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Relapse and Maintenance of Clinical Response In the Randomized Withdrawal Arm of the TRuE-V Long-Term Extension Phase 3 Study of Ruxolitinib Cream in Vitiligo

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Presenting Author Disclosures

- Consultant for AbbVie, Aclaris Therapeutics, BiologicsMD, EMD Serono, Genzyme/Sanofi, Incyte Corporation, Janssen, Pfizer, Rheos Medicines, Sun Pharmaceuticals, TeVido BioDevices, The Expert Institute, 3rd Rock Ventures, and Villaris Therapeutics
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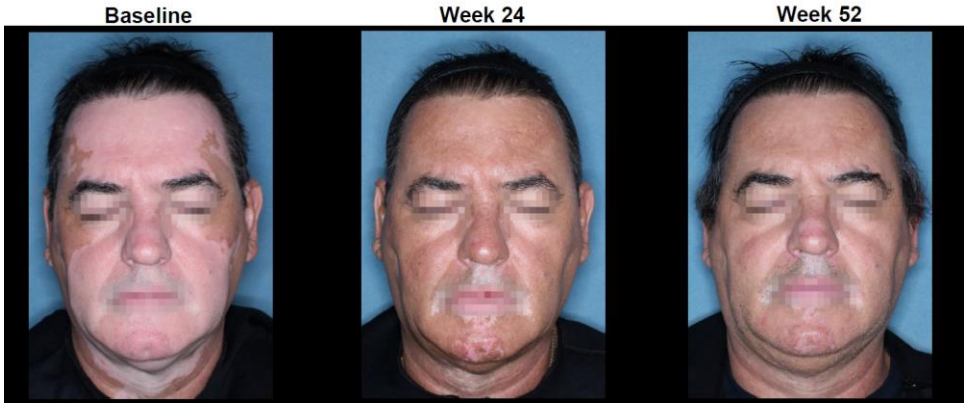
- Holds equity in Aldena Therapeutics, NIRA Biosciences, Rheos Medicines, TeVido BioDevices, and Villaris Therapeutics
- A scientific founder of Aldena Therapeutics, NIRA Biosciences, and Villaris Therapeutics
- Has patents pending for IL-15 blockade for treatment of vitiligo, JAK inhibition with light therapy for vitiligo, and CXCR3 antibody depletion for treatment of vitiligo

JAK-Targeted Therapy for Vitiligo

- Vitiligo is a chronic autoimmune disease that targets melanocytes, causing skin depigmentation[1]
- A cream formulation of ruxolitinib, a JAK1/JAK2 inhibitor, is approved by the US FDA for the topical treatment of nonsegmental vitiligo in adult and pediatric patients ≥12 years of age,[2] a milestone in vitiligo therapy
- In 2 randomized, double-blind, vehicle-controlled phase 3 studies of adults and adolescents with vitiligo (TRuE-V1 [NCT04052425]; TRuE-V2 [NCT04057573]), ruxolitinib cream was statistically superior to vehicle at Week 24 in the primary and all key secondary efficacy endpoints, with continued improvement in outcomes through Week 52[3]

Patient Who Achieved F-VASI90 at Week 52 in the TRuE-V Studies



FDA, US Food and Drug Administration; F-VASI90, ≥90% improvement from baseline in facial Vitiligo Area Scoring Index; JAK, Janus kinase; TRuE-V, Topical Ruxolitinib Evaluation in Vitiligo trials.

