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Efficacy and Safety of Ruxolitinib Cream for the Treatment of Vitiligo: Results of a 24-Week, Randomized, Double-Blind, Dose-Ranging, Vehicle-Controlled Study

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Presenting Author Disclosures

- Honoraria as a consultant for AbbVie, Celgene, Dermavant, Dermira, Janssen, Lilly, Novartis, Pfizer, and Regeneron Pharmaceuticals Inc.
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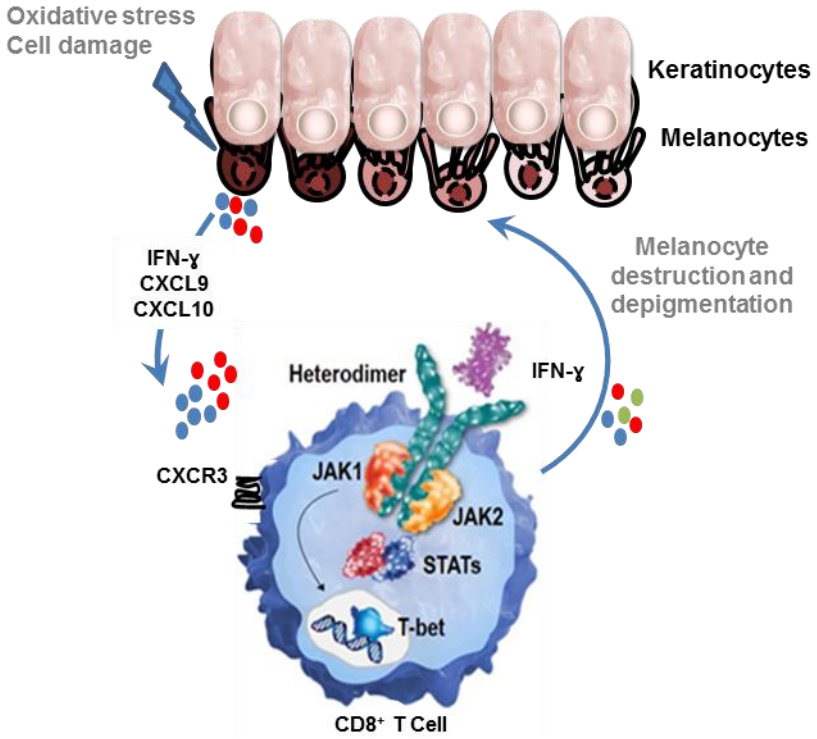
JAK-Targeted Therapy for Vitiligo

- Vitiligo is an autoimmune disease that targets melanocytes and leads to patches of depigmentation[1-2]
- Preclinical and translational studies suggest that IFN-γ drives disease pathogenesis by signaling through JAK1/JAK2[3,4]
- Ruxolitinib is a potent inhibitor of JAK1 and JAK2[5]
- Ruxolitinib cream provided significant repigmentation in facial vitiligo in a 20-week proof-of-concept study[6] and its 32-week extension[7]

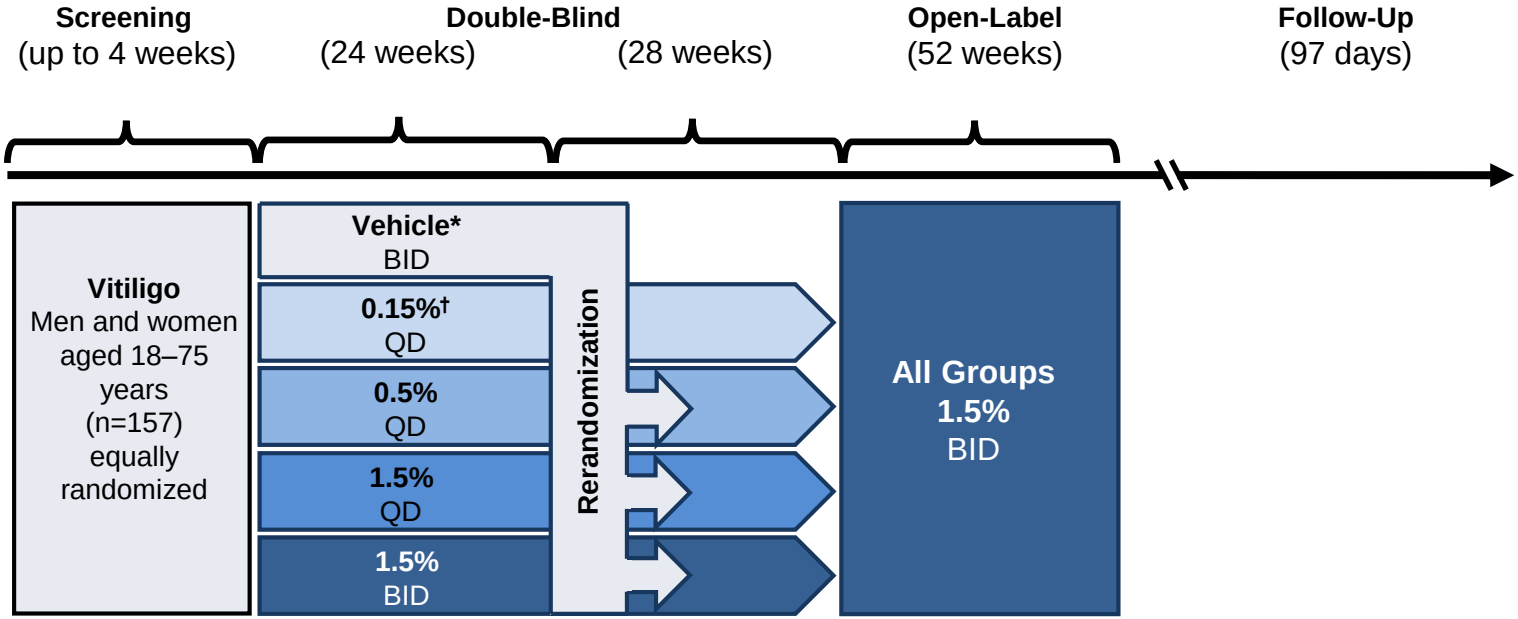
Objective: To report efficacy and safety of ruxolitinib cream in patients with vitiligo after 24 weeks of treatment (NCT03099304)



