Update on Treatment of Vitiligo

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Conflicts of Interest Disclosure

- Amit G. Pandya, MD
  - Investigator- Aclaris, Incyte, Pfizer, Immune Tolerance Network
  - Consultant- Pfizer
  - Board of directors and stock options- Clarify Medical

Vitiligo

- Common, progressive loss of skin pigmentation
- Affects 0.5-2% of population worldwide
- All races affected
- Significant effect on quality of life
- Disease course unpredictable
- No biomarkers

"Vitiligo: Truth, Hope and Change"

Vitiligo

- Peak age of onset is 10-30 yrs
- Increased risk of autoimmune disease, especially thyroid disease
- New discoveries
  - Pathogenesis
  - Clinical features
  - Epidemiology
  - Outcomes research
  - Psychological impact
  - Treatment

Markers of Vitiligo Activity

- Trichrome vitiligo
- Koebner phenomenon
- Confetti-like lesions
- Inflammatory vitiligo

The majority of patients presenting with vitiligo have a clinical sign of activity

To the Editor: Vitiligo is a common depigmenting disorder affecting 0.5%-1% of the world population.[1]

- Prospective cross-sectional study
- 200 new patients enrolled
- 61% had at least one sign of activity
  - Confetti-like 46%
  - Trichrome 27%
  - Koebner 30%
- Many had > 1 sign

Aboul-Fettouh N, Pandya AG, et al, JAAD 2017; 77:774–775

Dermoscopy in Vitiligo Patients

- Allows visualization of hairs
- Leukotrichia (white hairs) associated with poor prognosis
- Terminal and vellus hairs should be examined

Treatment of Vitiligo

- Long duration of therapy
- Importance of setting expectations
- Patience is a virtue
- > 75% repigmentation considered "successful" by physicians (not all patients)
- Few patients achieve 100% repigmentation
- Visible locations are of most concern to patients
- Good baseline images ⟶ **MOTIVATED PROVIDER AND PATIENT**

Prognosis

- Good response
  - Younger patients
  - Darker skin types
  - Short duration of vitiligo (< 2 years)
  - Face
  - Ears
  - Neck
  - Axillae
  - Hair bearing areas with pigmented hairs

Prognosis

- Poor response
  - Older patients
  - Lighter skin types
  - Long duration of vitiligo
  - Rapidly spreading vitiligo
  - Scalp
  - Lips
  - Fingers
  - Hands
  - Wrists
- Poor response (cont.)
  - Elbows
  - Genitalia
  - Toes
  - Feet
  - Ankles
  - Pretibial skin
  - Knees
  - Leukotrichia

Vitiligo- Treatment

- Camouflage makeup application
- Dihydroxyacetone (Chromelin, Pro tan)
- Antioxidants
- Topical corticosteroids
- Topical tacrolimus
- Topical pimecrolimus
- PUVA
- Narrow-band UVB
- Excimer laser
- Systemic corticosteroids
- Autologous skin grafting
- Depigmentation

Vitiligo- Antioxidants

- 35 patients
- Randomized, double-blind, placebo-controlled multicenter trial
- Low dose antioxidants (alpha lipoic acid, vit C, vit E, polyunsaturated fatty acids) given 2 months before NBUVB therapy and continued for 6 months vs. placebo
- 28 completed study
- After 2 months of supplementation, catalase activity rose 21% and reactive oxygen species fell 43% in PBMCs
- 47% of supplementation group achieved >75% repigmentation vs. 18% in placebo group

Dell'Anna ML, Picardo M, et al, Clin Exp Dermatol 2007; 32:631-636

Addition of oral minipulse dexamethasone to narrowband ultraviolet B phototherapy and topical steroids helps arrest disease activity in patients with vitiligo

DOI: 10.1111/bjd.17150

- Group A: 25 patients treated with dexamethasone 4 mg on 2 consecutive days per week + NBUVB + clobetasol once daily Mon-Fri
- Group B: 15 patients treated with NBUVB and clobetasol
- Disease arrest
  - Group A: 92% at 3.6 months
  - Group B: 53% at 3.9 months
- Moderate repigmentation in both groups
- Side effects in 7 patients (28%) in group A- insomnia, weight gain, steroid acne