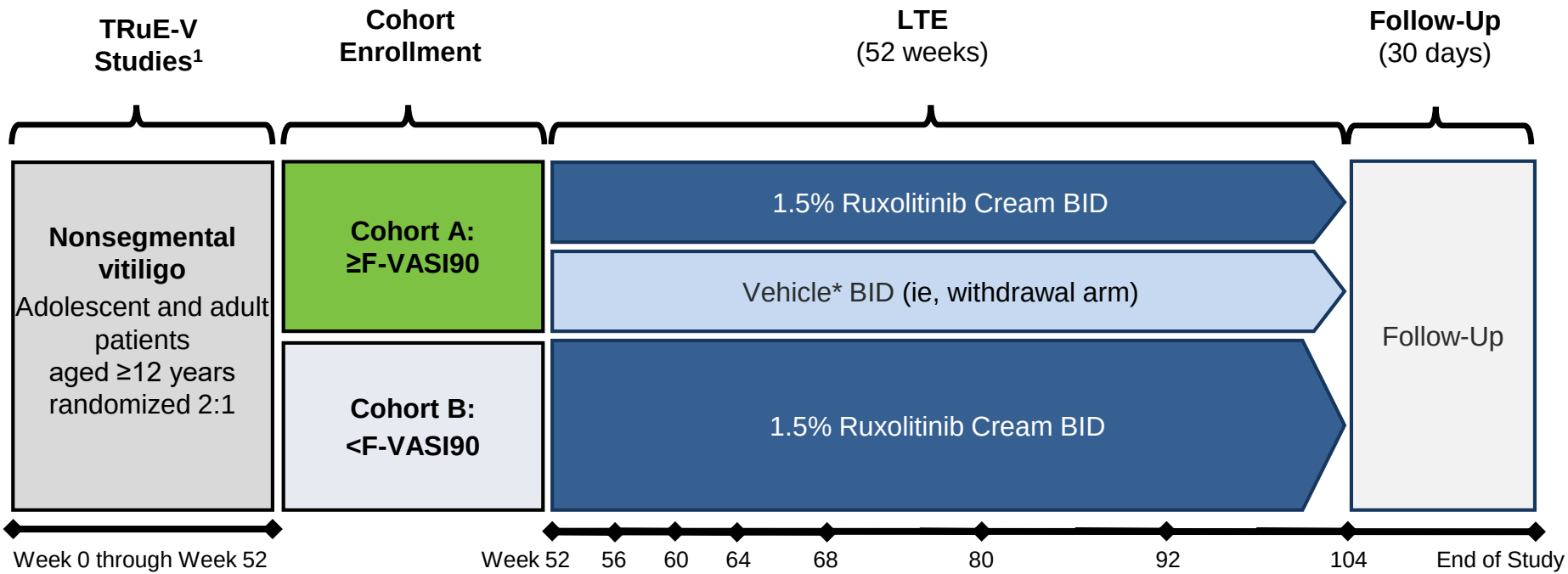
1. Rodrigues M, et al. *J Am Acad Dermatol*. 2017;77:1-13; 2. OPZELURA™ (ruxolitinib) cream). Full Prescribing Information. Incyte Corporation; July 2022; 3. Rosmarin D, et al. *N Engl J Med.* 2022;387:1445-1455.

Objectives

- To evaluate the time to relapse (a response of <F-VASI75) among adolescents and adults with nonsegmental vitiligo who achieved almost complete facial repigmentation (F-VASI90) in the TRuE-V parent studies and were randomized to vehicle (ruxolitinib cream withdrawal) in the TRuE-V long-term extension (LTE) study (NCT04530344)
- To evaluate the duration of F-VASI90 response maintenance in patients randomized to vehicle or ruxolitinib cream

F-VASI75, ≥75% improvement from baseline facial Vitiligo Area Scoring Index.

TRuE-V LTE Study Design



BID, twice daily.
* Patients randomized to vehicle who relapsed (ie, <F-VASI75) could apply 1.5% ruxolitinib cream BID rescue treatment for the remainder of the LTE period.
1. Rosmarin D, et al. *N Engl J Med.* 2022;387:1445-1455.

TRuE-V LTE Cohort A Study Endpoints

- **Primary Efficacy Endpoint**
  - Time to relapse, defined as <F-VASI75
- **Key Secondary Efficacy Endpoint**
  - Time to maintain ≥F-VASI90 response
- **Exploratory Efficacy Endpoints**
  - Time to regain ≥F-VASI90 response for patients who relapsed after entering the LTE
  - Time to regain ≥F-VASI75 response for patients who relapsed after entering the LTE
- **Safety and tolerability were also assessed**

Patient Demographics

Cohort A (≥F-VASI90 at Week 52)

- Baseline demographics and clinical characteristics were similar between treatment groups

Characteristic	Vehicle (n=58)*	Ruxolitinib Cream (n=58)*	Total (N=116)
Age, median (IQR), y	40.0 (32.0–47.0)	44.0 (35.0–55.0)	42.0 (33.5–50.0)
Female, n (%)	31 (53.4)	33 (56.9)	64 (55.2)
White, n (%)	42 (72.4)	48 (82.8)	90 (77.6)
Fitzpatrick skin type, n (%)			
I	0	0	0
II	15 (25.9)	22 (37.9)	37 (31.9)
III	18 (31.0)	17 (29.3)	35 (30.2)
IV	16 (27.6)	13 (22.4)	29 (25.0)
V	7 (12.1)	4 (6.9)	11 (9.5)
VI	2 (3.4)	2 (3.4)	4 (3.4)