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 Picard M. *N Engl J Med*. 2009;360(2):160-169; 2. van den Boorn JG, et al. *J Invest Dermatol*. 2009;129(9):2220-2232; 3. Harris JE, et al. *J Invest Dermatol*. 2012;132(7):1869-1876; 4. Rashighi M and Harris JE. *Ann Transl Med*. 2015;3(21):343; 5. Quintás-Cardama A, et al. *Blood*. 2010;115(15):3109-3117; 6. Rothstein B, et al. *J Am Acad Dermatol*. 2017;76(6):1054-1060; 7. Joshipura D, et al. *J Am Acad Dermatol*. 2018;78(6):1205-1207.

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.

BID, twice daily; F-VASI, facial Vitiligo Area Scoring Index; 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 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.

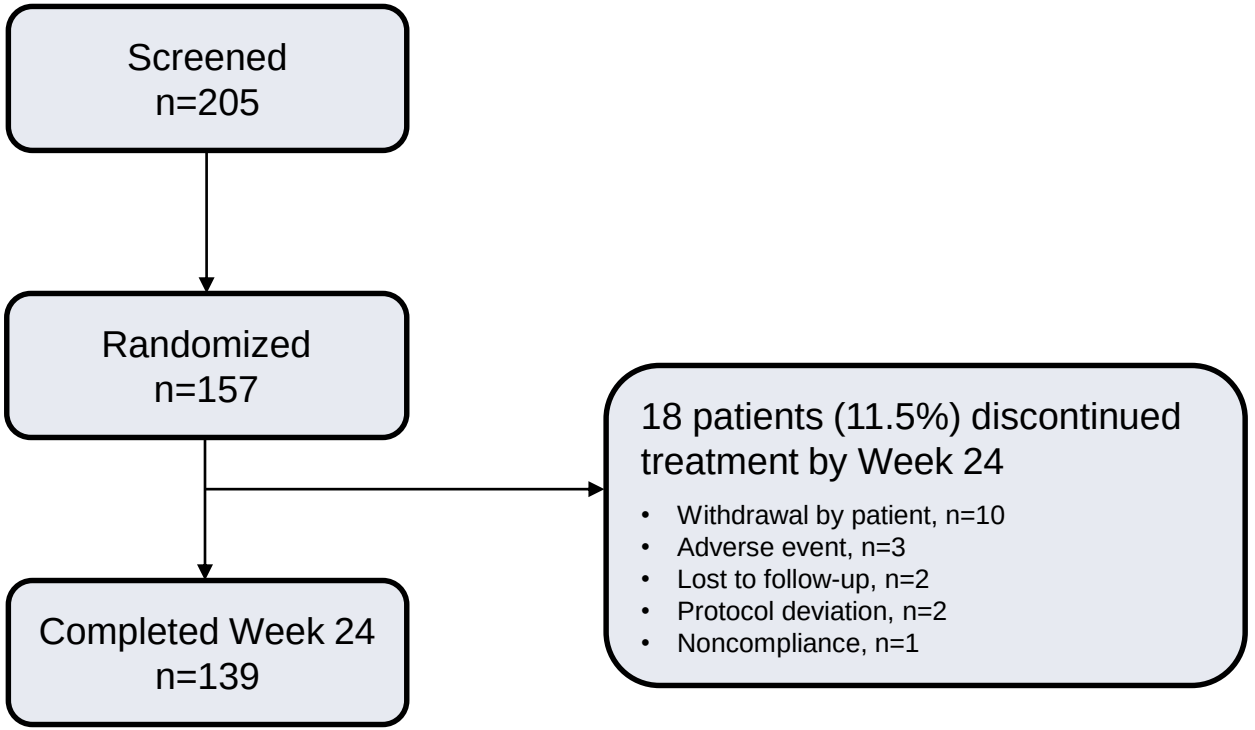
Eligibility Criteria

- **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**
  - Current or recent clinically meaningful infection
  - Dermatologic disease besides vitiligo
  - Use of biological, investigational, or experimental therapy within 12 weeks of screening
