
Repigmentation in vitiligo using the Janus kinase inhibitor tofacitinib may require concomitant light exposure



Lucy Y. Liu, BA,^a James P. Strassner, BS,^b Maggi A. Refat, MD,^b John E. Harris, MD, PhD,^b
and Brett A. King, MD, PhD^c

New Haven, Connecticut, and Worcester, Massachusetts

Background: Vitiligo is an autoimmune disease in which cutaneous depigmentation occurs. Existing therapies are often inadequate. Prior reports have shown benefit of the Janus kinase (JAK) inhibitors.

Objective: To evaluate the efficacy of the JAK 1/3 inhibitor tofacitinib in the treatment of vitiligo.

Method: This is a retrospective case series of 10 consecutive patients with vitiligo treated with tofacitinib. Severity of disease was assessed by body surface area of depigmentation.

Results: Ten consecutive patients were treated with tofacitinib. Five patients achieved some repigmentation at sites of either sunlight exposure or low-dose narrowband ultraviolet B phototherapy. Suction blister sampling revealed that the autoimmune response was inhibited during treatment in both responding and nonresponding lesions, suggesting that light rather than immunosuppression was primarily required for melanocyte regeneration.

Limitations: Limitations include the small size of the study population, retrospective nature of the study, and lack of a control group.

Conclusion: Treatment of vitiligo with JAK inhibitors appears to require light exposure. In contrast to treatment with phototherapy alone, repigmentation during treatment with JAK inhibitors may require only low-level light. Maintenance of repigmentation may be achieved with JAK inhibitor monotherapy. These results support a model wherein JAK inhibitors suppress T cell mediators of vitiligo and light exposure is necessary for stimulation of melanocyte regeneration. (J Am Acad Dermatol 2017;77:675-82.)

Key words: JAK; Janus kinase; narrowband ultraviolet B; nbUVB; phototherapy; ruxolitinib; tofacitinib; vitiligo.

From the Department of Dermatology,^c Yale University School of Medicine, New Haven,^a and Department of Dermatology, University of Massachusetts Medical School, Worcester.^b

Ms Liu and Mr Strassner contributed equally to this article.

Supported by National Center for Advancing Translational Sciences grant UL1-TR001453. Dr Harris is supported by National Institute of Arthritis and Musculoskeletal and Skin Diseases grant AR069114 and a Stiefel Scholar Award from the Dermatology Foundation. Dr King received funding support from The Ranjini and Ajay Poddar Resource Fund for Dermatologic Diseases Research.

Disclosure: Dr King has served on advisory boards or is a consultant for Aclaris Therapeutics, Concert Pharmaceuticals, Eli Lilly and Company, Pfizer, Regeneron Pharmaceuticals, and Roivant Sciences Ltd. Dr Harris has served on advisory boards, as a consultant, or as principal 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. Ms Liu and Mr Strassner and Dr Refat have no conflicts of interest to declare.

Accepted for publication May 21, 2017.

Reprints not available from the authors.

Correspondence to: John E. Harris, MD, PhD, Department of Dermatology, University of Massachusetts Medical School, 364 Plantation St, LRB 325, MA 01605. E-mail: john.harris@umassmed.edu. or Brett A. King, MD, PhD, Department of Dermatology, Yale University School of Medicine, PO Box 208059, New Haven, CT 06520. E-mail: brett.king@yale.edu.

Published online August 17, 2017.

0190-9622/\$36.00

© 2017 by the American Academy of Dermatology, Inc.

<http://dx.doi.org/10.1016/j.jaad.2017.05.043>

Vitiligo is a chronic autoimmune disease that results from the destruction of melanocytes, causing white spots on the skin. Vitiligo affects approximately 1% of people worldwide and can affect both adults and children, causing diminished quality of life and marked psychological distress.¹⁻⁴ Treatments include topical corticosteroids and calcineurin inhibitors, but the most effective treatment and mainstay of therapy is narrow-band ultraviolet B (nbUVB) phototherapy.⁵⁻¹⁰ However, incomplete response to treatment is common.