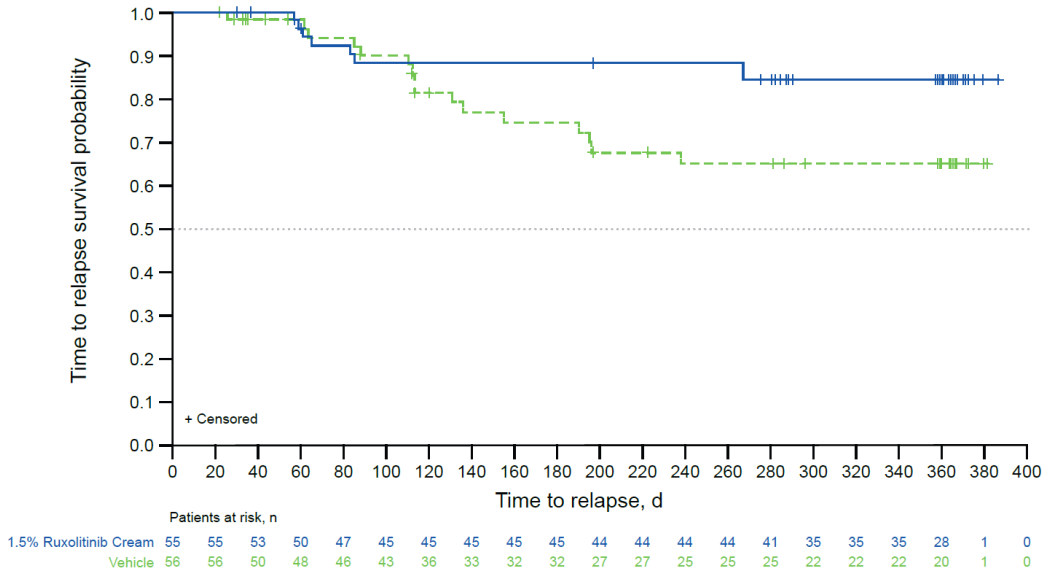
IQR, interquartile range; NB-UVB, narrow-band ultraviolet-B; PUVA, psoralen ultraviolet-A; T-BSA, total body surface area.
* One patient from the vehicle arm and 2 patients from the ruxolitinib cream arm were incorrectly assigned to this cohort and were not included in the efficacy analyses. Two other patients (1 in each arm) were also excluded from the efficacy analyses. † 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, PUVA photochemotherapy, and other phototherapy.

Characteristic	Vehicle (n=58)	Ruxolitinib Cream (n=58)	Total (N=116)
Baseline F-VASI, mean (SD)	0.87 (0.49)	0.99 (0.64)	0.93 (0.57)
Baseline T-VASI, mean (SD)	6.13 (2.10)	6.30 (2.02)	6.21 (2.06)
F-BSA,† mean (SD), %	0.92 (0.49)	1.09 (0.74)	1.01 (0.63)
T-BSA, mean (SD), %	6.84 (2.18)	6.86 (1.91)	6.85 (2.04)
Duration of disease, median (IQR), y	11.6 (3.2–19.3)	9.7 (4.3–17.4)	10.0 (4.2–17.5)
Diagnosed in childhood, n (%)	16 (27.6)	15 (25.9)	31 (26.7)
Disease stability,‡ n (%)			
Stable	42 (72.4)	40 (69.0)	82 (70.7)
Progressive	16 (27.6)	18 (31.0)	34 (29.3)
Other autoimmune disorders, n (%)	12 (20.7)	10 (17.2)	22 (19.0)
Previous therapy,§ n (%)	43 (74.1)	40 (69.0)	83 (71.6)
Topical calcineurin inhibitor	26 (44.8)	22 (37.9)	48 (41.4)
Topical corticosteroid	21 (36.2)	17 (29.3)	38 (32.8)
Phototherapy¶	24 (41.4)	20 (34.5)	44 (37.9)

Time to Relapse

Cohort A (≥F-VASI90 at Week 52)