  - Use of laser or light-based treatments within 8 weeks of screening
  - Use of immunomodulating systemic drugs or topical treatments within 4 weeks of screening
  - Prior JAK inhibitor therapy

BSA, body surface area.

Patient Disposition

Double-Blind (Day 1 to Week 24)



Patient Demographics and Clinical Characteristics

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

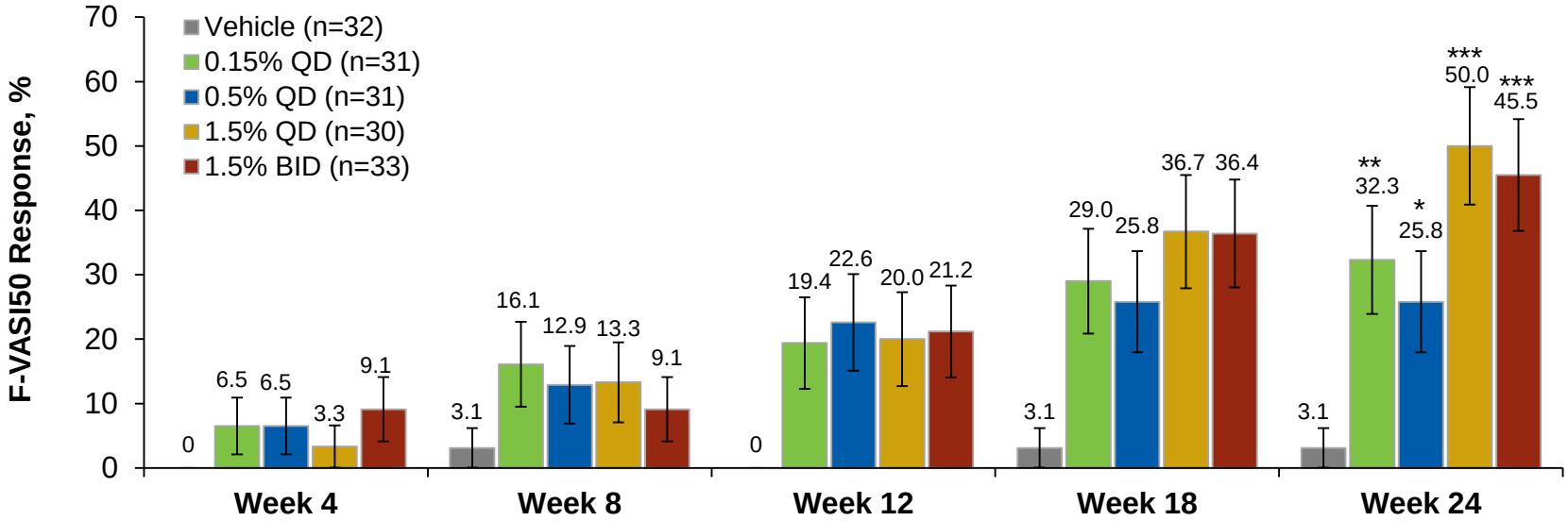
Demographics and Clinical Characteristics	Total (N=157)
Age, mean ± SD, years	48.3±12.85
Male, n (%)	73 (46.5)
Skin type, n (%)	
I	6 (3.8)
II	50 (31.8)
III	50 (31.8)
IV	31 (19.7)
V	10 (6.4)
VI	10 (6.4)

Clinical Characteristics	Total (N=157)
Baseline F-VASI, mean ± SD	1.26±0.82
Baseline T-VASI, mean ± SD	17.95±15.46
Facial BSA, mean ± SD, %	1.48±0.86
Total BSA, mean ± SD, %	22.05±18.38
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)

T-VASI, total Vitiligo Area Scoring Index.
* Including patients (n [%]) with thyroid disorders (39 [24.8]), juvenile diabetes mellitus (2 [1.3]), and pernicious anemia (1 [0.6]).

