Ruxolitinib Cream: Phase 2 Data in Vitiligo

June 17, 2019

Speakers on Today's Webcast

- **Hervé Hoppenot**
  Chief Executive Officer
  Incyte

- **John E. Harris, MD, PhD**
  Associate Professor and Vice Chair Department of Dermatology
  Director Vitiligo Clinic and Research Center
  University of Massachusetts Medical School

- **Jim Lee, MD, PhD**
  Group Vice President, Inflammation and Autoimmunity
  Incyte

Forward-looking Statements

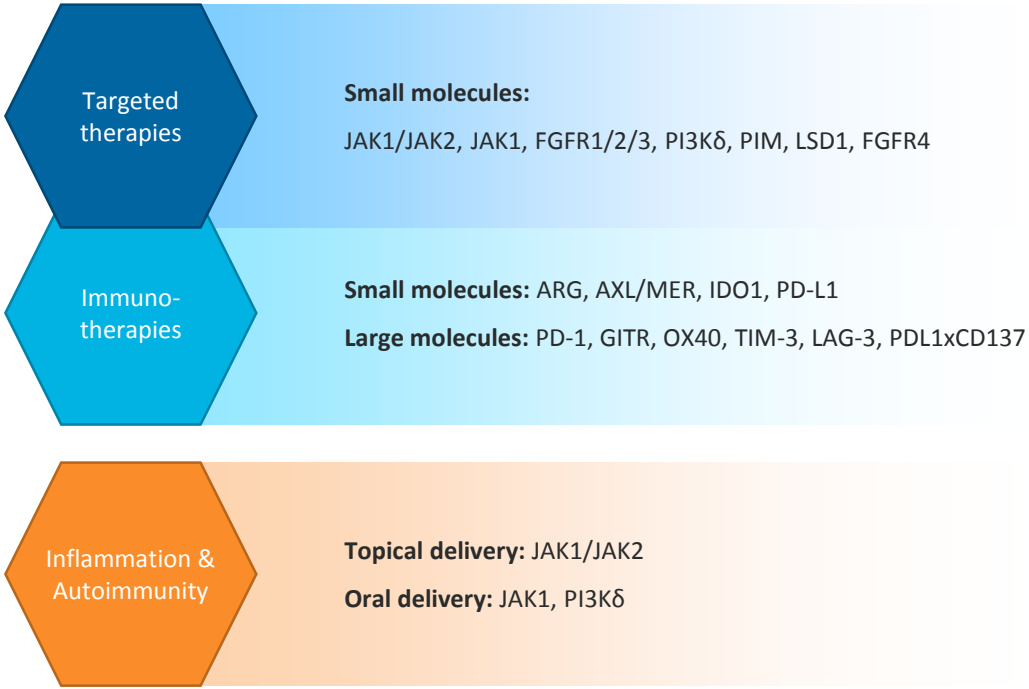
Except for the historical information set forth herein, the matters set forth in this presentation contain predictions, estimates and other forward-looking statements, including without limitation statements regarding: expectations regarding ruxolitinib cream trial results and implications of those results; expectations to commence and the expected timing of commencement of Phase 3 clinical trials for ruxolitinib cream for vitiligo; our views of the commercial opportunities, including our views of market size and market opportunities, for our drug product candidates, including ruxolitinib cream for vitiligo; and our expectations regarding further clinical development for ruxolitinib cream and the timing of clinical trial results.

These forward-looking statements are based on our current expectations and are subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: unanticipated delays; further research and development and the results of clinical trials possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials; determinations made by the FDA; assuming approval of ruxolitinib cream for vitiligo or other indications, the acceptance of ruxolitinib cream in the marketplace and the effects of market competition; manufacturing, sales and marketing requirements; and other risks detailed from time to time in our reports filed with the Securities and Exchange Commission, including our quarterly report on Form 10-Q for the quarter ended March 31, 2019. We disclaim any intent or obligation to update these forward-looking statements.

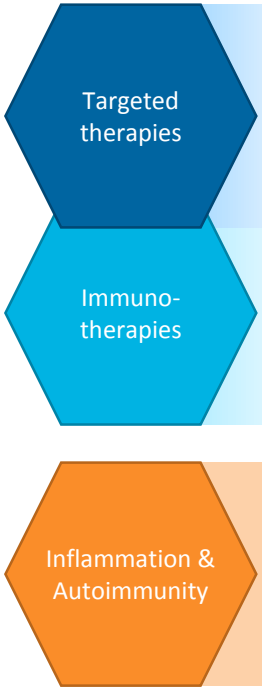
Inflammation and Autoimmunity Development

Hervé Hoppenot

Incyte has Three Groups within Clinical Development



Capitalizing on our Expertise in Inflammation and Autoimmunity



Ruxolitinib cream

Atopic dermatitis

- ✓ Phase 2 data presented at EADV 2018
- ✓ Phase 3 underway; results expected 2020

Vitiligo

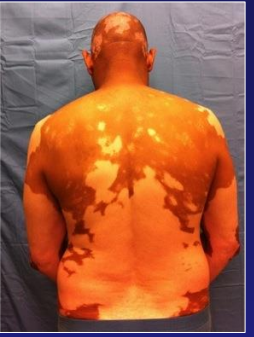
- ✓ Proof-of-concept achieved; Phase 3 in preparation

Oral JAK1

- ➢ Itacitinib: PoC trial in ulcerative colitis
- ➢ INCB54707: PoC trial in moderate to severe hidradenitis suppurativa

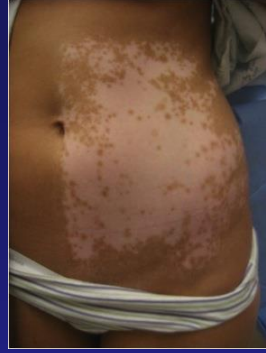
Oral PI3Kδ

- ➢ Parsaclisib: PoC trial in autoimmune hemolytic anemia
- ➢ Parsaclisib: PoC trial in Sjögren's syndrome



VITILIGO
CLINIC & RESEARCH CENTER

Department of Dermatology
University of Massachusetts
Medical School

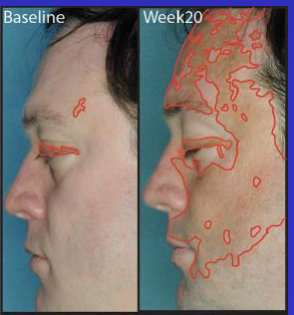


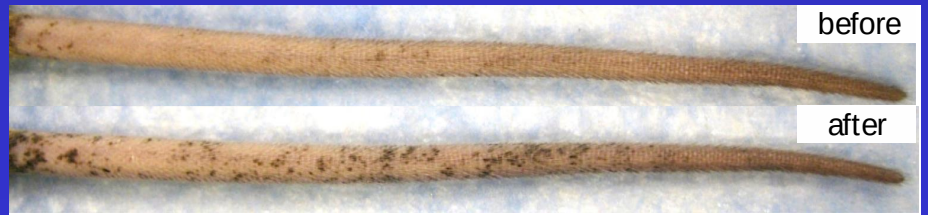
Targeting JAK signaling as a novel treatment for vitiligo

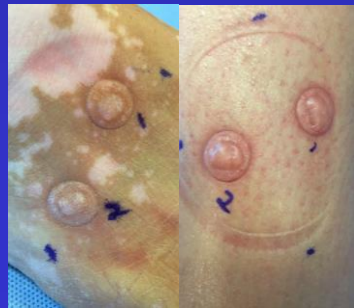
Website:
Umassmed.edu/vitiligo

Twitter:
@HarrisVitiligo

John E. Harris, MD, PhD
Associate Professor
University of Massachusetts Medical School

