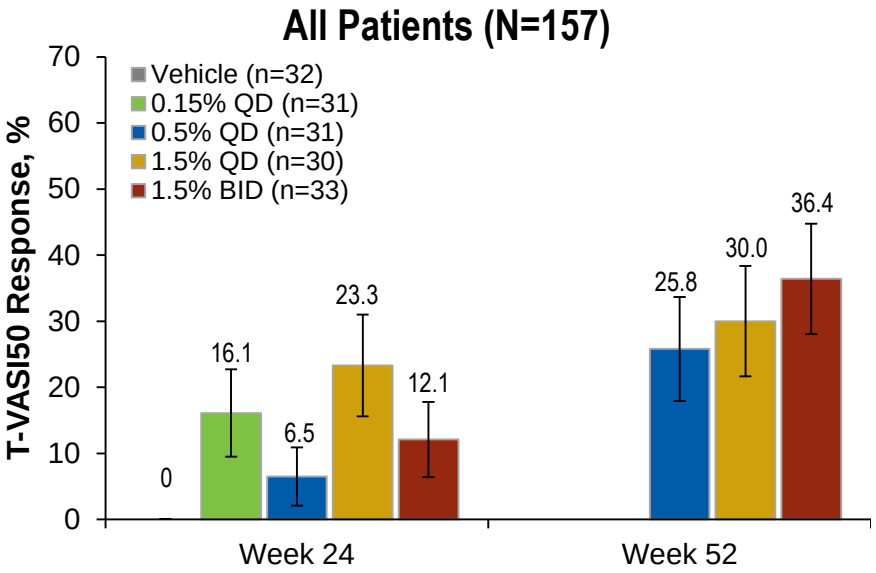


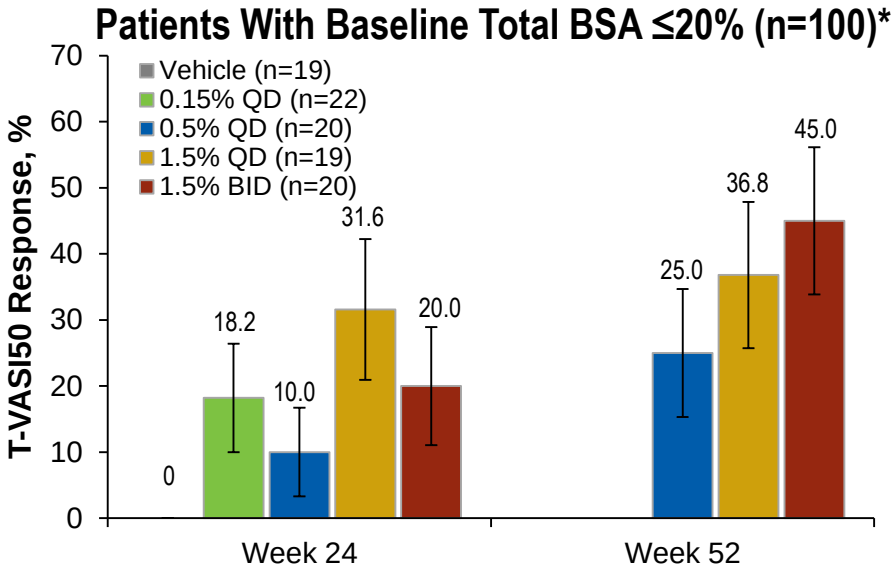


Error bars indicate standard error.

T-VASI50 Response

- T-VASI50 at Week 52 was achieved by patients in a dose-dependent manner
- Among patients who treated all depigmented skin (baseline total BSA ≤20%), T-VASI50 response was 45.0% with the 1.5% BID regimen at Week 52