The pathogenesis of vitiligo involves the destruction of melanocytes via cell-mediated immunity, and studies show that interferon gamma (IFN- γ) and CD8⁺ T cells play a key role in this process.^{7,11-16} A similar pattern of CD8⁺ T cell-driven autoimmunity is also seen in alopecia areata,¹⁷ a disease that often co-occurs with vitiligo, suggesting that targeted therapy in 1 disease may be effective in the other.¹⁸ Two case reports described successful repigmentation in vitiligo, 1 using tofacitinib, a Janus kinase (JAK) 1/3 inhibitor,¹⁹ and the other using ruxolitinib, a JAK 1/2 inhibitor,²⁰ presumably via inhibition of IFN- γ signaling in the skin. Recently, an open-label clinical trial reported efficacy of topical ruxolitinib in patients with vitiligo, in particular, for facial involvement.²¹

Here we report the results of 10 consecutive patients with vitiligo treated with oral tofacitinib.

METHODS

This study is a retrospective case series of 10 patients seen between July 2014 and January 2017. Medical records of patients with vitiligo, age 18 years and older, who were treated with tofacitinib for at least 3 months were reviewed. Clinical and demographic information, including biological sex, age, disease duration and course, medical history, family history, and prior treatments, were collected. Before initiation of tofacitinib therapy, all patients underwent baseline laboratory evaluation, including a comprehensive metabolic panel, complete blood cell count with differential, fasting lipid panel, screening for tuberculosis with the QuantiFERON-TB Gold test (Cellestis Limited, Melbourne, Australia), and screening for HIV and hepatitis B and C. Body surface area (BSA) of depigmentation was assessed before and at the end of treatment. Serial laboratory monitoring, physical

examinations, and review of systems were used to monitor for adverse events.

Suction blister sampling was performed in 1 patient before the start of tofacitinib treatment and again 10 months later to assess changes in T cell recruitment and chemokine expression; this patient had previously responded to tofacitinib but then

relapsed after discontinuing treatment.¹⁹ Three sites were selected for sampling: 1 was a site of vitiligo that did not previously respond to treatment with tofacitinib, 1 was a recently active site (featuring confetti depigmentation²²) that previously responded to tofacitinib, and 1 was unaffected skin.

Suction blister sampling and processing

The Negative Pressure Instrument Model NP-4 (Electronic Diversities, Finksburg, MD) was used to induce suction blisters (1 cm in diameter). Blisters formed at a pressure between 10 and 15 mm Hg negative pressure and at a constant temperature of 40°C. Once blisters formed, the blister fluid was aspirated through the roof with a 1-mL insulin syringe. Cells in the blister fluid were pelleted at 330 g for 10 minutes and prepared for flow cytometry. The supernatant of the blister fluid was stored at -80°C until analysis by enzyme-linked immunosorbent assay (ELISA) for chemokines. None of the blisters were hemorrhagic.

ELISA

Chemokines were assayed using the Human CXCL9/MIG DuoSet ELISA and Human CXCL10/IP-10 DuoSet ELISA (R&D Systems, Minneapolis, MN) per the manufacturer's instructions. Optical densities were measured with a Perkin Elmer EnVision 2102 multilabel reader (Perkin Elmer, Waltham, MA) and analyzed using a 4-parameter logarithmic standard curve.

Flow cytometry

Cells were blocked with Human TruStain and incubated with an antibody cocktail for 30 minutes at 4°C. Anti-human CD45 (2D1) and CD8 (SK1) were used at 1:20 dilution. Anti-human CD3 (OKT3) was used at 1:200 dilution (BioLegend, San Diego, CA) and Fixable Viability Dye eFluor 455UV at 1:1000 (eBioscience, San Diego, CA). Before cell staining of the peripheral blood mononuclear cells (PBMCs), 10⁶ PBMCs were treated with desatinib for 30 minutes at 36°C, pelleted, and incubated with Mart-1

CAPSULE SUMMARY

- Vitiligo is driven by the destruction of melanocytes by T cells, which is inhibited by tofacitinib treatment.
- Janus kinase inhibitors are a promising targeted treatment for vitiligo.
- Combination therapy using tofacitinib plus light exposure may be required for effective responses in vitiligo.

Abbreviations used:

BSA:	body surface area
CXCL9:	C-X-C motif chemokine ligand 9
ELISA:	enzyme-linked immunosorbent assay
IFN- γ :	interferon gamma
JAK:	Janus kinase
nbUVB:	narrowband ultraviolet B
PBMCs:	peripheral blood mononuclear cells

Pentamer (ProImmune, Oxford, United Kingdom) for 10 minutes at room temperature.