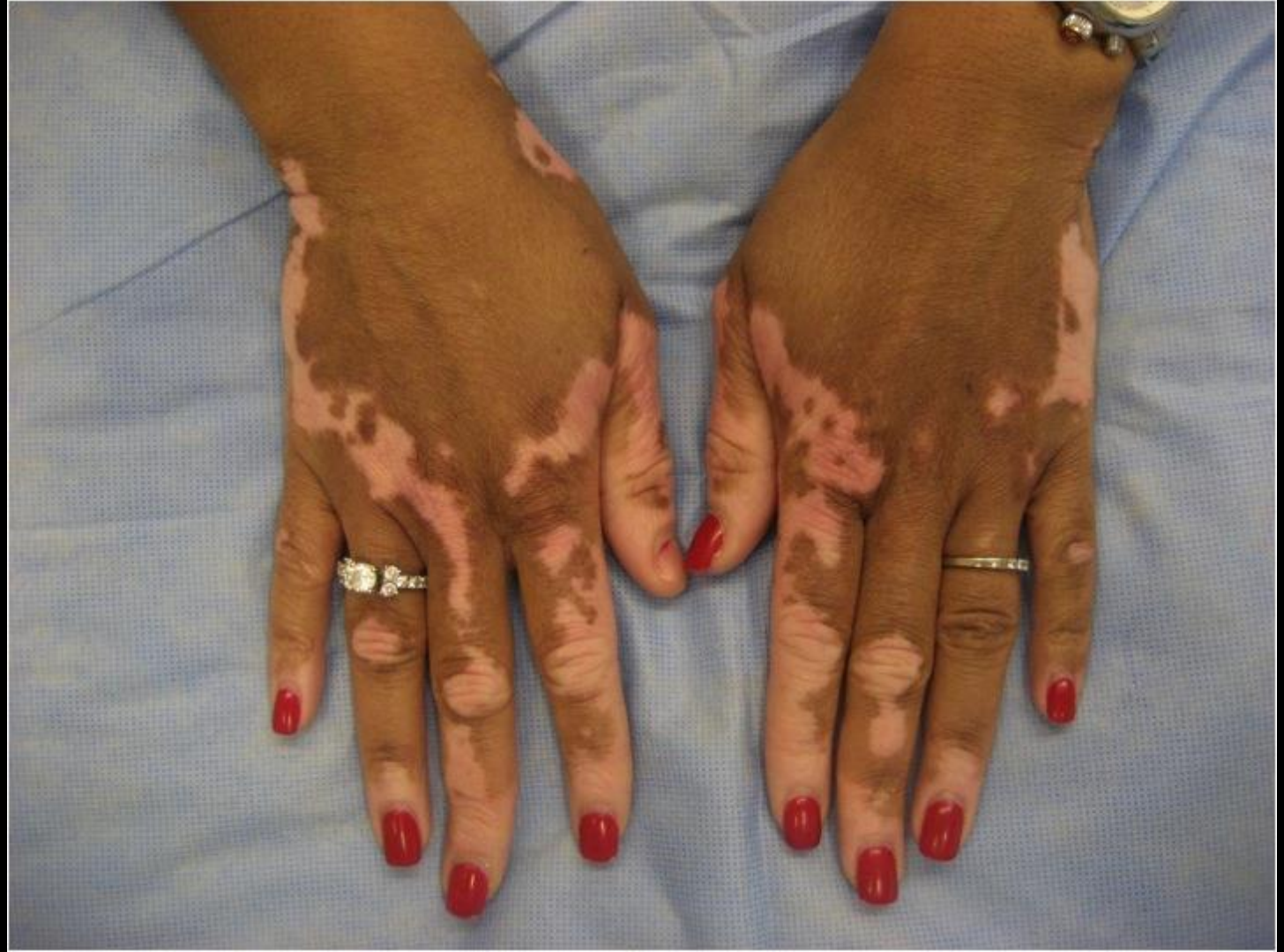


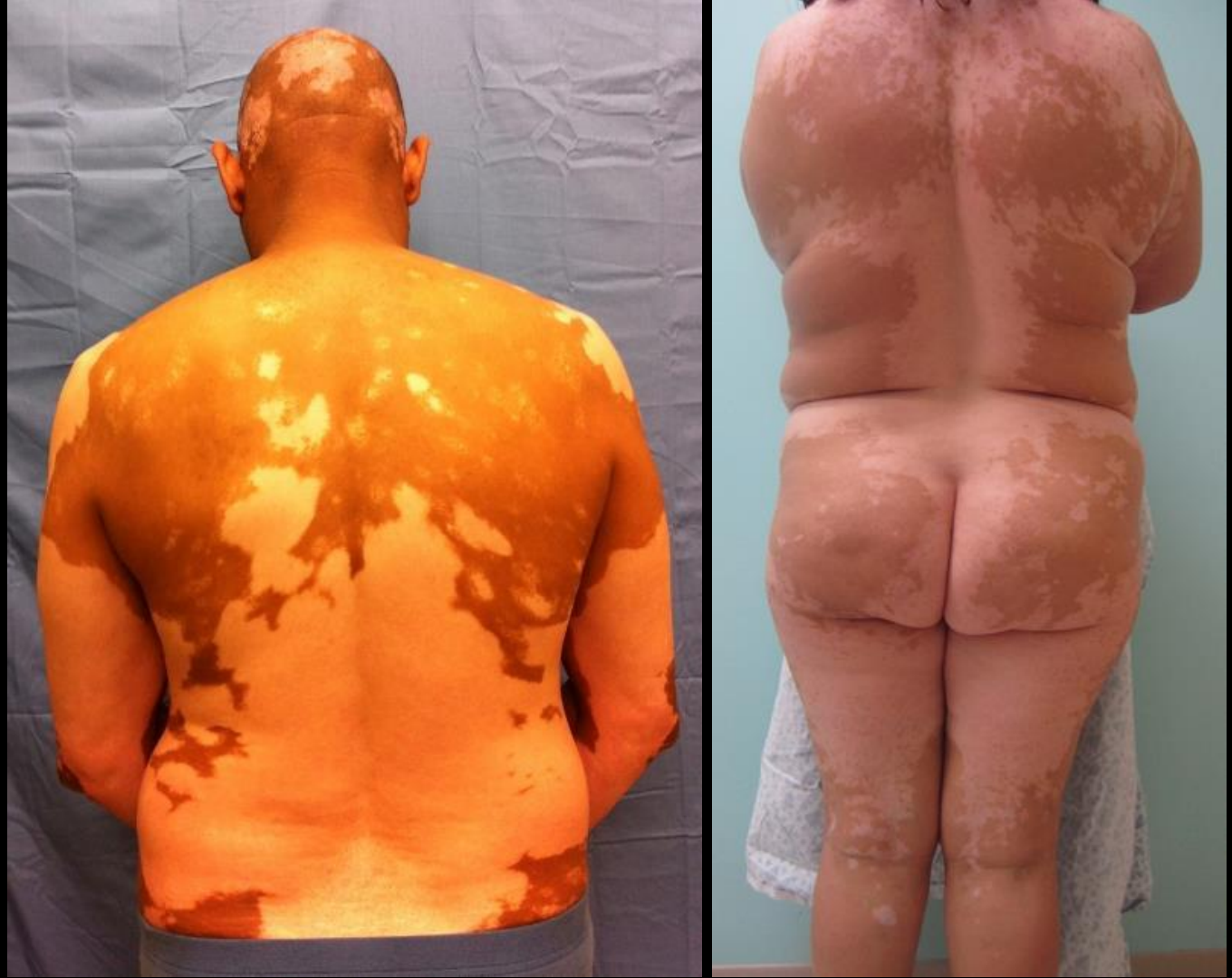


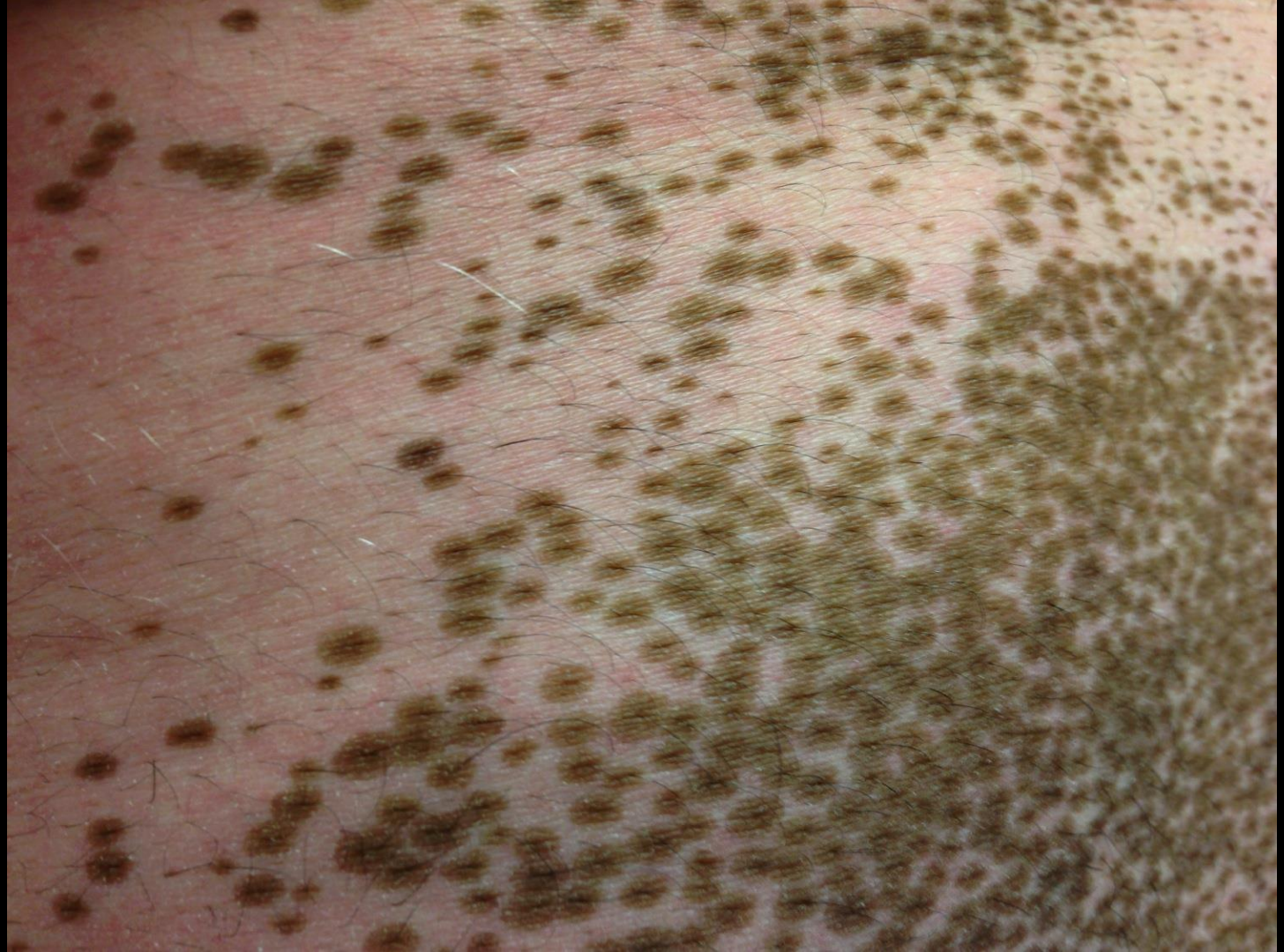


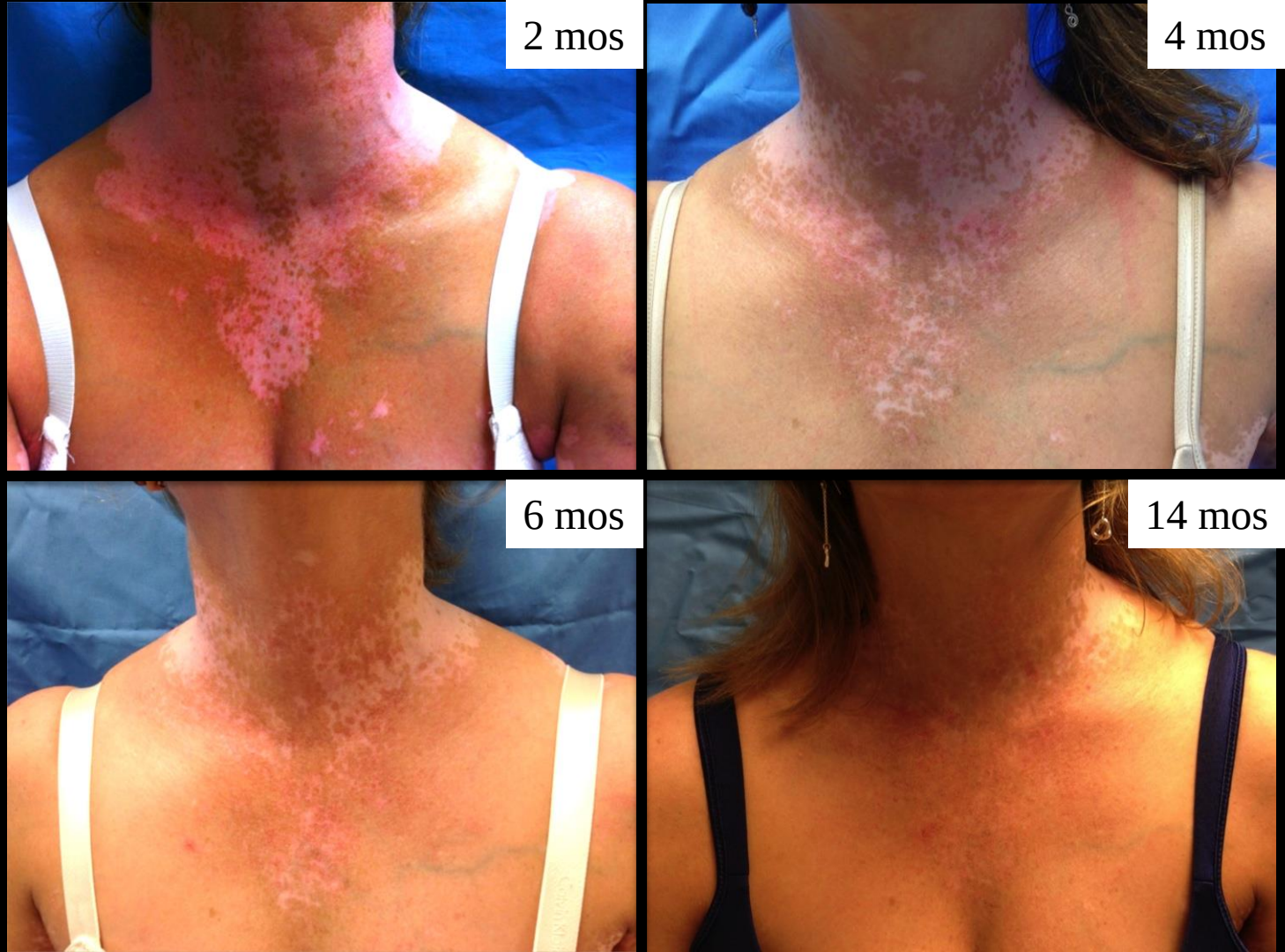
Vitiligo

- 1-2% incidence
- 3-6.5 million (US)
- 75-150 million (world)
- 50% onset before age 20
- Disease associations
  - Type 1 diabetes
  - Lupus
  - Hashimoto thyroiditis
  - Pernicious anemia
  - Addison’s disease








2 mos
4 mos
6 mos
14 mos

Vitiligo is not a cosmetic disease

J Am Acad Dermatol
November 2015

Khaled Ezzedine, MD, PhD,[a] Vaneeta Sheth, MD,[b] Michelle Rodrigues, MBBS (Hons), FACD,[c] Viktoria Eleftheriadou, MD, PhD,[d] John E. Harris, MD, PhD,[e] Iltefat H. Hamzavi, MD,[f] and Amit G. Pandya, MD,[g] on behalf of the Vitiligo Working Group
Bordeaux, France; Boston and Worcester, Massachusetts; Melbourne, Australia; Nottingham, United Kingdom; Detroit, Michigan; and Dallas, Texas

The burden of vitiligo: Patient characteristics associated with quality of life

May W. Linthorst Homan, MD,[a,b] Phyllis I. Spuls, MD, PhD,[b] John de Korte, MA, PhD,[b] Jan D. Bos, MD, PhD,[b] Mirjam A. Sprangers, MA, PhD,[c] and J. P. Wietze van der Veen, MD, PhD[a,b]
Amsterdam, The Netherlands