F-VASI50 Response

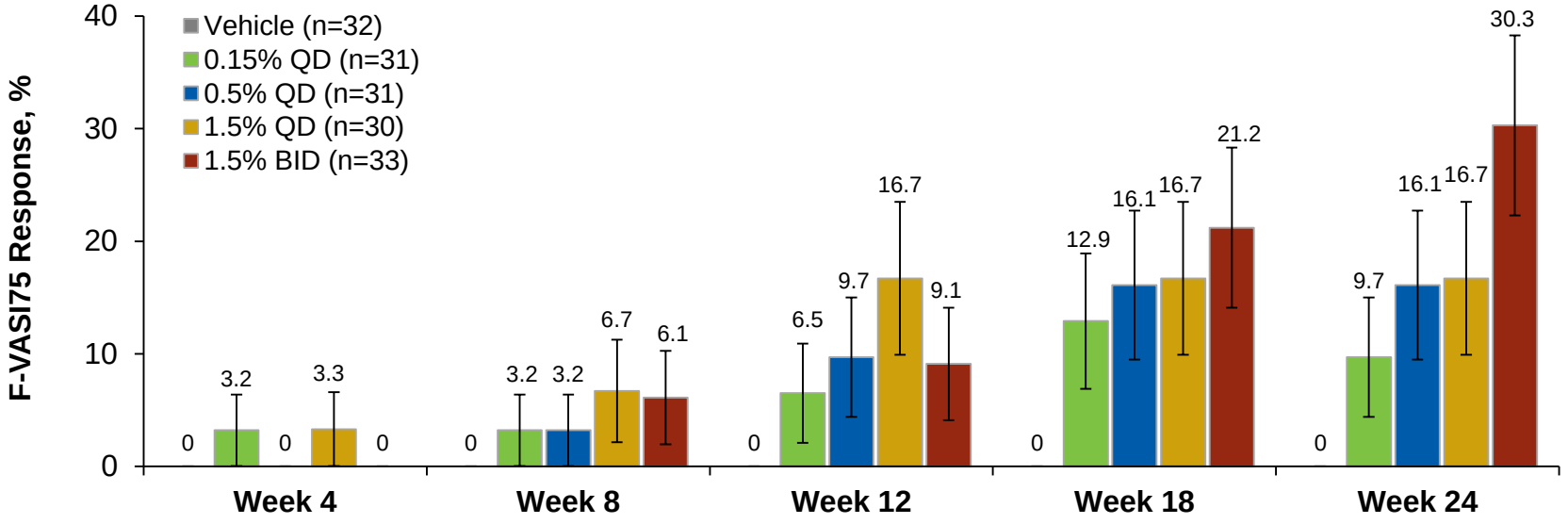
- At Week 24, the highest F-VASI50 response was achieved with the ruxolitinib cream 1.5% QD and BID regimens



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

F-VASI75 Response

- At Week 24, the highest F-VASI75 response was achieved with the ruxolitinib cream 1.5% BID regimen

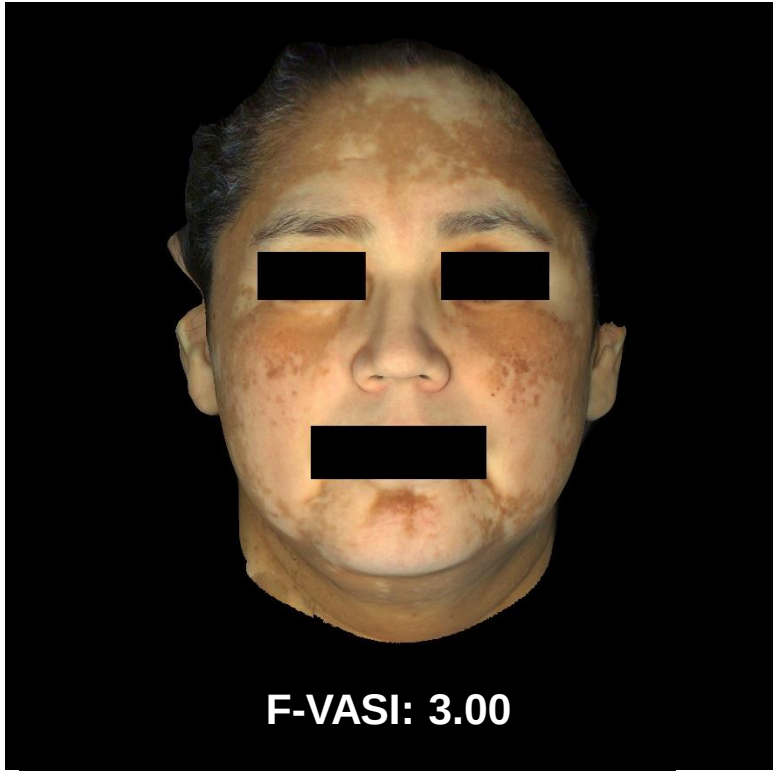


Error bars indicate standard error.