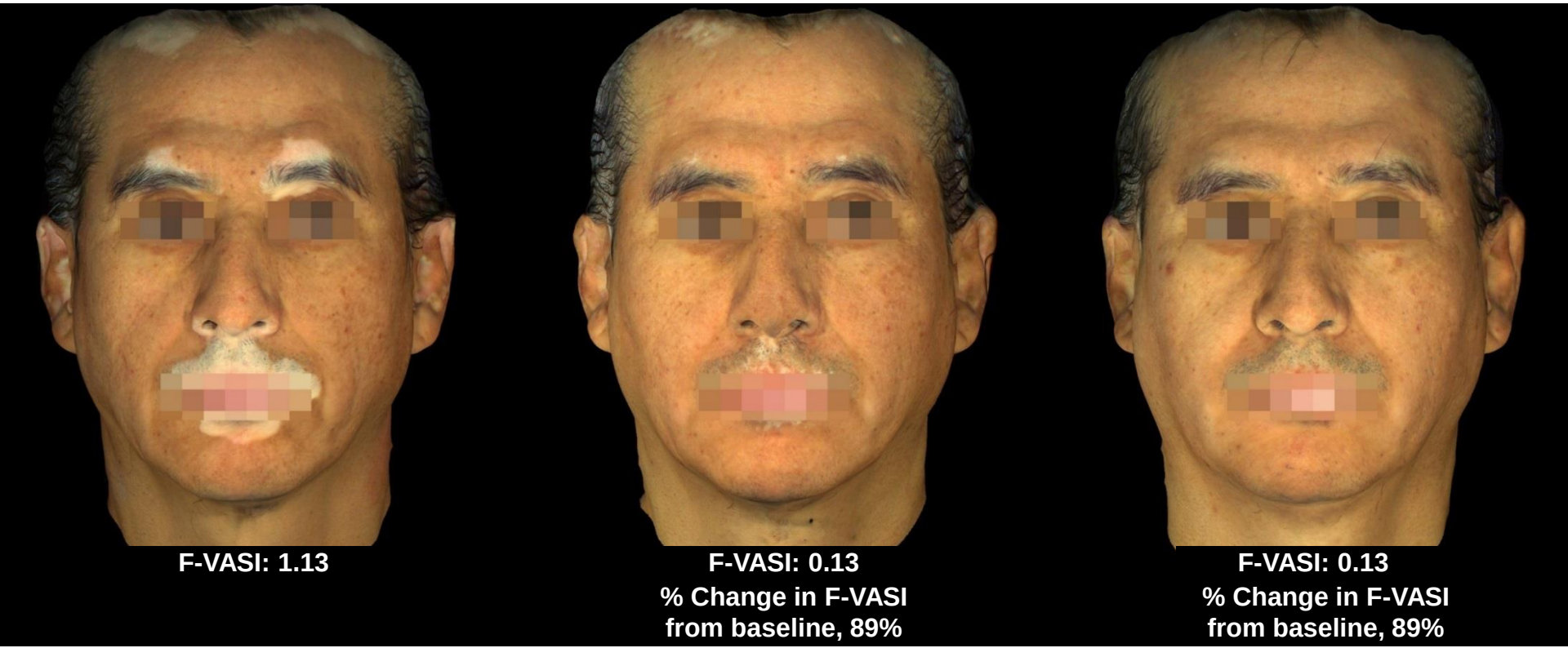


Error bars indicate standard error.

* T-VASI50 response is reported for the subset of patients with baseline total BSA ≤20% because treatment was limited to lesions constituting ≤20% of total BSA.