Background: Vitiligo is commonly regarded as a harmless cosmetic skin problem in Western societies, and the importance of treating patients with vitiligo is often underestimated.

Objective: We sought to determine the clinical and sociodemographic variables that adversely affect the quality of life in adult patients with generalized vitiligo so that these variables can be considered in the treatment and care.

Methods: A total of 245 adult patients with generalized vitiligo completed two quality-of-life questionnaires (the Medical Outcomes Study 36-Item Short-Form General Health Survey and the Skindex-29). Physicians assessed sociodemographic and clinical characteristics of these patients.

Results: Dark skin type, vitiligo located on the chest, and treatment in the past appeared to have an adverse impact on the psychosocial domains of quality of life. Moreover, itch was reported by 20% of the patients in this study.

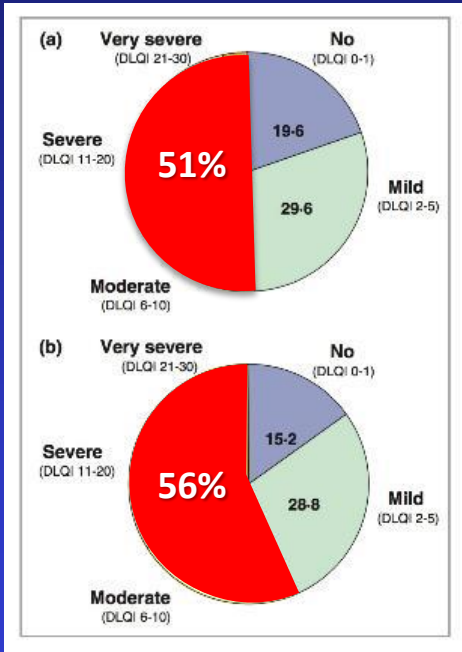
Limitations: Psychiatric comorbidity was not evaluated in the analyses.

Conclusion: Generalized vitiligo is a serious skin disorder with an adverse impact on the emotional state, comparable with that of other major skin diseases. (J Am Acad Dermatol 2009;61:411-20.)