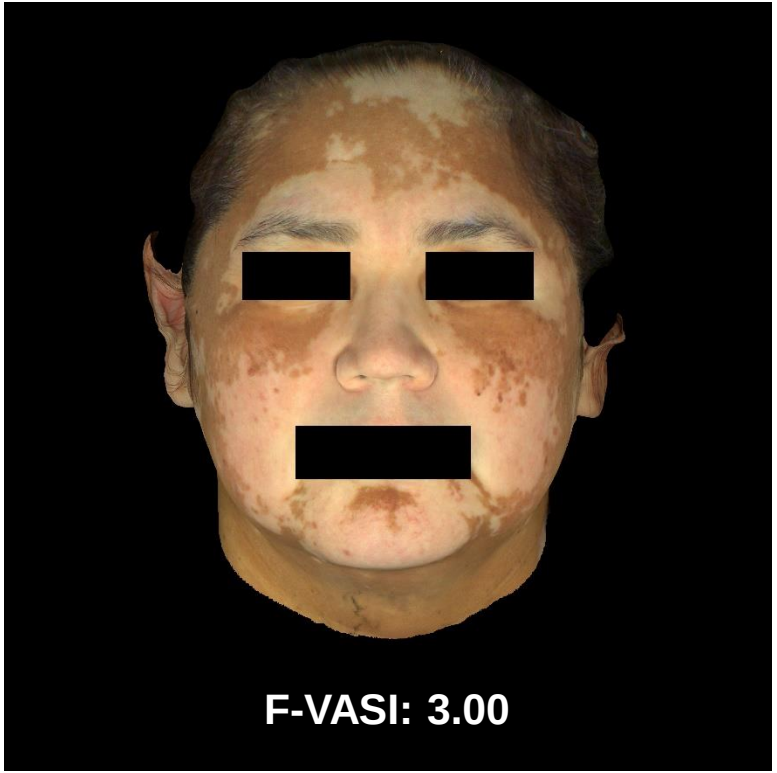
Clinical Images Showing F-VASI Response

Vehicle

Day 1



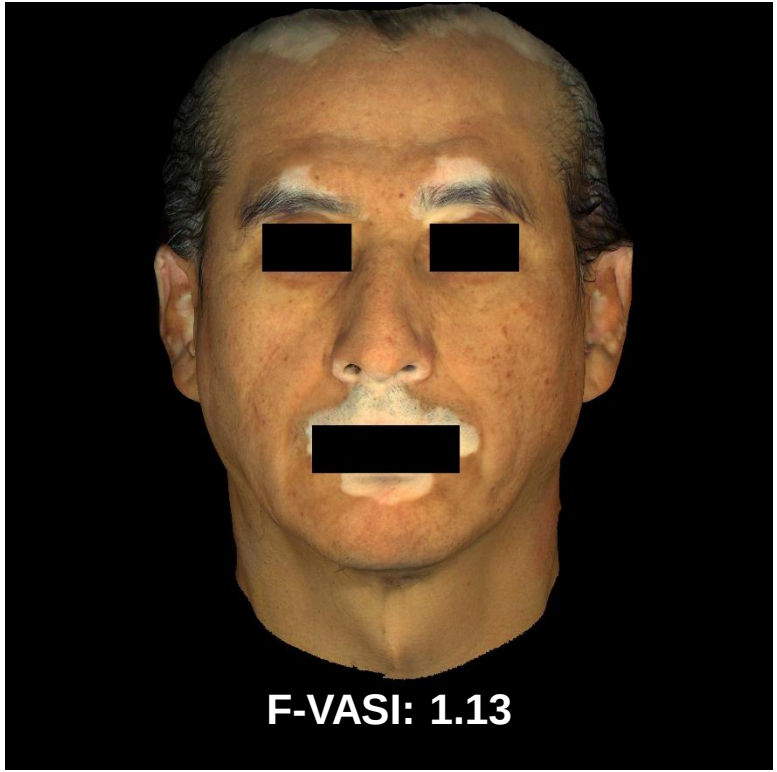
Week 24



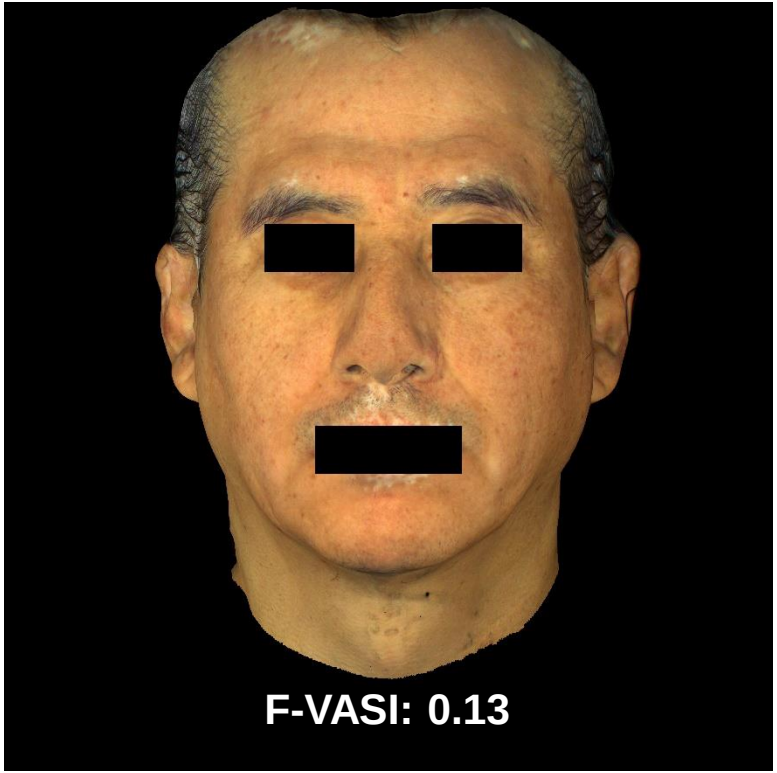
Clinical Images Showing F-VASI Response

Ruxolitinib Cream 1.5% BID

Day 1



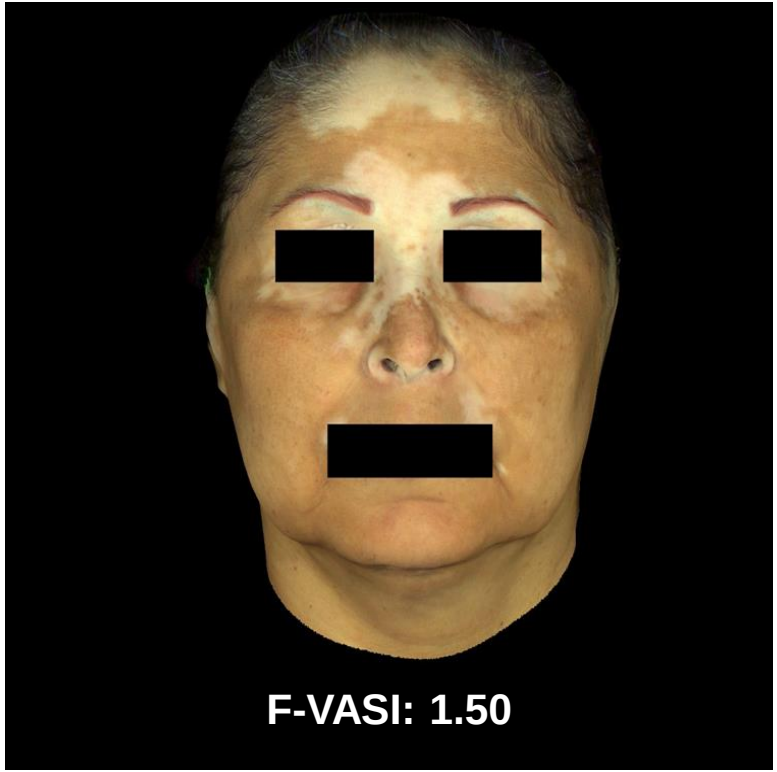
Week 24



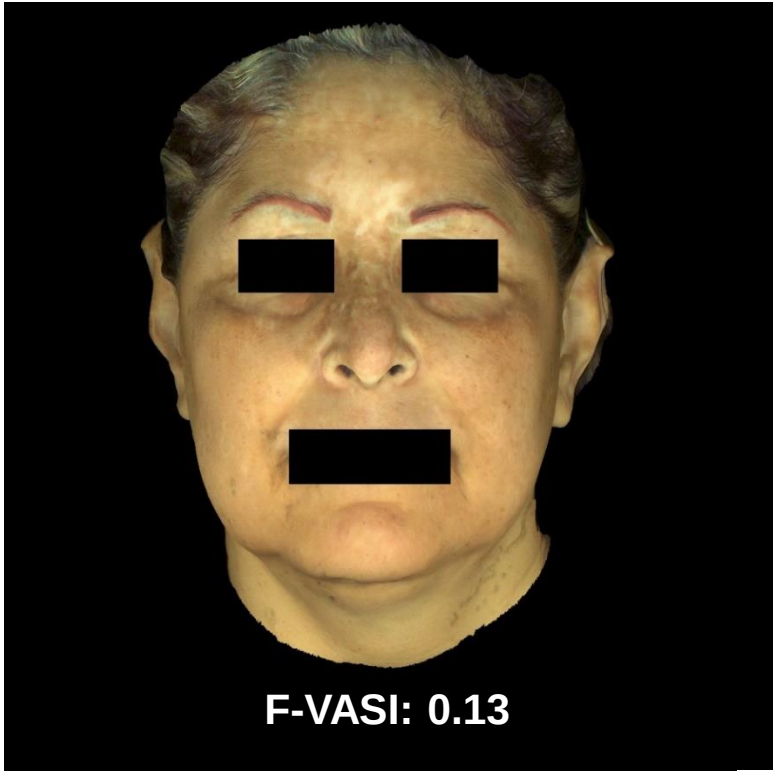
Clinical Images Showing F-VASI Response

Ruxolitinib Cream 1.5% BID

Day 1



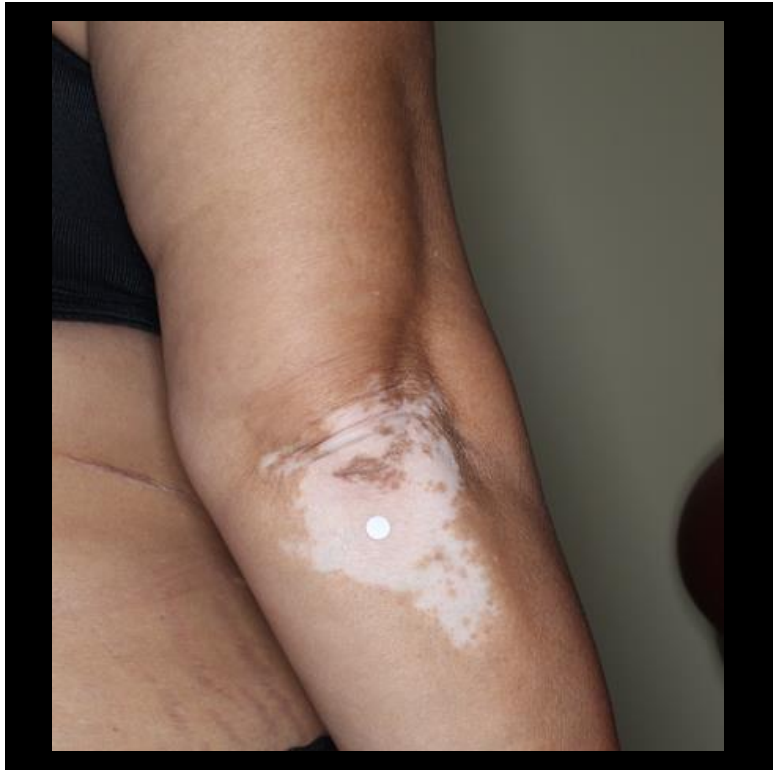
Week 24



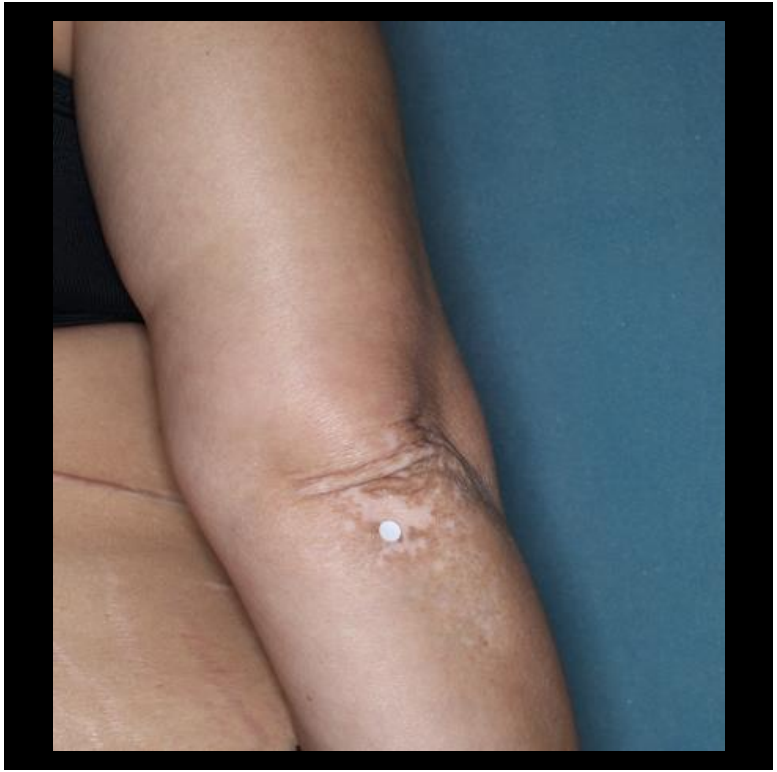
Clinical Images Showing T-VASI Response

Ruxolitinib Cream 1.5% BID

Day 1