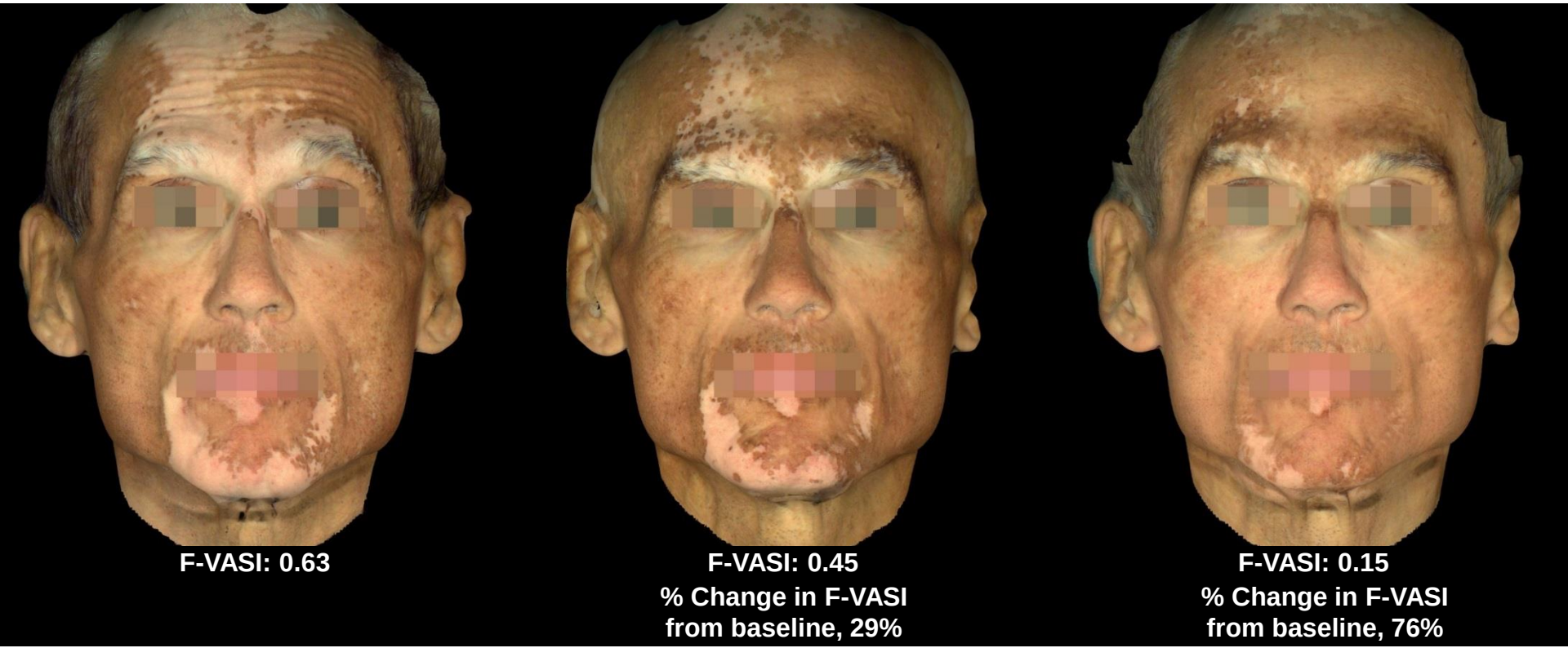
Clinical Images Showing F-VASI Response

Ruxolitinib Cream 1.5% BID



Clinical Images Showing F-VASI Response

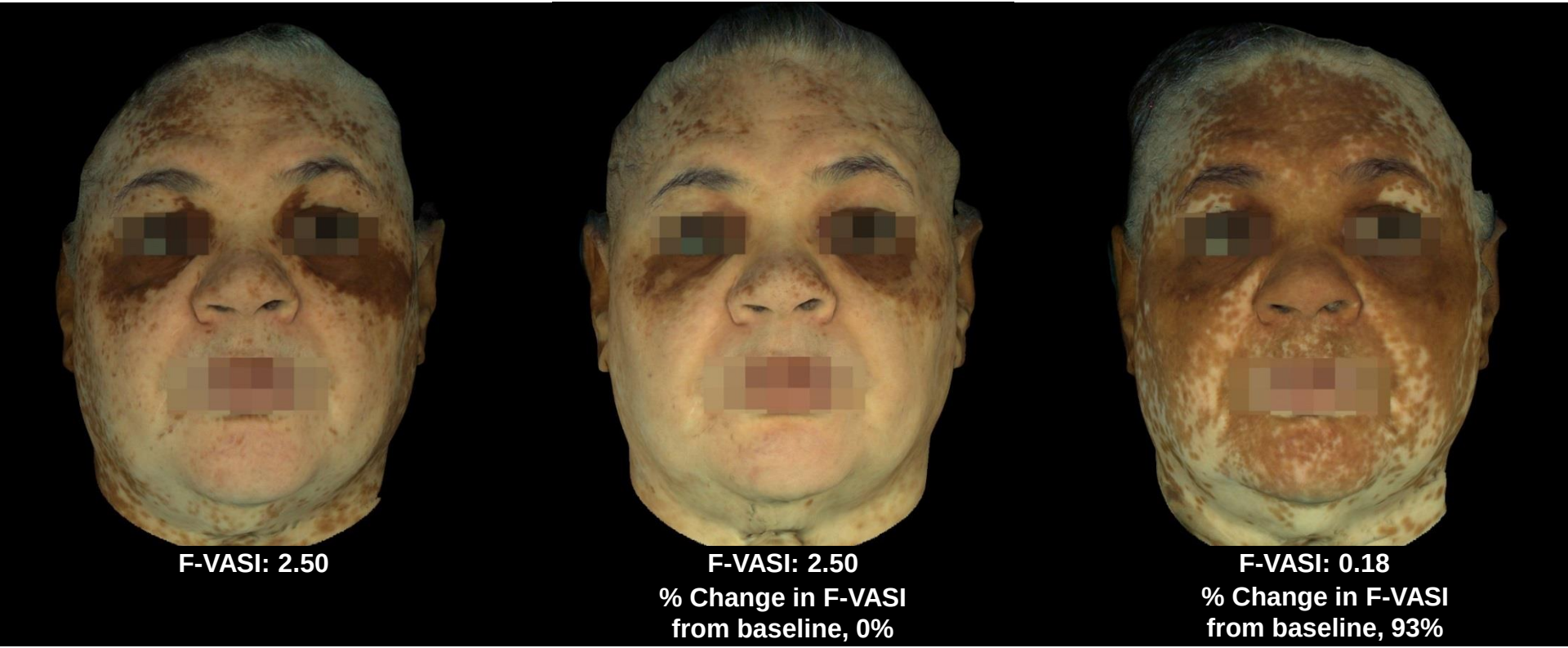
Ruxolitinib Cream 1.5% BID