Dermatology Life Quality Index (DLQI)

Vitiligo

Psoriasis



Radtke, et al. *BJD* 2009

Vitiligo – unmet medical need

- **Poor Quality of Life**: Similar to psoriasis/eczema
- **Willingness to pay for a cure**: Greater than eczema
- No FDA-approved medical treatments!
- Current topicals used off-label have significant side effects

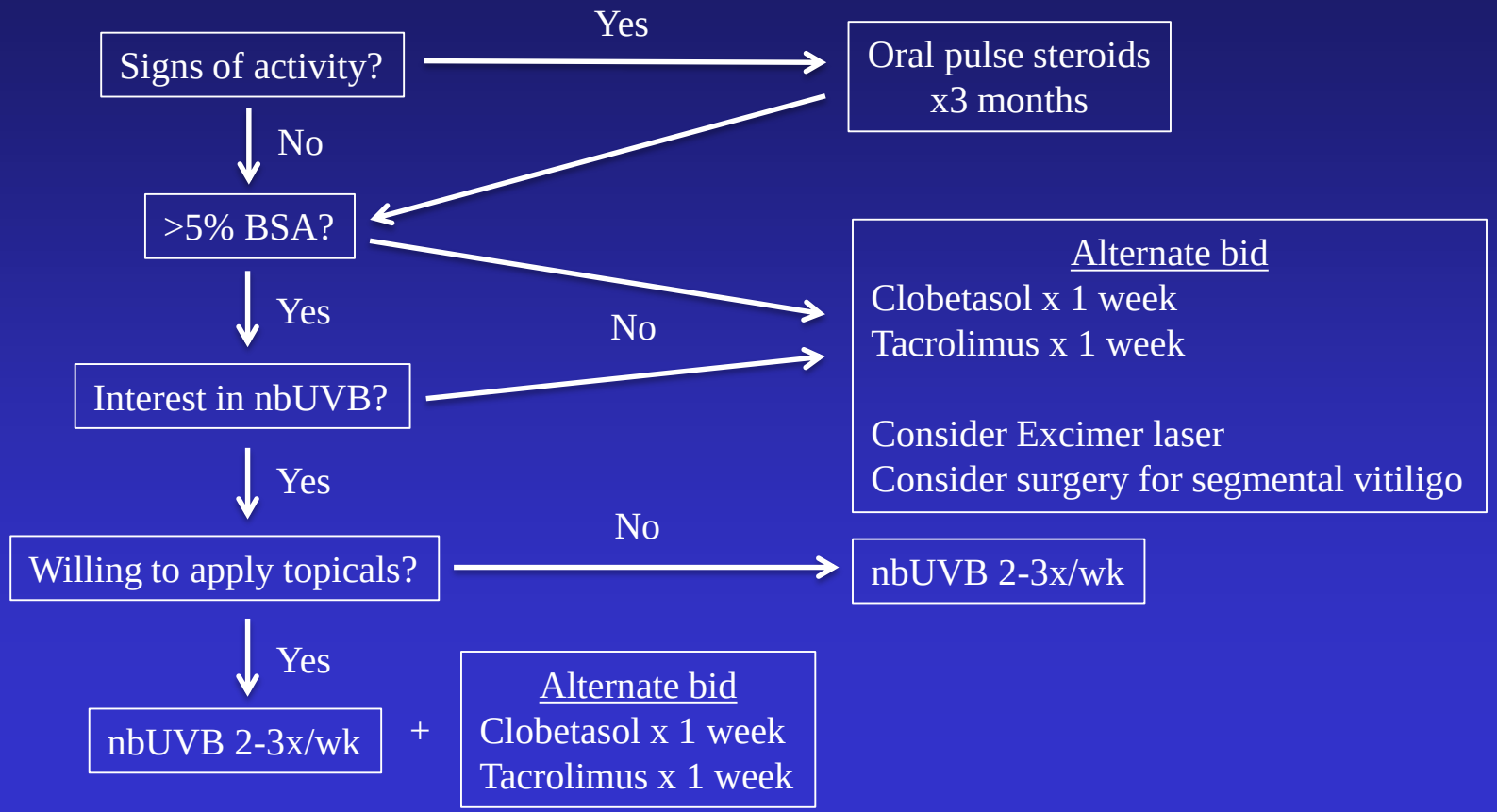
Current vitiligo treatments

Segmented and Incomplete

- Topical steroids (striae, atrophy)
- Topical calcineurin inhibitors (burning sensation, hyperpigmentation)
- nbUVB phototherapy (time-consuming-3x/wk >1yr, moderately effective)
- Surgical transplantation (for stable disease only, <5% are candidates)
- Depigmentation (for very severe disease only, <1%, worsens vitiligo)

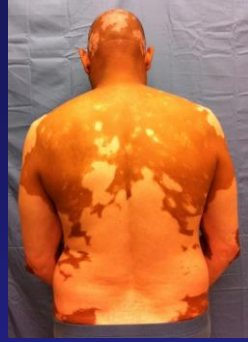
Current treatments have significant limitations and thus have only penetrated a small part of market, likely <20%

My (simple) Treatment Algorithm



Vitiligo – “Severity”

Data from 3 vitiligo specialty clinics



58%	<5% BSA
25%	5-10% BSA
11%	>10-25% BSA
5%	>25-50% BSA
2%	>50% BSA

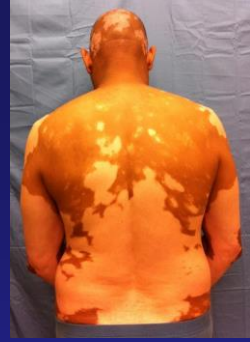
Worcester

Dallas

Paris

Vitiligo – "Severity"

Decision Tree



Signs of activity? —Yes→ Systemic + Topical 20%

↓ No

More than 5% BSA? —Yes→ Systemic + Topical 32%

↓ No

Topical 48%

	US	World
Topical only	1.6M	37M
Topical + Systemic	1.6M	37M

Phototherapy, a current vitiligo treatment, is reimbursed at a high level

$24,000 per year

$42,000 per year

Vitiligo – The Opportunity

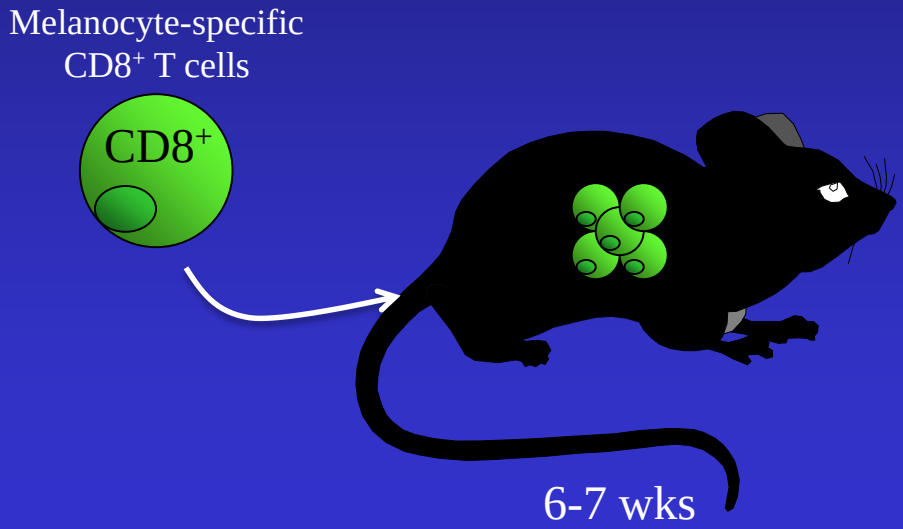
- Vitiligo analogous to psoriasis market 30 years ago: topicals, phototherapy, oral immunosuppressant (methotrexate)
- Psoriasis (7.4M in US/125M worldwide) – now with effective therapies, $8B annual market, estimated to be $21B by 2022; mostly shared by 10-12 drugs
- Vitiligo (3-6M in US/75-150M world) with no effective, FDA-approved medication

ORIGINAL ARTICLE

A Mouse Model of Vitiligo with Focused Epidermal Depigmentation Requires IFN-γ for Autoreactive CD8$^+$ T-Cell Accumulation in the Skin

John E. Harris[1], Tajie H. Harris[2], Wolfgang Weninger[3,4], E. John Wherry[5], Christopher A. Hunter[2] and Laurence A. Turka[6]

Journal of Investigative Dermatology advance online publication, 2 February 2012; doi:10.1038/jid.2011.463