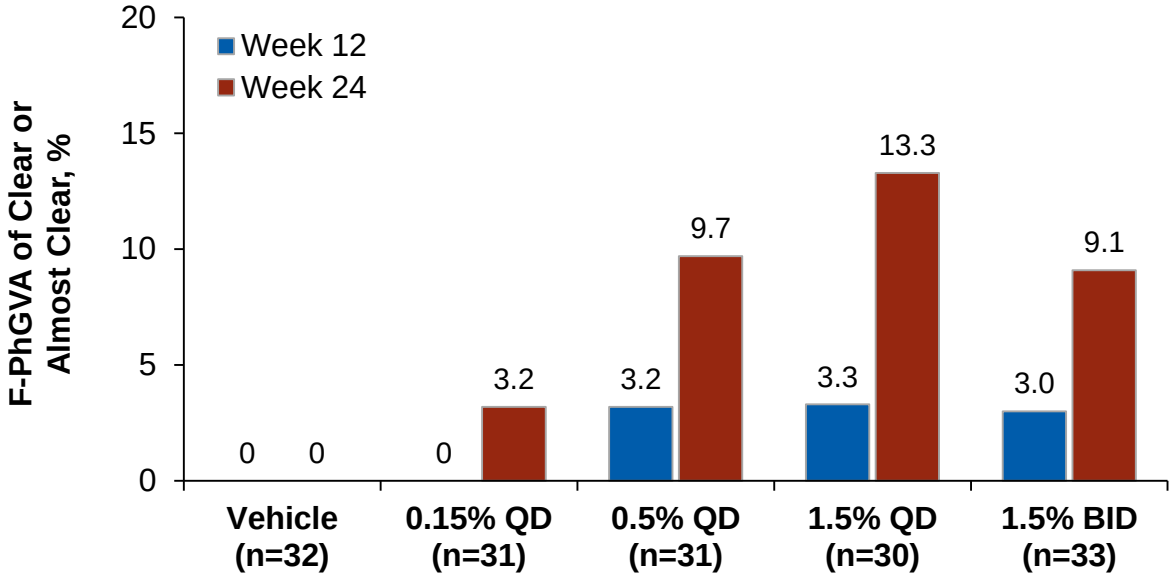


Week 24



F-PhGVA of Clear or Almost Clear at Week 24

- F-PhGVA scores of clear (no signs of vitiligo) or almost clear (only specks of depigmentation present) at Week 24 were achieved only by patients who received ruxolitinib cream



Safety

Treatment-Emergent Adverse Events Through 24 Weeks

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

		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)**	**Total (n=157)**
Patients with TEAE, n (%)	20 (62.5)	20 (64.5)	22 (71.0)	22 (73.3)	20 (60.6)	104 (66.2)
Most common TEAEs,* n (%)						
Acne	1 (3.1)	4 (12.9)	3 (9.7)	3 (10.0)	5 (15.2)	16 (10.2)