Tovar-Garza A, Pandya AG, et al, Br J Dermatol 2018

Phototherapy for Vitiligo

- Full body NBUVB
- Localized NBUVB
- Full body PUVA
- Localized PUVA
- Topical PUVA
- PUVASOL
- Excimer laser/light
- Sunlight
- Solarium

NBUVB vs. PUVA for Vitiligo

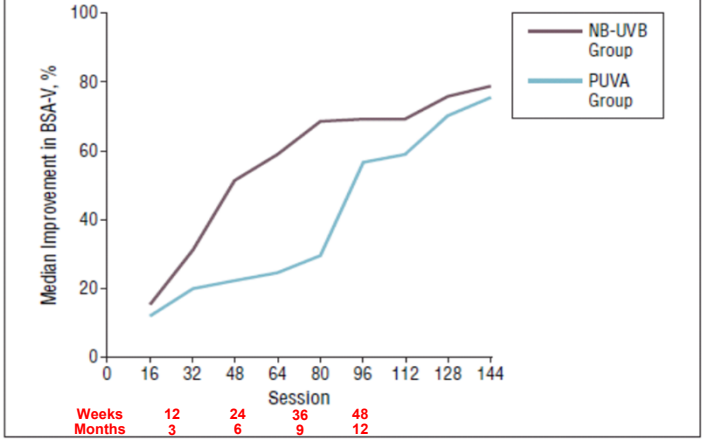


Figure 2. Improvement in body surface area affected by vitiligo (BSA-V). The data at each time point refer only to patients who received at least that number of sessions. NB-UVB indicates narrowband UV-B; PUVA, oral psoralen followed by irradiation with UV-A.

Yones SS, Hawk JLM, et al, Arch Dermatol 2007; 143:578-584

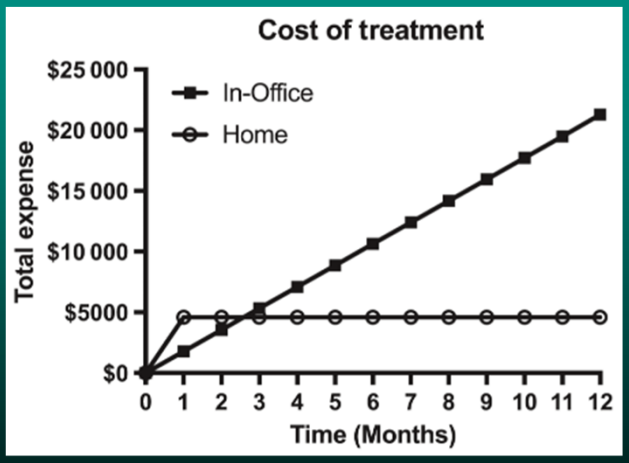
Phototherapy for Vitiligo

- Home NBUVB therapy
  - Handheld Unit: $650
  - 18 inch unit: $1500
  - 6 bulb unit: $2400
  - 8 bulb unit: $3200
  - 10 bulb unit: $4600

In-Office vs. Home NBUVB

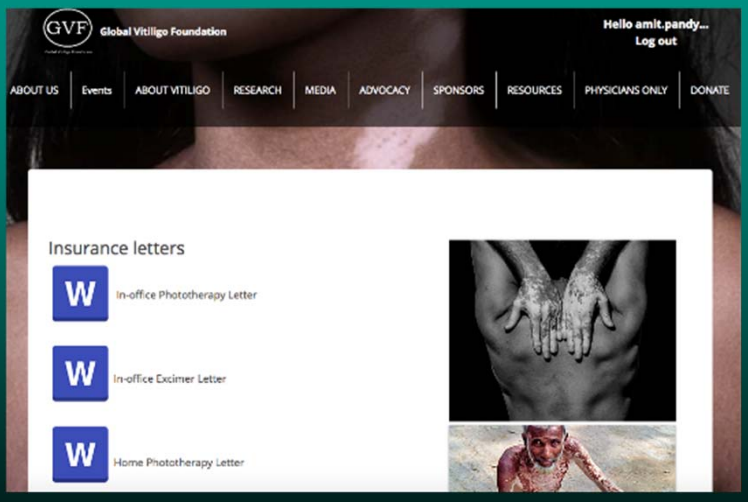
TABLE 1 Mean treatment time for three phototherapy sessions in patients with vitiligo receiving in-office vs home phototherapy