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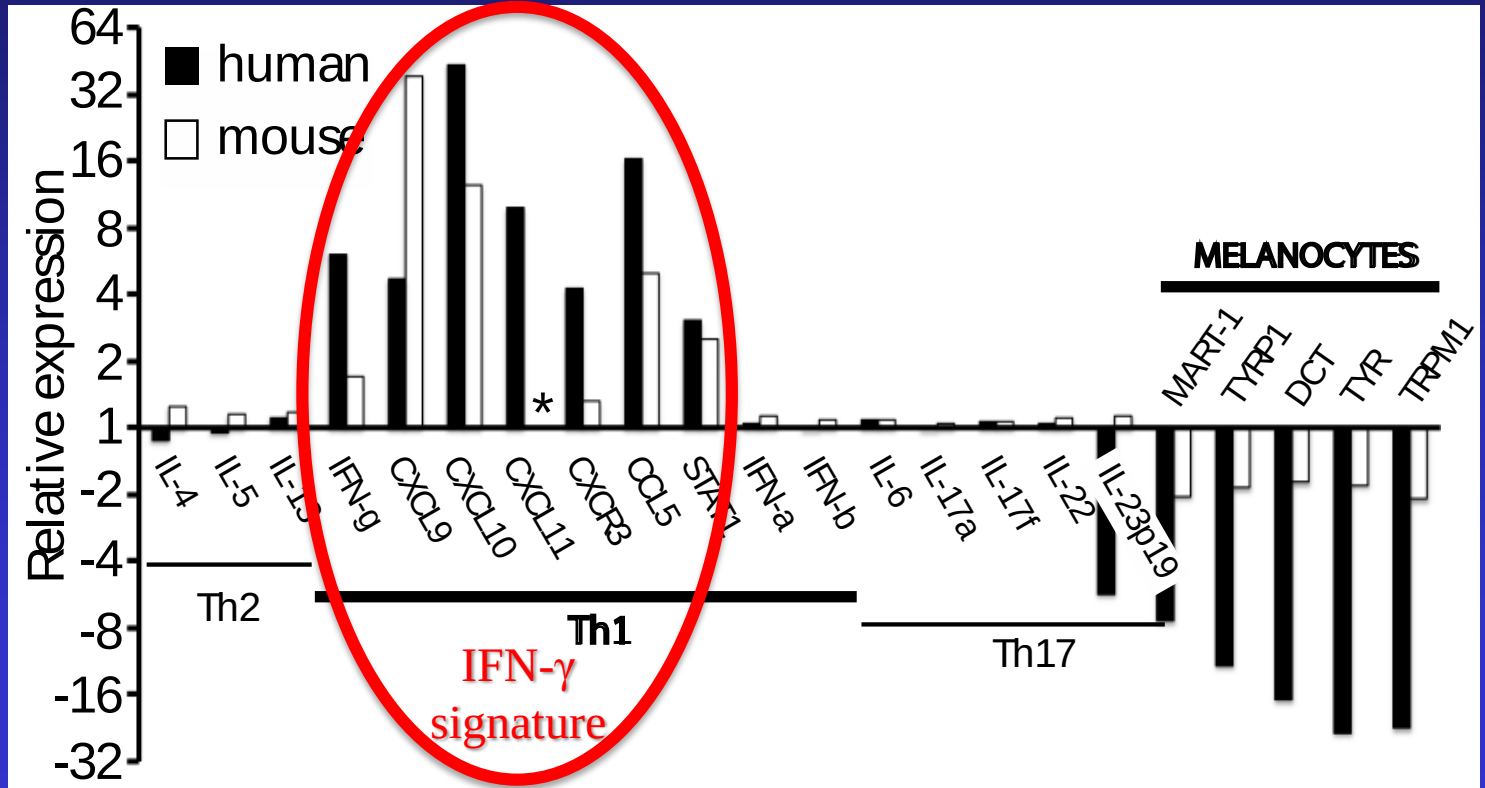
- Clinical and histological appearance same as human
- Gene expression in mouse and human identical
- Only mouse model of skin depigmentation (not hair)
- Only reversible model of vitiligo
- Ongoing studies parallel observations in mouse and human
- Has predicted therapies now in clinical trials (JAK)
- Many companies using this model for preclinical testing

Harris, JID 2012	Richmond, JID 2017a	Rodrigues, JAAD 2017
Rashighi, STM 2014	Richmond, JID 2017b	Frisoli, JACI 2017
Harris, JAAD 2016	Strassner, JAAD 2017	Richmond, STM 2018

Gene expression is similar in mouse and human vitiligo



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Science Translational Medicine
AAAS

RESEARCH ARTICLE

VITILIGO

CXCL10 Is Critical for the Progression and Maintenance of Depigmentation in a Mouse Model of Vitiligo

Mehdi Rashighi,[1] Priti Agarwal,[1] Jillian M. Richmond,[1] Tajie H. Harris,[2]* Karen Dresser,[3] Ming-Wan Su,[4] Youwen Zhou,[4] April Deng,[3] Christopher A. Hunter,[2] Andrew D. Luster,[5] John E. Harris[1†]

www.ScienceTranslationalMedicine.org 12 February 2014 Vol 6 Issue 223 223ra23

Science Translational Medicine

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RESEARCH ARTICLE

VITILIGO

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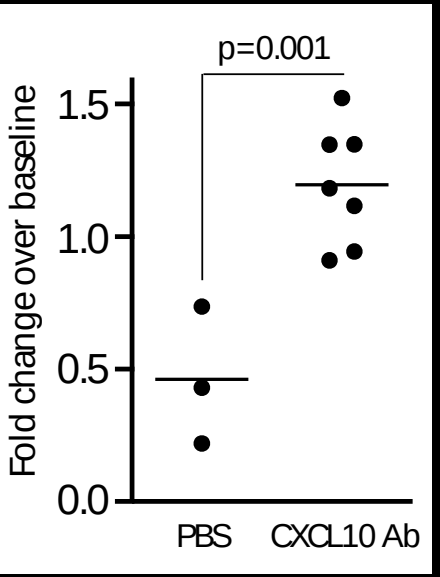
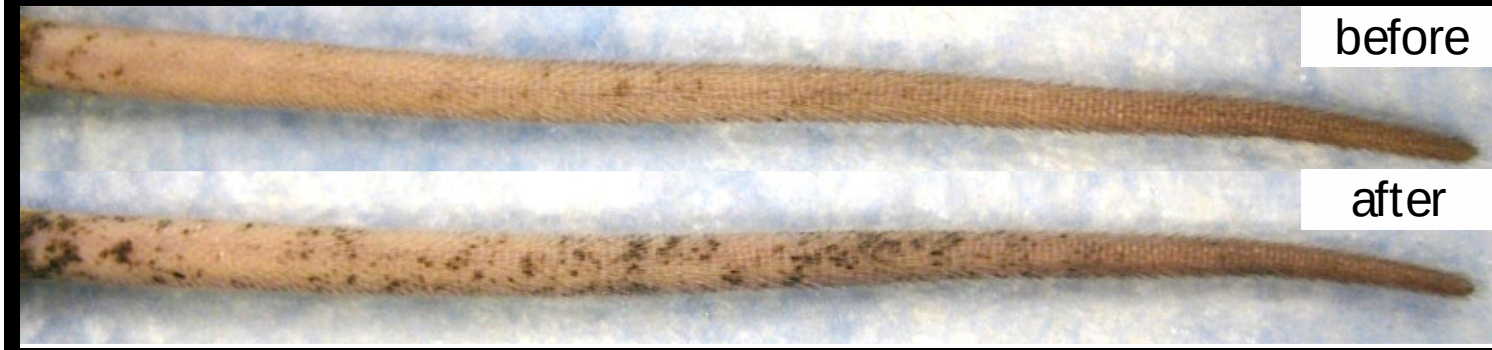
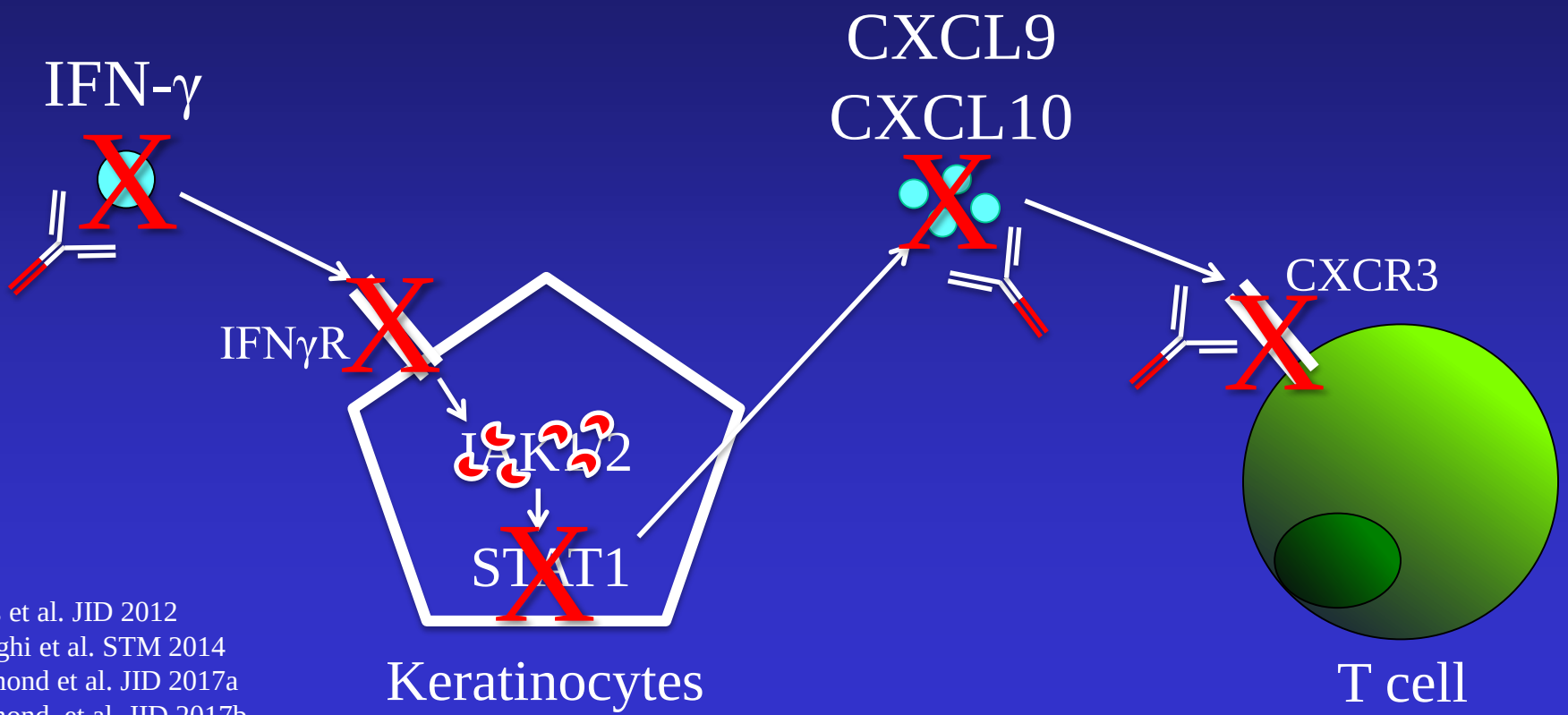