Clinical Images Showing F-VASI Response

Vehicle Rerandomized to Ruxolitinib Cream 1.5% QD After Week 24

Day 1 —Vehicle→ **Week 24** —1.5% QD→ **Week 52**



F-VASI: 2.50

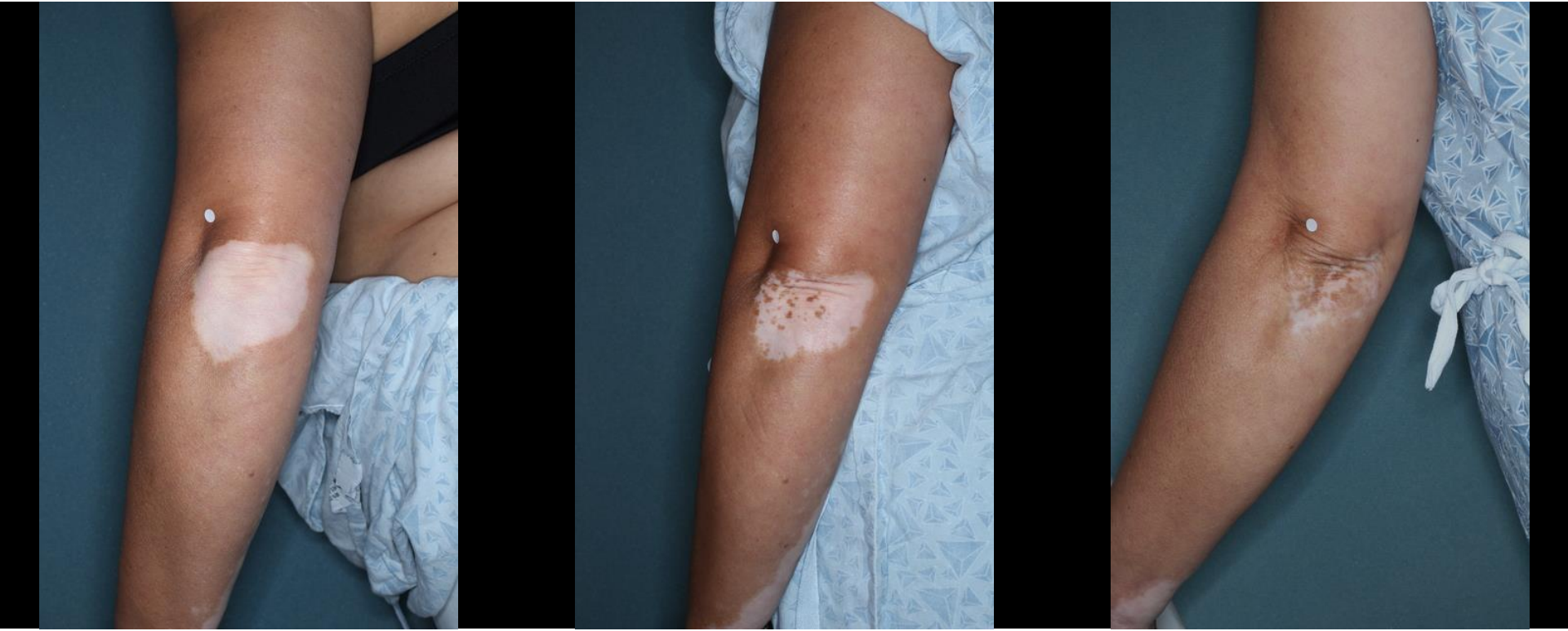
F-VASI: 2.50
% Change in F-VASI from baseline, 0%