	Home Phototherapy (min)	In-Office Phototherapy (min)
Pair 1	25	91
Pair 2	20	62
Pair 3	11	95
Pair 4	15	181
Pair 5	45	84
Pair 6	13	103
Pair 7	40	53
Pair 8	13	62
Pair 9	16	41
Average	22	86



Dillon JC, Pandya AG, et al, Photodermatol, Photoimmunol, Photomed 2017;33:282–283

Global Vitiligo Foundation



Phototherapy Dosing Chart and Treatment Log

Treatment Number	10% Increase (min:sec)	15% Increase (min:sec)	Date	Dose (min:sec)
1	:20	:20		
2	:22	:23		
3	:24	:26		
4	:26	:30		
5	:29	:35		
6	:32	:40		
7	:35	:46		
8	:39	:53		
9	:43	1:01		
10	:47	1:10		
11	:52	1:21		
12	:57	1:33		
13	1:03	1:47		
14	1:09	2:03		
15	1:16	2:21		
16	1:24	2:42		
17	1:32	3:06		
18	1:41	3:34		
19	1:51	4:06		
20	2:02	4:43		
21	2:14	5:25		
22	2:27	6:14		
23	2:42	7:10		
24	2:58	8:15		
25	3:16	9:29		
26	3:36	10:54		
27	3:58	12:32		
28	4:22	14:25		
29	4:48	16:35		
30	5:17	19:04		
31	5:49	21:56		
32	6:24			
33	7:02			
34	7:44			
35	8:30			
36	9:21			
37	10:17			
38	11:19			
39	12:27			
40	13:42			
41	15:04			
43	16:34			
44	18:13			
45	20:02			

Early Treatment Gives Better Results

Table 3. Percentile prevalence of different groups of overall clinical response in relation to disease duration shows statistically significant difference between recent and long-standing vitiligo ($P = 0.023$)

Disease duration grouping	Mild response	Moderate response	Good or excellent response	Total
Recent	11.5	26.9	61.5	100
Long standing	21.6	51.4	27	100

Hallaji Z, et al, Photodermatology, Photoimmunology & Photomedicine 2012, 28, 115–119

Safety of Phototherapy in Vitiligo

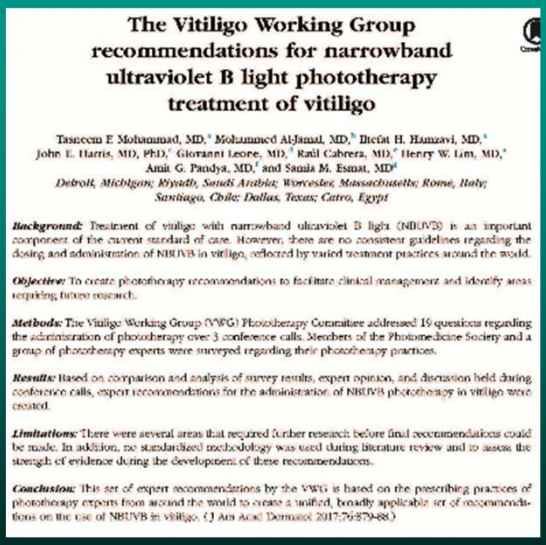
- 477 patients at Henry Ford with vitiligo treated with NBUVB compared to age adjusted cohort
- Average duration of observation 4.3 years
- 6 patients with NMSC identified, all Caucasian
- Risk of NMSC double, but only in Caucasians
- Additional studies from the Netherlands and Scotland do not show an increased risk of melanoma or NMSC with NBUVB

Hexsel CL, et al, J Am Acad Dermatol, 2009:929-33

Maximizing Efficacy and Minimizing Toxicity

- Set expectations:
  - 25% repigmentation in 3 months
  - 50% repigmentation in 6 months
  - 75% repigmentation in 9 months
- Expose all areas evenly minimize shielding initially
- Start at 200 mj and increase by 15% per treatment
- Provide a small stool to maximize exposure to feet
- Extra exposure to hands and feet
- Mineral oil to dry areas of hands, feet, elbows, knees
- 3 X weekly is ideal
- If 2 X weekly is used, minimum of 2 days between treatments