CXCL10 antibody reverses vitiligo



Emerging Treatments



Harris et al. JID 2012
Rashighi et al. STM 2014
Richmond et al. JID 2017a
Richmond, et al. JID 2017b

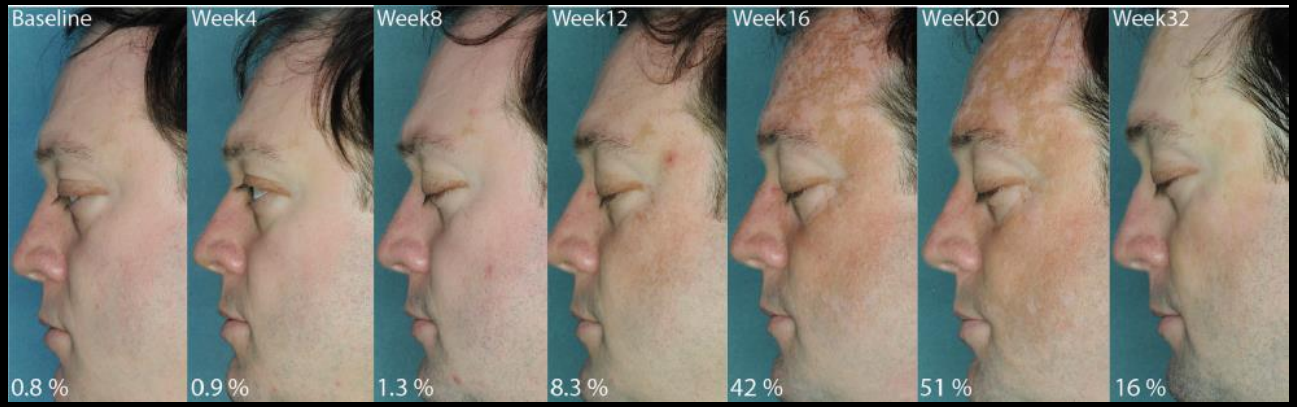
Rapid skin repigmentation on oral ruxolitinib in a patient with coexistent vitiligo and alopecia areata (AA)

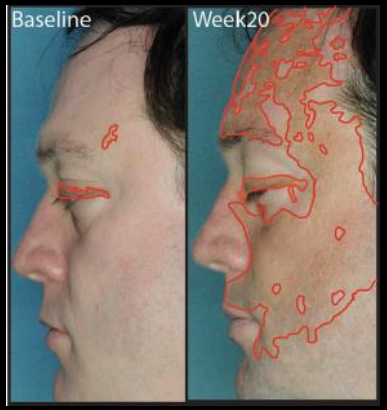
RESEARCH LETTER

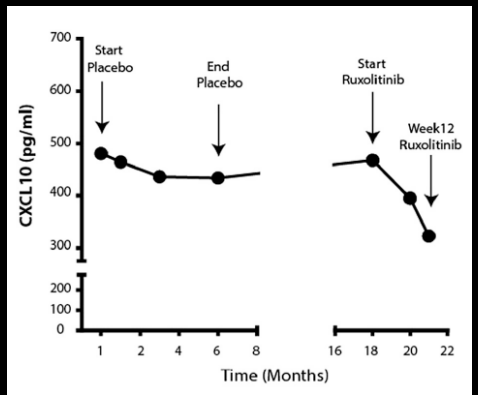
John E. Harris, MD, PhD,[a] Mehdi Rashighi, MD,[a] Nhan Nguyen, MD,[b] Ali Jabbari, MD, PhD,[b] Grace Ulerio, BA,[b] Raphael Clynes, MD, PhD,[b] Angela M. Christiano, PhD,[b,c] and Julian Mackay-Wiggan, MD, MS[b]

370 FEBRUARY 2016

J AM ACAD DERMATOL
VOLUME 74, NUMBER 2







Ongoing Trials:

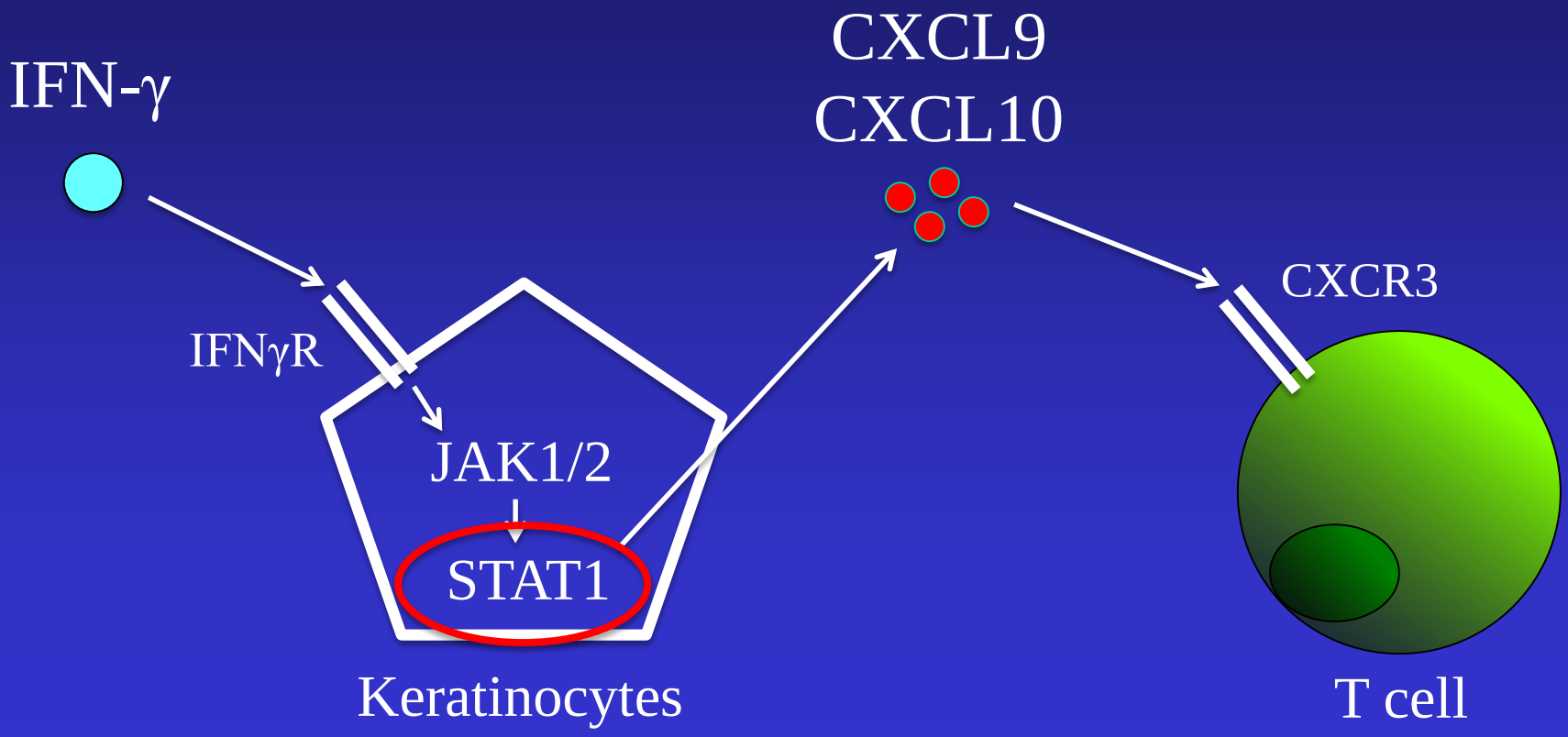
Aclaris

Incyte

Pfizer

Where does JAK signaling matter?