RESULTS

Patient characteristics

All 10 patients in this case series were adults. Duration of disease ranged from 4 to 33 years (mean, 16.6; standard deviation, 8.8). Eight patients had generalized vitiligo and 2 patients had primarily acral involvement, with BSA 1% to 100%. Additional patient characteristics, together with previous treatments, are described in [Table I](#).

Clinical response to treatment

Ten patients underwent treatment with tofacitinib, 5 to 10 mg daily or twice daily, for an average of 9.9 months (standard deviation, 4.1; range, 3-15). A mean decrease of 5.4% BSA involvement with vitiligo was observed in 5 of 10 patients, whereas the other 5 patients did not achieve any repigmentation.

In the 5 patients who achieved some reversal of disease, repigmentation occurred only in sun-exposed areas of skin of 3 of them, diffusely in another patient undergoing concomitant full-body nbUVB phototherapy, and to the dorsal surface of the hands in another patient after initiation of concomitant hand nbUVB phototherapy. [Fig 1](#) shows clinical images of patient 1 before and after treatment, and [Table II](#) summarizes the clinical course of each patient.

Of the 5 patients who did not experience repigmentation, only 1 reported significant sunlight exposure, and the others either avoided sunlight or practiced photoprotection.

Adverse events

The most common adverse event was upper respiratory infection in 2 patients. One patient reported weight gain of 5 pounds and 1 patient reported arthralgia. Mild elevations of lipid levels were noted in 4 patients. There were no serious adverse events.

Suction blister sampling

Previous analysis of suction blisters of active vitiligo lesions demonstrated that T cell number

and C-X-C motif chemokine ligand 9 (CXCL9) protein level were both sensitive and specific to predict disease activity.¹⁵ We used this method to measure the treatment response of patient 1 who had previously responded to tofacitinib but then relapsed after discontinuing treatment.¹⁹ Before retreatment with tofacitinib, she underwent suction blister sampling of a previously treatment-unresponsive site (intermammary cleft), a previously treatment-responsive site (forearm), and skin unaffected by vitiligo (arm). After 10 months of tofacitinib, she underwent blister sampling again at the same sites, where responses to retreatment were the same as with the original treatment (ie, no repigmentation of the intermammary cleft and repigmentation of the forearm were observed).

A small number of T cells were detected in all sites at baseline and during treatment. At baseline, there were 29 CD8⁺ T cells in the previously nonresponding lesion and a greater number in the recently developed lesion (69 cells). Both lesional sites had more cells than in unaffected skin. Following treatment with tofacitinib, the absolute numbers in each site were reduced ([Fig 2, A and B](#)). Similarly, melanocyte-specific T cells (human leukocyte antigen pentamer-positive) were detected in the PBMCs at baseline; this percentage did not change with tofacitinib treatment, and even increased slightly ([Supplemental Fig 1, A](#); available at: <http://www.jaad.org>).

CXCL9 level was elevated in all 4 lesional blisters (2 blisters were induced and sampled at each site) compared with in unaffected skin at baseline ([Fig 2, C](#)), and C-X-C motif chemokine ligand 10 (CXCL10) was elevated in 3 of 4 lesional blisters ([Fig 2, D](#)). Following treatment, chemokine levels became undetectable in both the blister fluid (responding and nonresponding sites [[Fig 2, C and D](#)]), and serum ([Supplemental Fig 1, B](#)).

In summary, tofacitinib effectively decreased T cell numbers and chemokine proteins (a measure of IFN- γ signaling) in the skin. In the blood, tofacitinib did not affect the number of autoreactive T cells but did decrease the levels of chemokines.

DISCUSSION

The pathogenesis of vitiligo involves CD8⁺ T cell production of IFN- γ , which leads to CXCL9/CXCL10 expression by keratinocytes and further recruitment of CD8⁺ T cells, resulting in melanocyte destruction.^{7,13-16,23} Originally, we hypothesized that inhibition of IFN- γ signaling using JAK inhibitors would lead to repigmentation, and the results in 2 patients^{19,20} using 2 different oral JAK inhibitors,