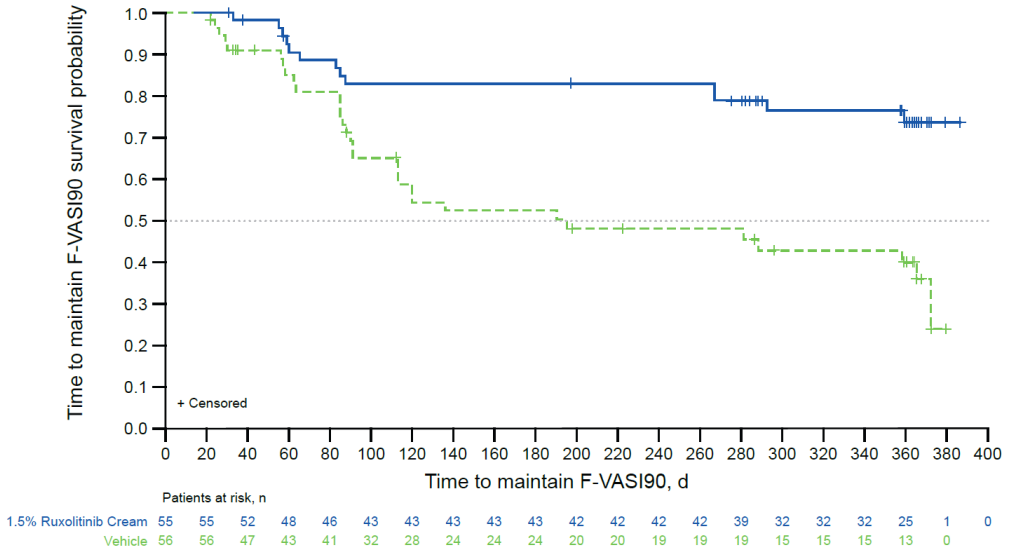
- ≥F-VASI75 response was maintained for 1 year among 39.3% of patients in the withdrawal arm
- Relapse (ie, <F-VASI75) occurred in 28.6% of patients in the withdrawal arm
  - Half of the relapse events occurred within 4 months, although median time to relapse was not estimable
  - 23.2% of patients in the withdrawal arm discontinued treatment prior to 1 year



Maintenance of ≥F-VASI90 Response

Cohort A (≥F-VASI90 at Week 52)

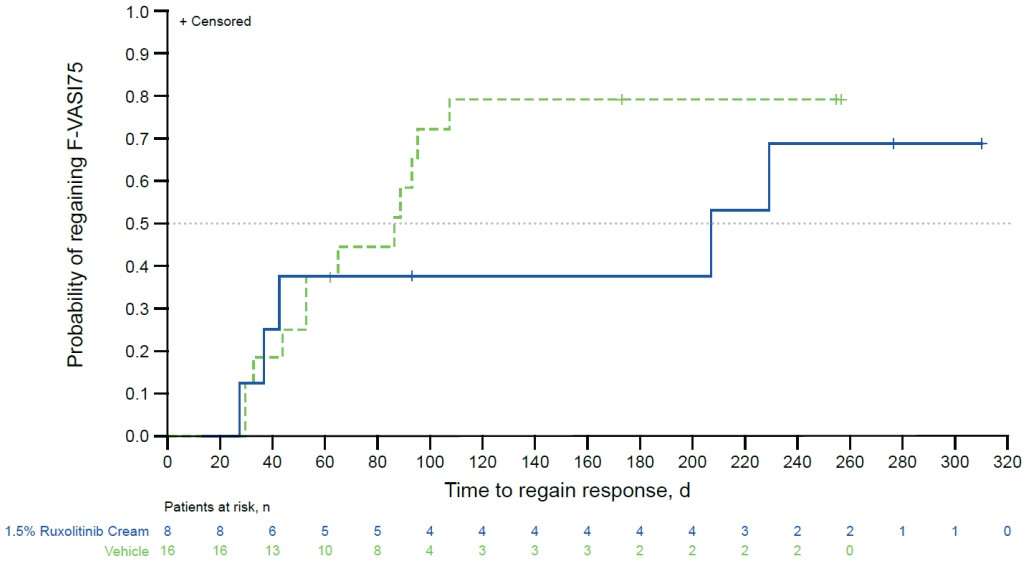
- ≥F-VASI90 response was maintained for 1 year in 21.4% of patients applying vehicle cream and 61.8% of patients applying ruxolitinib cream
  - 17.9% of patients applying vehicle and 10.9% of patients applying ruxolitinib cream discontinued treatment prior to 1 year
  - Median duration of ≥F-VASI90 response was 195.0 days for vehicle and not estimable for ruxolitinib cream



Time to Regain ≥F-VASI75 Response

Cohort A (≥F-VASI90 at Week 52)