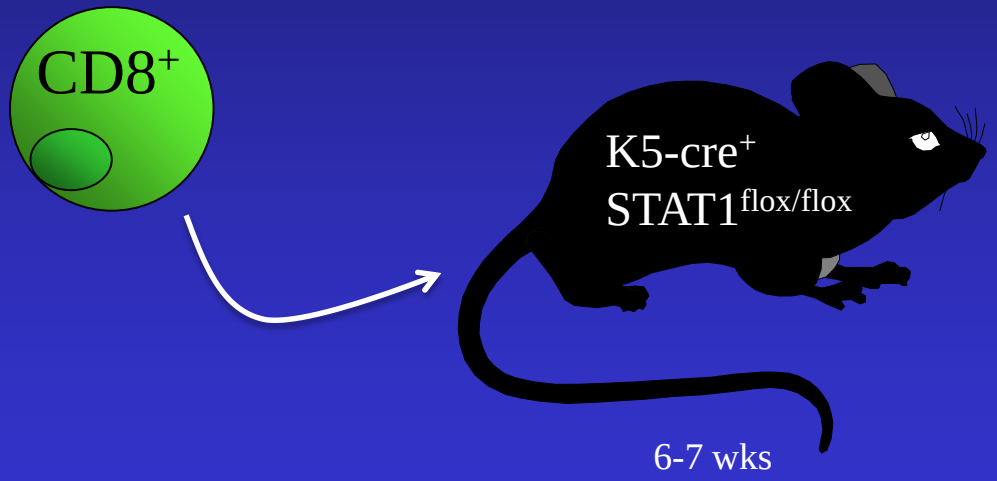
K5-cre/STAT1^{flox}



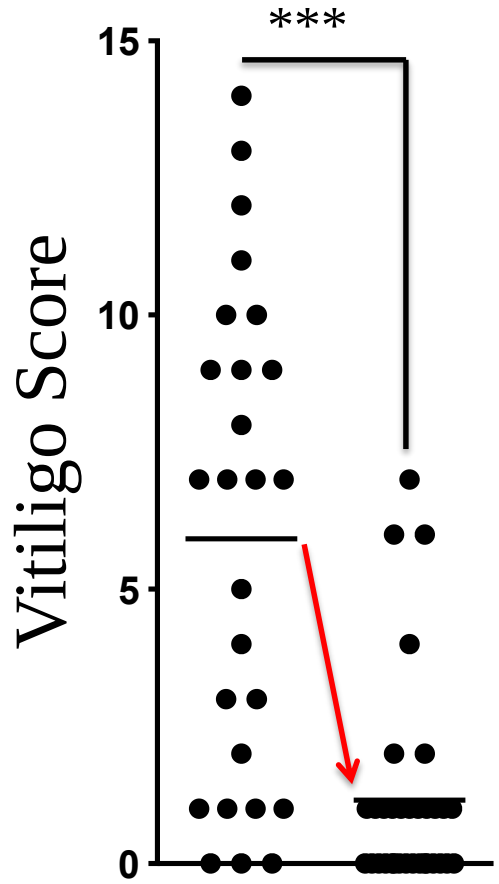
Is there a functional role for keratinocytes?

K5-cre/STAT1^{flox}

Melanocyte-specific
CD8$^+$ T cells

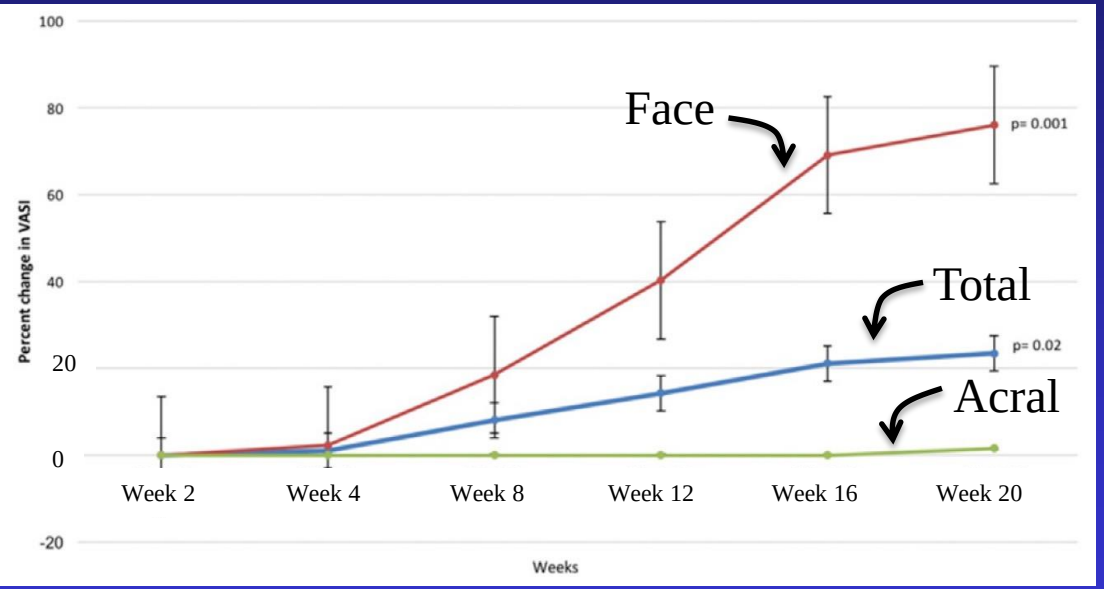


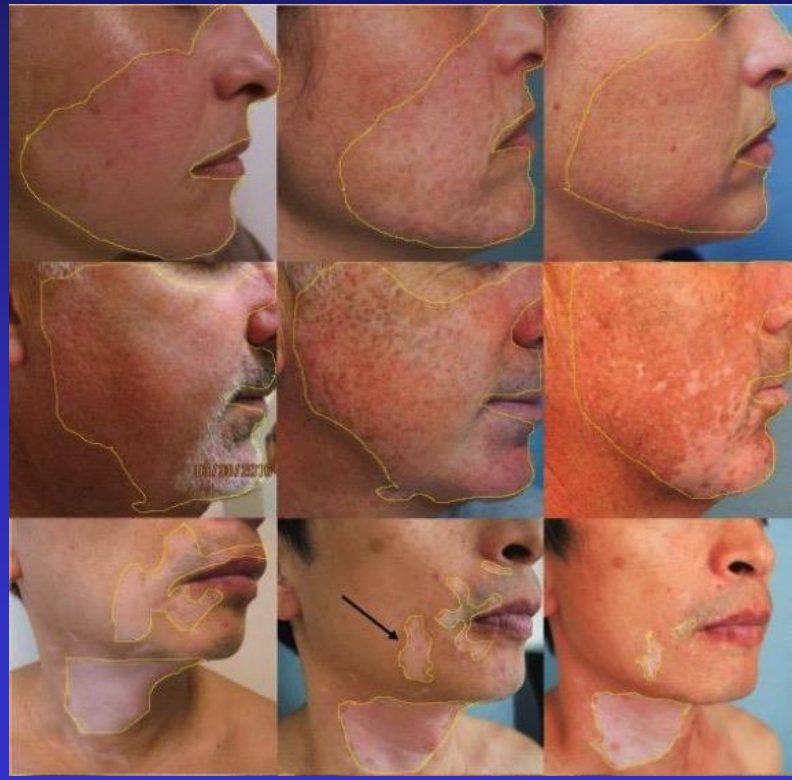
KERATINOCYTES



Richmond, et al. JID 2017

Topical ruxolitinib for vitiligo





Rothstein R, et al. JAAD 2017

Ruxolitinib cream: Phase 2 data in vitiligo

Jim Lee, MD, PhD

Presented at the 24th World Congress of Dermatology
June 10–15, 2019; Milan, Italy

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

David Rosmarin, MD,[1] Amit G. Pandya, MD,[2] Mark Lebwohl, MD,[3] Pearl Grimes, MD,[4] Iltefat Hamzavi, MD,[5] Alice B. Gottlieb, MD, PhD,[6] Kathleen Butler, MD,[7] Fiona Kuo, PhD,[7] Michael D. Howell, PhD,[7] Kang Sun, PhD,[7] John E. Harris, MD, PhD[8]