Table I. Clinical characteristics of patients with vitiligo

Patient No.	Age	Sex	Race	BSA before tofacitinib	BSA after tofacitinib treatment	Body site involvement	Tofacitinib treatment duration, mo	Vitiligo disease duration, y	Responder status	Previous treatments
1	54	F	White	10%	4%	Face, torso, arms and hands, legs and feet	10	4	R	nbUVB, topical tacrolimus
2	45	M	White	28%	24%	Face, neck, torso, arms and hands, legs and feet	8	23	R	Prednisone
3	46	F	White	39%	24%	Face, neck, torso, arms and hands, legs and feet	11	16	R	nbUVB, topical steroids, pseudocatalase cream, blister grafting
4	55	F	White	10%	8%	Face, neck, torso, hands, feet	14	24	R	nbUVB, secukinumab
5	45	M	East Indian	2%	2%*	Torso, elbows and hands	14	5	R	nbUVB, topical tacrolimus
6	28	M	White	7%	7%	Face, neck, arms and hands, legs	3	14	NR	nbUVB, topical steroids, topical tacrolimus
7	47	F	Hispanic	1%	1%	Face, neck, arms and hands, legs	9	18	NR	nbUVB, excimer laser, topical PUVA, topical steroids
8	49	M	White	4%	4%	Forehead, torso, arms and hands, legs	15	17	NR	nbUVB, topical steroids, topical tacrolimus
9	32	M	Hispanic	6%	6%	Lower forehead, eyelids, perioral, axillae, elbows and hands, lower back, gluteal cleft, feet	4	12	NR	nbUVB, fraxel laser, cryotherapy, topical tacrolimus
10	73	F	White	100%	100%	Entire body	11	33	NR	nbUVB, PUVA

BSA, Body surface area; F, female; M, male; nbUVB, narrow band ultraviolet B; NR, nonresponder; PUVA, psoralen with ultraviolet A; R, responder.

*Islands of repigmentation, which were apparent after 12 treatments with nbUVB phototherapy over 4 weeks, did not change the BSA appreciably at this early time point.

Table II. Clinical course of patients with vitiligo who responded to treatment

Patient No.	Clinical course
1	Near-complete repigmentation of face, forearms, and dorsal surface of the hands over 5 months of treatment with tofacitinib, 5 mg QD, followed by recurrence of depigmentation after discontinuation of tofacitinib. Retreatment with tofacitinib, 5 mg QD, starting in late spring, led to repigmentation of the face, forearms, dorsal surface of the hands, chest, upper back, and shoulders over 10 months; sun-protected body sites remained unchanged.
2	Partial repigmentation of the face, lateral and posterior surfaces of the neck, and forearms over 3 months and near-complete repigmentation of the same areas (notably, not the submental chin), as well as islands of repigmentation involving the dorsal surface of the hands and lower legs over 8 months of treatment with tofacitinib, 5 mg BID; sun-protected body sites remained unchanged. Repigmentation maintained during tofacitinib treatment in winter, when sunlight exposure was minimal.
3	Complete repigmentation of the face and significant repigmentation of the torso and extremities over 11 months of treatment with tofacitinib, 5 mg BID, plus nbUVB (150 mJ/cm ² TIW).
4	Near-complete repigmentation of the face over 14 months of tofacitinib, 5 mg BID; sun-protected body sites remained unchanged.
5	No repigmentation of the dorsal surface of the hands over 1 year of treatment with tofacitinib, 5-10 mg BID. Patient wore dark brown makeup on his hands to disguise the white patches. Subsequently, after 12 treatments of concomitant nbUVB hand phototherapy (350 mJ/cm ² over 4 weeks), islands of repigmentation were apparent.

BID, Twice daily; nbUVB, narrowband ultraviolet B; QD, daily; TIW, three times weekly.