Mohammad T, et al, J Am Acad Dermatol, 2017; 76:879-888



The Vitiligo Working Group recommendations for narrowband ultraviolet B light phototherapy treatment of vitiligo

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Detroit, Michigan; Riyadh, Saudi Arabia; Worcester, Massachusetts; Rome, Italy; Santiago, Chile; Dallas, Texas; Cairo, Egypt

Background: Treatment of vitiligo with narrowband ultraviolet B light (NBUVB) is an important component of the current standard of care. However, there are no consistent guidelines regarding the dosing and administration of NBUVB in vitiligo, reflected by varied treatment practices around the world.

Objective: To create phototherapy recommendations to facilitate clinical management and identify areas requiring future research.

Methods: The Vitiligo Working Group (VWG) Phototherapy Committee addressed 19 questions regarding the administration of phototherapy over 3 conference calls. Members of the Photomedicine Society and a group of phototherapy experts were surveyed regarding their phototherapy practices.

Results: Based on comparison and analysis of survey results, expert opinion, and discussion held during conference calls, expert recommendations for the administration of NBUVB phototherapy in vitiligo were created.

Limitations: There were several areas that required further research before final recommendations could be made. In addition, no standardized methodology was used during literature review and to assess the strength of evidence during the development of these recommendations.

Conclusion: This set of expert recommendations by the VWG is based on the prescribing practices of phototherapy experts from around the world to create a unified, broadly applicable set of recommendations on the use of NBUVB in vitiligo. (J Am Acad Dermatol 2017;76:879-88.)

Maximizing Efficacy and Minimizing Toxicity

- Goal is to maintain a “pink carnation flower” color
- Protect skin from sun exposure
- Avoid photosensitizing medications and foods
- Images taken at every visit
- Use prints or I pad to show patient the lesions while using a mirror
- Oral antioxidants- Vitamins C, E, alpha lipoic acid
- Clobetasol to stabilize disease
- For scalp vitiligo, cut hair as much as possible
- Home phototherapy for selected patients to improve compliance
- For unusual rashes, check ANA
- Systemic pulse corticosteroids for rapidly advancing disease

Mohammad T, et al, J Am Acad Dermatol, 2017; 76:879-888

Tofacitinib Citrate for the Treatment of Vitiligo A Pathogenesis-Directed Therapy