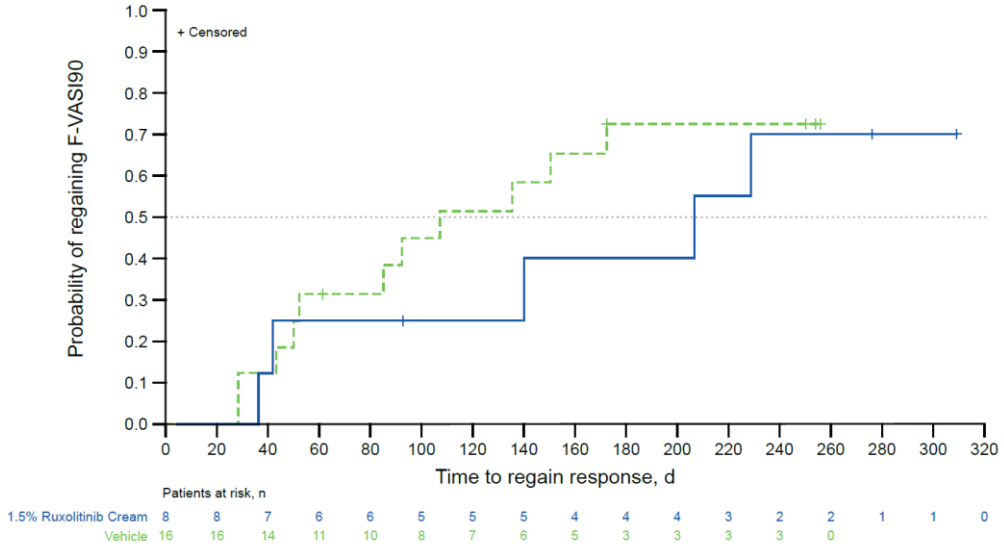
- Upon restarting treatment with ruxolitinib cream, ≥F-VASI75 response was regained in a median of 12 weeks
  - 12/16 (75.0%) of patients who relapsed during treatment withdrawal regained ≥F-VASI75 response



Time to Regain ≥F-VASI90 Response

Cohort A (≥F-VASI90 at Week 52)

- Upon restarting treatment with ruxolitinib cream, ≥F-VASI90 response was regained in a median of 15 weeks
  - 11/16 (68.8%) of patients who relapsed during treatment withdrawal regained ≥F-VASI90



Safety

TEAEs in Cohort A (≥F-VASI90 at Week 52) Through Week 104

- Ruxolitinib cream was well tolerated
- There were no cases of application site acne or application site pruritus among patients who applied ruxolitinib cream in Cohort A
- Treatment-related TEAEs (all mild or moderate; none serious) among patients who applied ruxolitinib cream were application site dermatitis (n=1), application site rash (n=1), and hyperlipidemia (n=1)

Characteristic, n (%)	Vehicle (n=58)	Ruxolitinib Cream* (n=81)
Patients with TEAE	21 (36.2)	35 (43.2)
Most common TEAEs†		
COVID-19	6 (10.3)	10 (12.3)
Upper respiratory tract infection	0	4 (4.9)
Application site dermatitis	0	3 (3.7)
Headache	2 (3.4)	2 (2.5)
Nasopharyngitis	2 (3.4)	2 (2.5)
Toothache	2 (3.4)	1 (1.2)
Bronchitis	2 (3.4)	0
Cough	2 (3.4)	0
Muscle strain	2 (3.4)	0
Skin papilloma	2 (3.4)	0
Patients with treatment-related TEAE	3 (5.2)	3 (3.7)
Patients with application site reactions	2 (3.4)	5 (6.2)
Patients with serious TEAE‡	0	1 (1.2)‡
Patients with TEAE leading to discontinuation	0	0
Patients with TEAE leading to dose reduction	0	1 (1.2)

TEAE, treatment-emergent adverse event.
* Including 23 patients restarted active treatment upon relapse
† Occurring in ≥3% of patients in any treatment group.
‡ Uterine leiomyoma was considered by the investigators to be unrelated to treatment.

Conclusions

- Many patients who achieved a high level of facial repigmentation (≥F-VASI90) in TRuE-V1/TRuE-V2 were able to maintain durable response for 1 year after discontinuing ruxolitinib cream treatment in the TRuE-V LTE study
  - 39.3% in the withdrawal arm maintained ≥F-VASI75 response
  - 21.4% in the withdrawal arm maintained ≥F-VASI90 response
- Among patients who relapsed (<F-VASI75) upon stopping active treatment, response was regained upon reinitiating ruxolitinib cream treatment
- Ruxolitinib cream was well tolerated, with no serious treatment-related AEs reported through 104 weeks