Application site pruritus	3 (9.4)	6 (19.4)	3 (9.7)	3 (10.0)	1 (3.0)	16 (10.2)
Pruritus	3 (9.4)	1 (3.2)	4 (12.9)	4 (13.3)	2 (6.1)	14 (8.9)
Viral upper respiratory tract infection	5 (15.6)	3 (9.7)	2 (6.5)	2 (6.7)	1 (3.0)	13 (8.3)
Headache	3 (9.4)	1 (3.2)	0	3 (10.0)	2 (6.1)	9 (5.7)
Treatment-related TEAE, n (%)	12 (37.5)	11 (35.5)	11 (35.5)	10 (33.3)	10 (30.3)	54 (34.4)
TEAE leading to discontinuation, n (%)	1 (3.1)	1 (3.2)†	0	0	0	2 (1.3)
Serious TEAE, n (%)	0	0	0	0	1 (3.0)‡	1 (0.6)

TEAE, treatment-emergent adverse event.
* Occurring in ≥5% of the total patient population; † Headache related to treatment; ‡ Subdural hematoma not related to treatment.

Conclusions

- Significantly more patients achieved F-VASI50 after 24 weeks of treatment with ruxolitinib cream (all regimens) vs vehicle
  - F-VASI50 was most notably achieved with ruxolitinib cream 1.5% BID (45.5%) and 1.5% QD (50.0%); both $P<0.001$ vs vehicle
- F-VASI75 was achieved by 30.3% and 16.7% of patients in the 1.5% BID and 1.5% QD groups, respectively
- F-PhGVA scores of clear or almost clear were achieved only by patients who received ruxolitinib cream (3.2%–13.3% across doses at Week 24)
- All doses of ruxolitinib cream were well tolerated