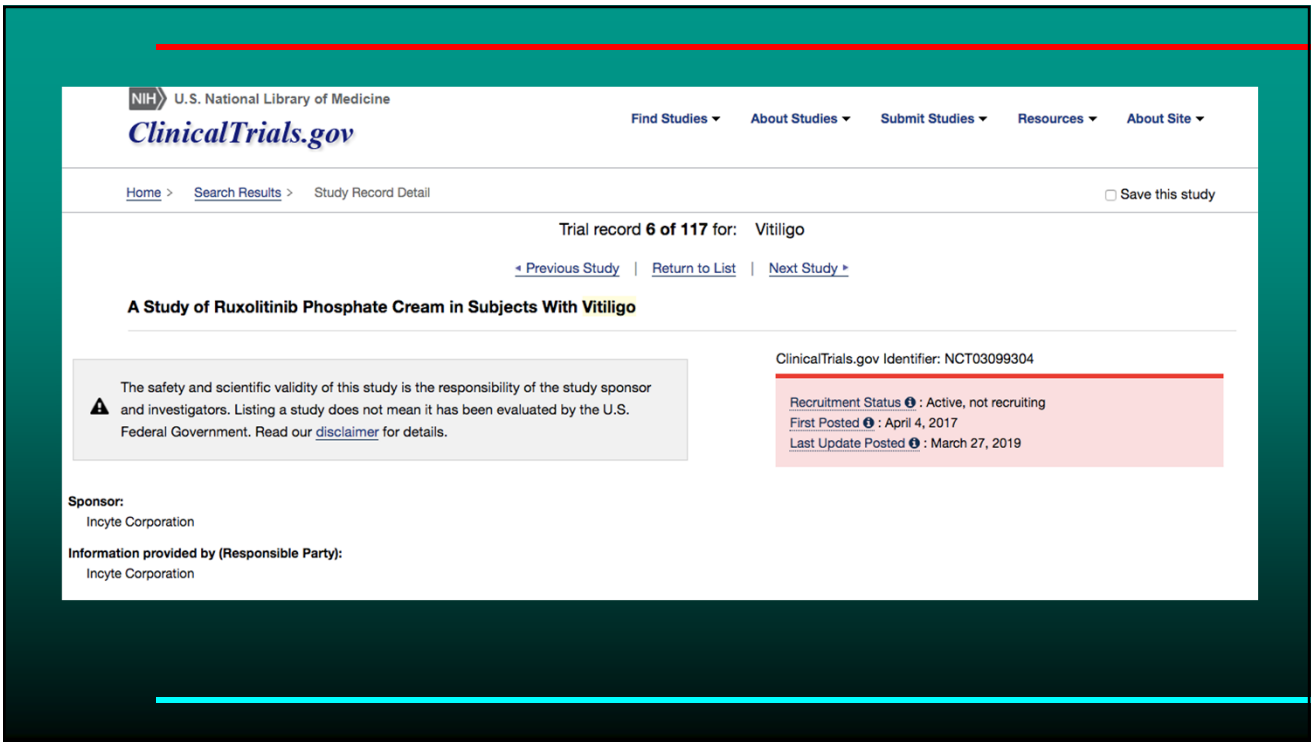
- 50 y/o WF; progressive vitiligo for one year
- Tacrolimus and triamcinolone ineffective
- 10% BSA affected
- Oral tofacitinib (Xeljanz) 5 mg every other day initiated
- After 3 weeks, the dosage was increased to 5 mg per day
- Repigmentation started at 2 months and was nearly complete at 5 months
- 5% BSA remained depigmented at the end of treatment
- No side effects

Craiglow BG, King BA, JAMA Dermatol 2015; 151:1110

Rapid Response to Oral Tofacitinib and Low-Dose NBUVB

- 35 y/o LAF with vitiligo for 12 years
- Tofacitinib 5 mg twice daily
- NBUVB 400-500 mj twice weekly
- >75% repigmentation of face, neck, chest, forearms and shins after 3 months
- Cost of 60 tablets- $4200