[1]Tufts Medical Center, Boston, MA, USA; [2]University of Southwestern Medical Center, Dallas, TX, USA; [3]Mount Sinai Hospital, New York, NY, USA; [4]The Vitiligo & Pigmentation Institute of Southern California, Los Angeles, CA, USA; [5]Henry Ford Medical Center, Detroit, MI, USA; [6]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [7]Incyte Corporation, Wilmington, DE, USA; [8]University of Massachusetts Medical School, Worcester, MA, USA

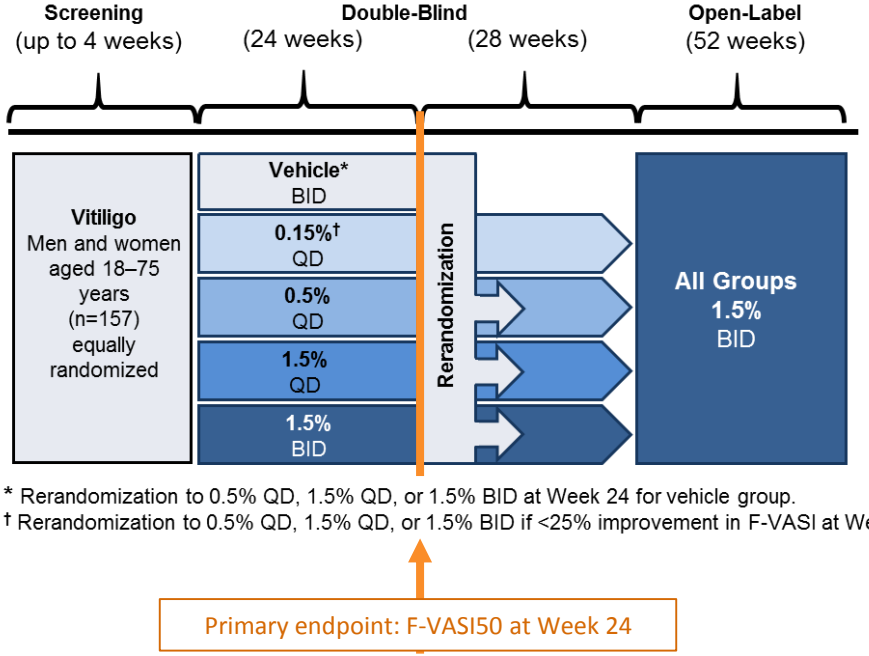
Eligibility Criteria and Study Design

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



BID, twice daily; BSA, body surface area; F-VASI, facial Vitiligo Area Scoring Index; QD, once daily.

Patient Demographics and Clinical Characteristics

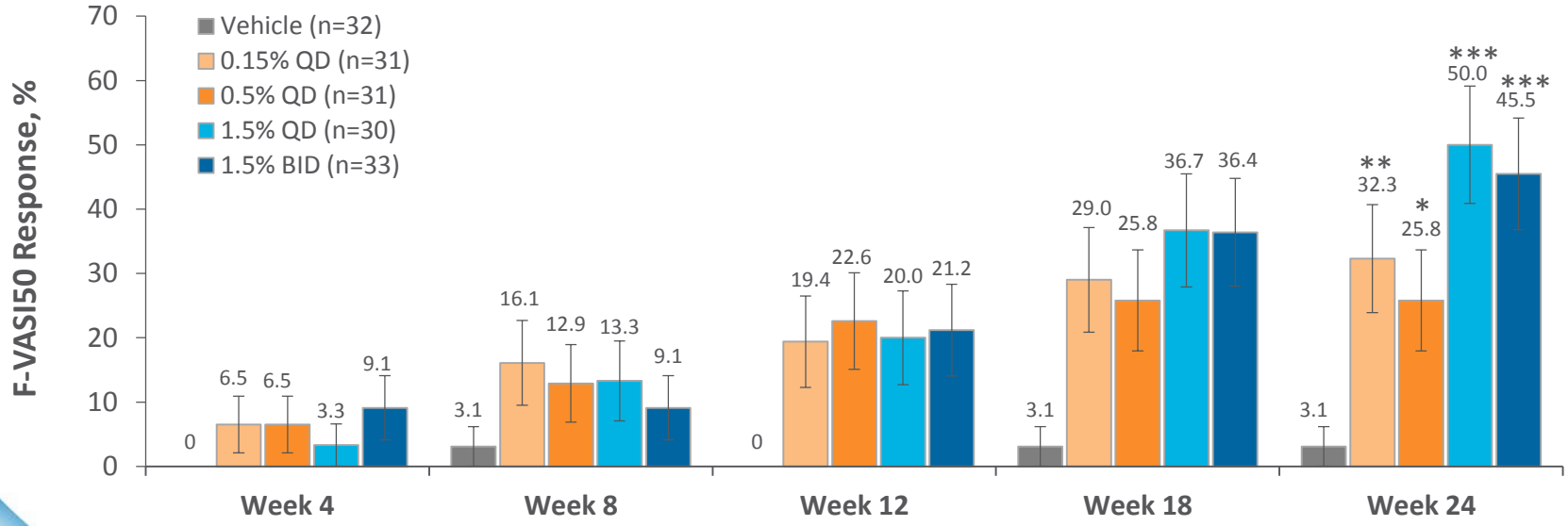
Demographics and Clinical Characteristics	Total (N=157)
Age, mean ± SD, years	48.3±12.85
Male, n (%)	73 (46.5)
Skin type, n (%)	
I	6 (3.8)
II	50 (31.8)
III	50 (31.8)
IV	31 (19.7)
V	10 (6.4)
VI	10 (6.4)

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]).

Primary Efficacy Endpoint: F-VASI50 Response

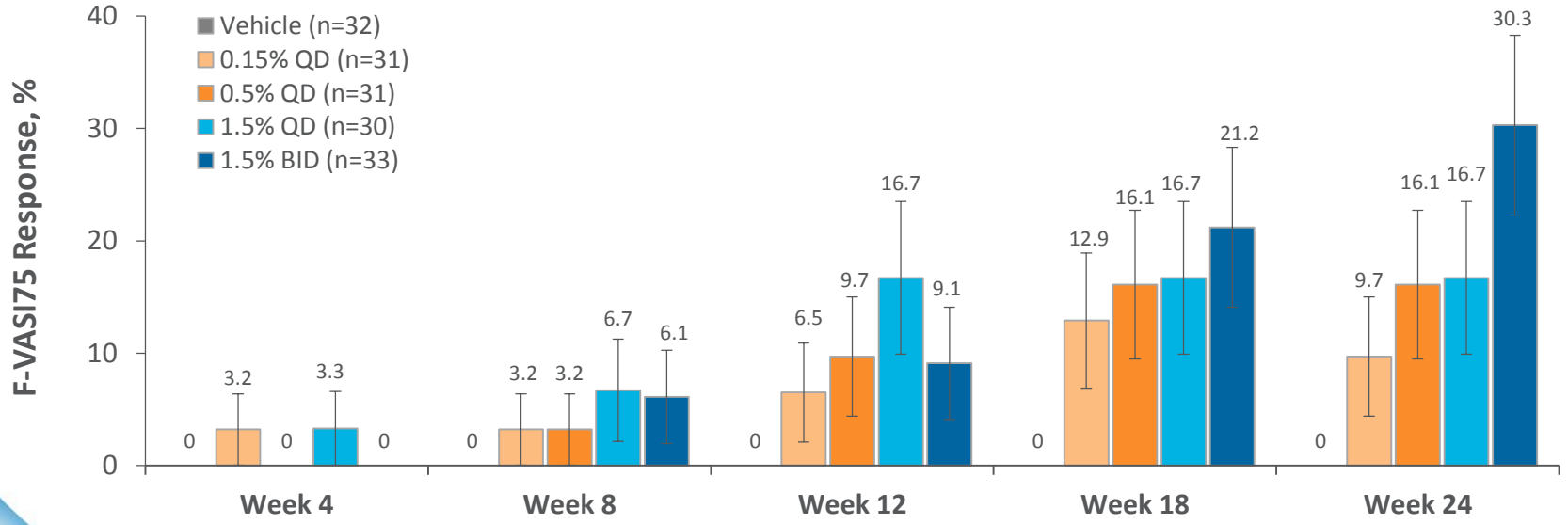
- At Week 24, the highest F-VASI50 response was achieved with the 1.5% QD and BID regimens



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 1.5% BID regimen



Error bars indicate standard error.

Treatment-Emergent Adverse Events Through 24 Weeks

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

	Vehicle (n=32)	Ruxolitinib Cream				Total (n=157)
		0.15% QD (n=31)	0.5% QD (n=31)	1.5% QD (n=30)	1.5% BID (n=33)	
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
- All doses of ruxolitinib cream were well tolerated

Next Steps in Ruxolitinib Cream Development

Vitiligo — Phase 3 initiation — Phase 3 results →

Atopic dermatitis — Phase 3 results →

Q&A

Building Value through Innovative Medicines

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