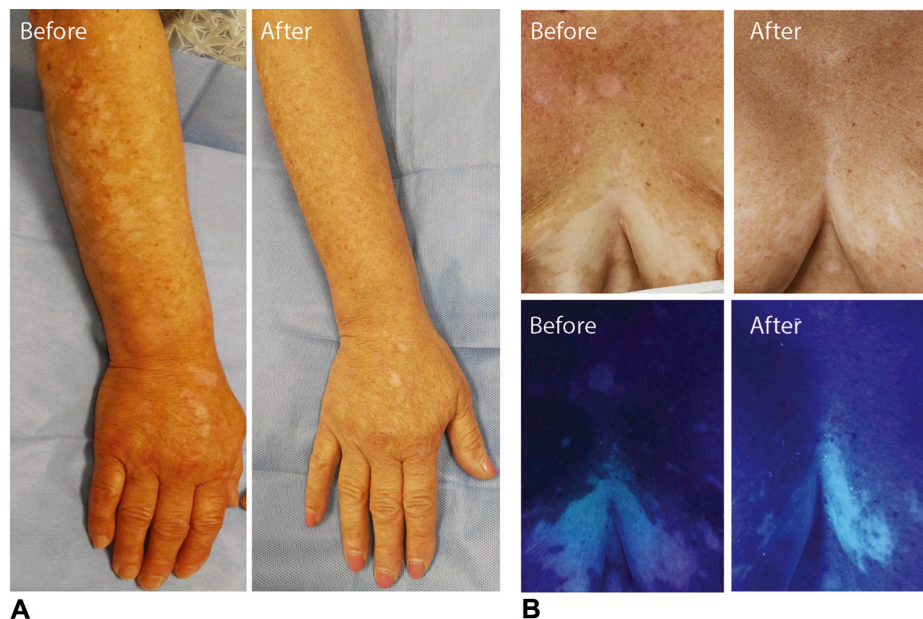


Fig 1. Clinical images of patient 1. **A**, The sun-exposed forearm and dorsal surface of the hand, before and during treatment, demonstrates repigmentation. **B**, The chest, before and during treatment under room light (*top panels*) and Wood's lamp (*bottom panels*), demonstrates repigmentation of sun-exposed lesions involving the upper chest but not sun-protected lesions involving the intermammary cleft.

tofacitinib and ruxolitinib, supported this hypothesis. Recently, a case series evaluating topical ruxolitinib also demonstrated efficacy.²¹ Interestingly, both of the patients taking oral JAK inhibitors repigmented mainly in sun-exposed areas, and the topical study reported the best response on the face, also a sun-exposed location.

Here we report the results of 10 patients in whom treatment with tofacitinib led only to repigmentation when there was concomitant light exposure, either sunlight or nbUVB phototherapy. Notably, the low doses of nbUVB that were beneficial would not typically be effective as monotherapy in vitiligo.

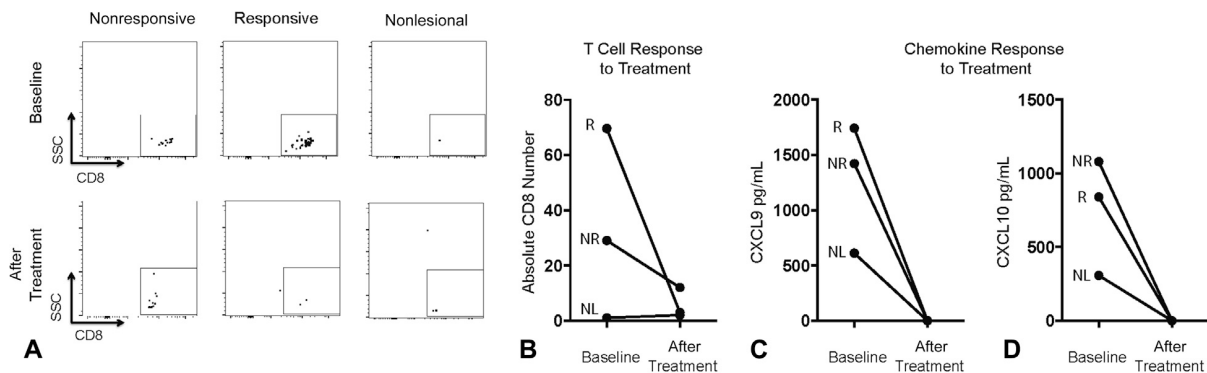


Fig 2. CD8⁺ T cell quantification and chemokine protein levels in blister fluid in patient 1. **A**, Representative CD8⁺ T cells in the CD8⁺ gate for each site at baseline and after treatment. CD8⁺ T cells were first gated on singlets and then by physical parameters side scatter (SSC) and forward scatter (FSC), all live cells, all CD45⁺ cells, all CD3⁺ cells, and all CD8⁺ T cells. **B-D**, Comparison of CD8⁺ T cell number (**B**), C-X-C motif chemokine ligand 9 (CXCL9) (**C**), and C-X-C motif chemokine ligand 10 (CXCL10) (**D**) in each site before and after treatment. NL, Nonlesional site; NR, nonresponding site; R, responding site.