Kim SR, Heaton H, Liu LY, King BA, JAMA Dermatol 2018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Recruitment Status : Active, not recruiting
First Posted : April 4, 2017
Last Update Posted : March 27, 2019
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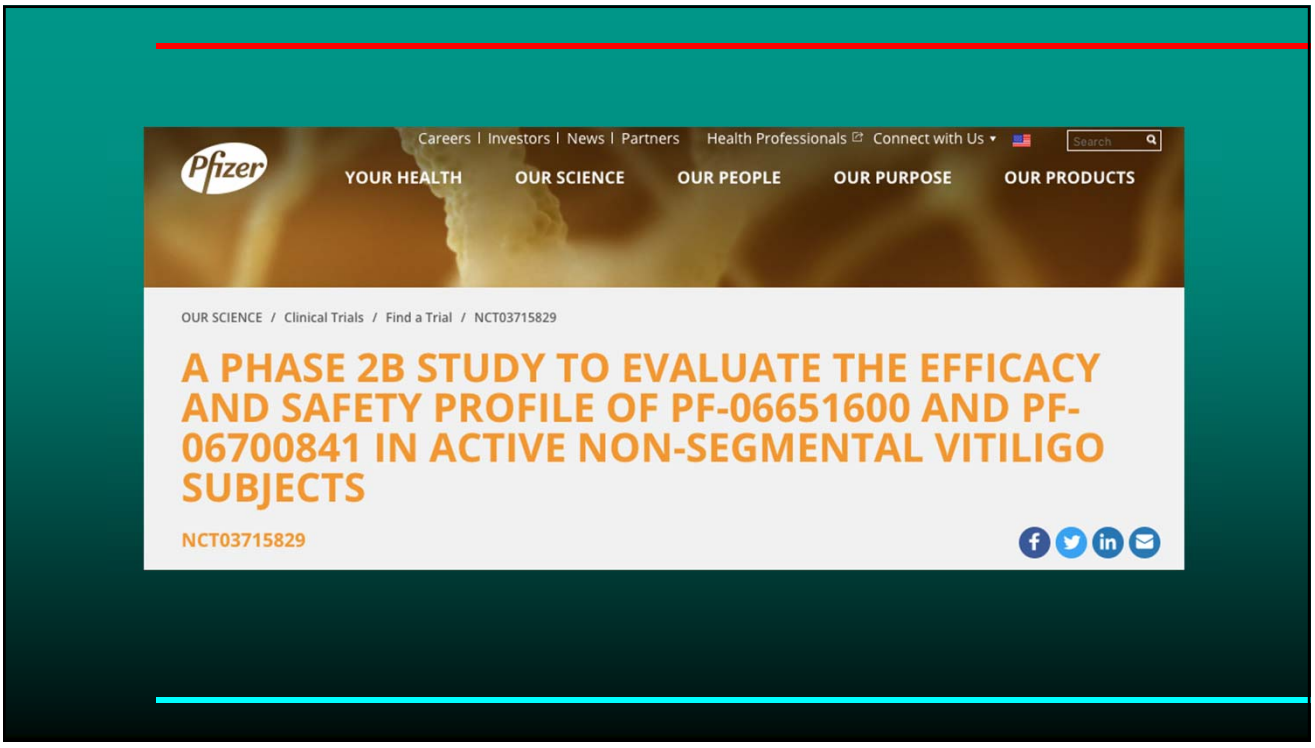
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A PHASE 2B STUDY TO EVALUATE THE EFFICACY AND SAFETY PROFILE OF PF-06651600 AND PF-06700841 IN ACTIVE NON-SEGMENTAL VITILIGO SUBJECTS
NCT03715829

Current and emerging treatments for vitiligo

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Victoria, Australia; Creteil, France; Detroit, Michigan; Dallas, Texas; and Worcester, Massachusetts

Learning objectives
After completing this learning activity, participants should be able to choose an optimal approach to management of all patients with vitiligo; list the risks associated with treatment for vitiligo; and discuss emerging treatment options for vitiligo.

Disclosure
Editors
The editors involved with this CME activity and all content validation/peer reviewers of the journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Authors
The authors involved with this journal-based CME activity other than Dr Harris have reported no relevant financial relationships with commercial interest(s). Dr Harris has served on advisory boards, as a consultant, or as principle investigator on research agreements with Pfizer, AbbVie, Genzyme/Sanofi, Concert Pharmaceuticals, Stiefel/GSK, Mitsubishi Tanabe Pharma, Novartis, Aclaris Therapeutics, The Expert Institute, Celgene, Biologics MD, and Dermira. Dr Harris' relevant relationship with Pfizer was resolved by nonconflicted reviewers and editors.

Planners
The planners involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s). The editorial and education staff involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Clinicians should be aware that vitiligo is not merely a cosmetic disease and that there are safe and effective treatments available for vitiligo. It is important to recognize common and uncommon presentations and those with active disease, as well as their implications for clinical management; these were discussed in the first article in this continuing medical education series. Existing treatments include topical and systemic immunosuppressants, phototherapy, and surgical techniques, which together may serve to halt disease progression, stabilize depigmented lesions, and encourage repigmentation. We discuss how to optimize the currently available treatments and highlight emerging treatments that may improve treatment efficacy in the future. (J Am Acad Dermatol 2017;77:17-29.)

Rodrigues M, et al, J Am Acad Dermatol, 2017; 77:17-29

Summary

- Treatment of vitiligo is effective but requires a prolonged course
- Patients should be examined carefully to detect signs of activity
- Treatment should be aimed at
  - Decreasing the immune-mediated attack on melanocytes
  - Stimulating melanocytes to proliferate and repigment the skin
- JAK inhibitors show promise as future treatments for vitiligo
- Other treatments are being developed to target newly discovered pathways

2017 Vitiligo Walkathon