F-VASI: 0.18
% Change in F-VASI from baseline, 93%

Clinical Images Showing T-VASI Response

Ruxolitinib Cream 1.5% QD

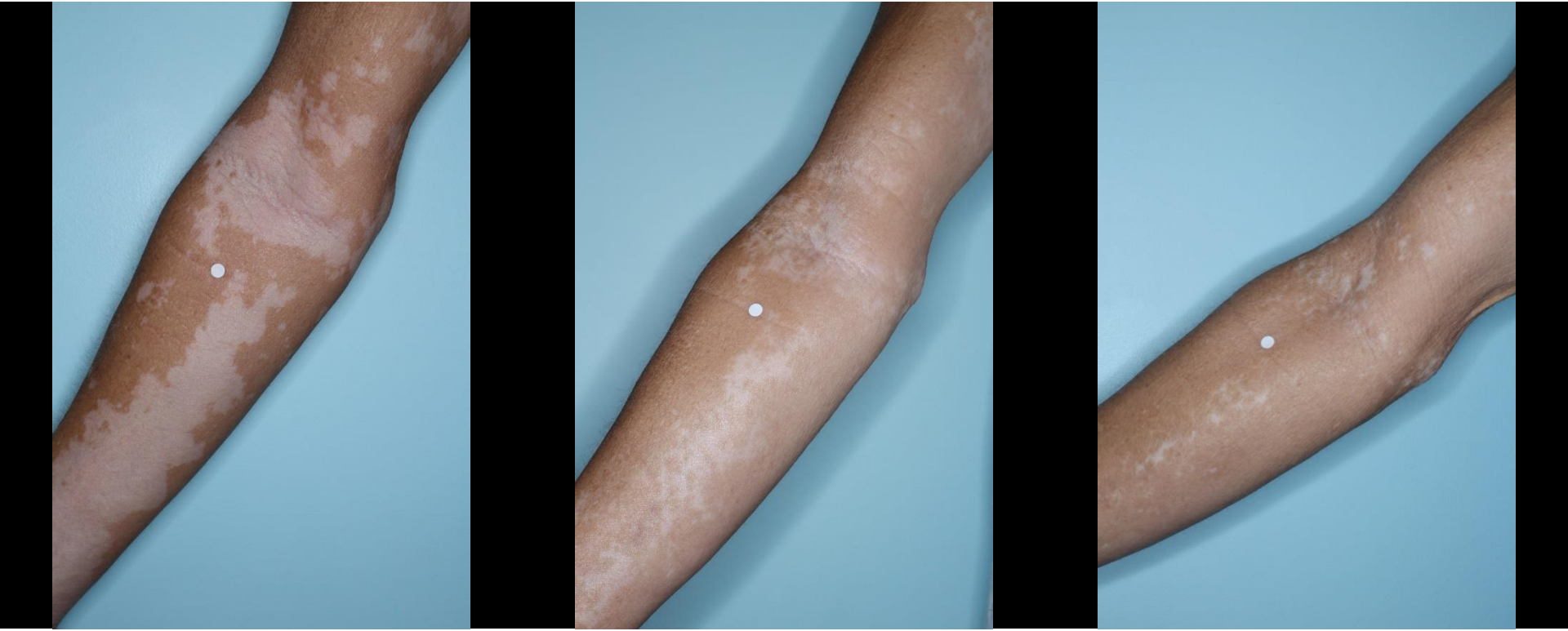
Day 1 **Week 24** **Week 52**



Clinical Images Showing T-VASI Response

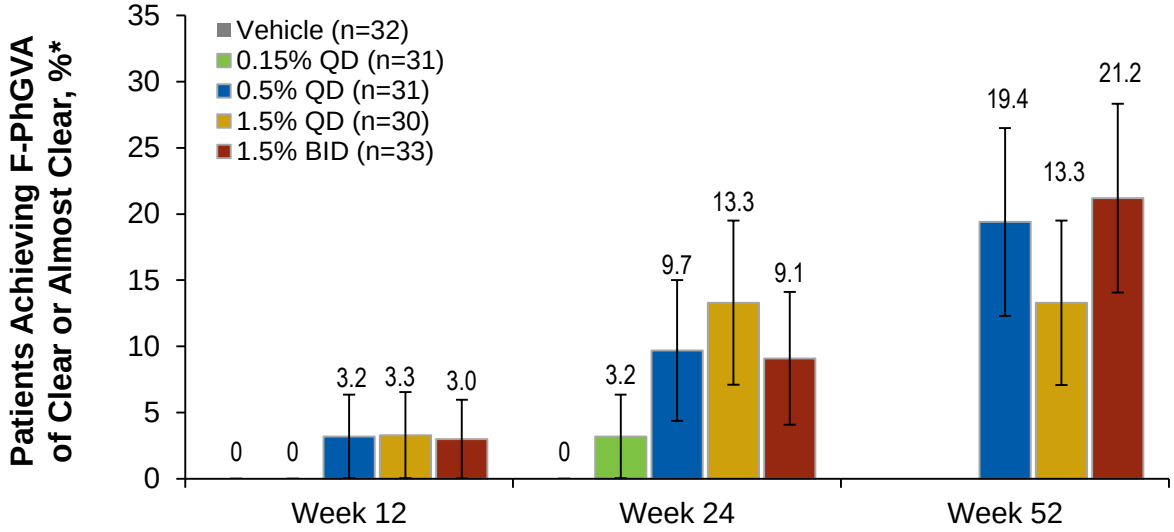
Ruxolitinib Cream 1.5% BID

Day 1 **Week 24** **Week 52**



F-PhGVA of Clear or Almost Clear

- The proportion of patients who attained F-PhGVA scores of clear or almost clear at Week 24 increased by Week 52



Error bars indicate standard error.
* No patients had F-PhGVA values of clear or almost clear at baseline.

Safety

TEAEs Through 52 Weeks

- Ruxolitinib cream was not associated with clinically significant application site reactions or serious treatment-related adverse events

Parameter, n (%)	Week 24	Week 52			
		Ruxolitinib Cream			
	Vehicle (n=32)	0.15% QD (n=31)	0.5% QD (n=31)	1.5% QD (n=30)	1.5% BID (n=33)
Patients with TEAE	20 (62.5)	20 (64.5)	26 (83.9)	23 (76.7)	23 (76.7)
Most common TEAEs*					
Acne	1 (3.1)	4 (12.9)	5 (16.1)	3 (10.0)	6 (18.2)
Pruritus	3 (9.4)	1 (3.2)	5 (16.1)	4 (13.3)	3 (9.1)
Upper respiratory tract infection	0	1 (3.2)	5 (16.1)	1 (3.3)	3 (9.1)
Headache	3 (9.4)	1 (3.2)	0	3 (10.0)	2 (6.1)
Sinusitis	1 (3.1)	2 (6.5)	1 (3.2)	2 (6.7)	2 (6.1)
Viral upper respiratory tract infection	5 (15.6)	3 (9.7)	3 (9.7)	6 (20.0)	1 (3.0)
Application site pruritus	3 (9.4)	6 (19.4)	3 (9.7)	3 (10.0)	1 (3.0)
Patients with treatment-related TEAE	12 (37.5)	11 (35.5)	12 (38.7)	12 (40.0)	10 (30.3)
Patients with TEAE leading to discontinuation†	1 (3.1)	1 (3.2)‡	0	1 (3.3)	0
Patients with serious TEAE§	0	0	2 (6.5)	1 (3.3)	1 (3.0)

TEAE, treatment-emergent adverse event.

* Occurring in >5% of the total patient population; † TEAEs leading to discontinuation were not related to treatment unless otherwise indicated; ‡ Headache related to treatment; § No serious TEAEs were related to treatment.

Conclusions

- Ruxolitinib cream monotherapy produced substantial facial and total body repigmentation of vitiligo lesions after Week 24
- Continued improvement was seen through 52 weeks of treatment (highest responses with 1.5% BID), suggesting that ruxolitinib cream is an effective treatment option for patients with vitiligo
- A longer duration of therapy was associated with greater repigmentation, as objectively assessed using the VASI
  - Near-complete facial repigmentation as assessed by F-VASI75
  - Substantial total body repigmentation as assessed by T-VASI50
- All doses of ruxolitinib cream were well tolerated, and no treatment-related serious AEs were reported