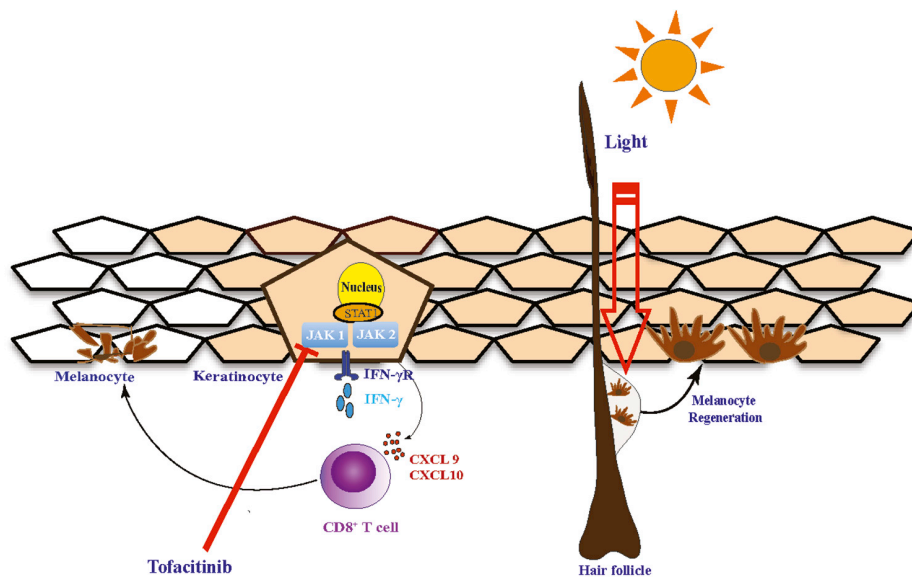


Fig 3. Model of vitiligo treatment with Janus kinase (JAK) inhibitor plus light exposure. Interferon gamma (IFN- γ) (blue ovals) signals through the IFN- γ receptor (IFN- γ R) via JAK1 and JAK2, initiating phosphorylation of signal transducer and activator of transcription 1 (STAT1) and STAT1 translocation to the nucleus where IFN- γ -dependent genes, including C-X-C motif chemokine ligand 9 gene (CXCL9) and C-X-C motif chemokine ligand 10 gene (CXCL10), are transcribed. CXCL9 and CXCL10 recruit autoreactive CD8⁺ T cells to the skin, where they attack melanocytes, leading to depigmentation (white keratinocytes). Tofacitinib inhibits this process by blocking JAK signaling. Even under JAK inhibitor suppression of vitiligo, repigmentation depends on photoactivation to stimulate melanocytes to leave their stem cell niche in the hair follicle bulge and seed the epidermis to make pigment.

There are several important observations that emerge from this case series: (1) tofacitinib treatment of vitiligo appears to require light exposure, for which low doses may be sufficient (even regular exposure to sunlight was sufficient to achieve

repigmentation in some patients); (2) repigmentation may again be achieved after depigmentation recurs upon discontinuation of tofacitinib; (3) areas of repigmentation are maintained with tofacitinib monotherapy after light exposure ceases; (4)

tofacitinib treatment in 1 patient eliminated IFN- γ signaling and reduced T cell numbers in the skin, even in lesions that did not repigment; and (5) suction blister sampling may be used to understand the effects of treatment on the immunological milieu of the skin. Altogether, these results lead to the model shown in Fig 3. Repigmentation requires both suppression of inflammation in the skin (which is achieved with JAK inhibitor treatment) and melanocyte stimulation (via light exposure). The requirement for only low-dose nbUVB phototherapy or sunlight to induce repigmentation during tofacitinib treatment suggests that the higher doses of nbUVB normally required to induce repigmentation may specifically be for the immunosuppressive effect. It may be that high doses are necessary to suppress autoimmunity in the skin but low doses are sufficient to promote melanocyte regeneration. Future studies are needed to test this hypothesis. The lack of response of patient 8, who received both tofacitinib and sun exposure, highlights that there are yet unidentified factors influencing treatment response. For instance, IFN- γ signaling is mediated by JAK1/2, and therefore, tofacitinib, which is a JAK1/3 inhibitor, may be less efficacious than a JAK1/2 inhibitor, such as ruxolitinib.

Adverse events were mild and infrequent, which is consistent with other studies of off-label use of tofacitinib in the treatment of skin disease.²⁴⁻²⁶

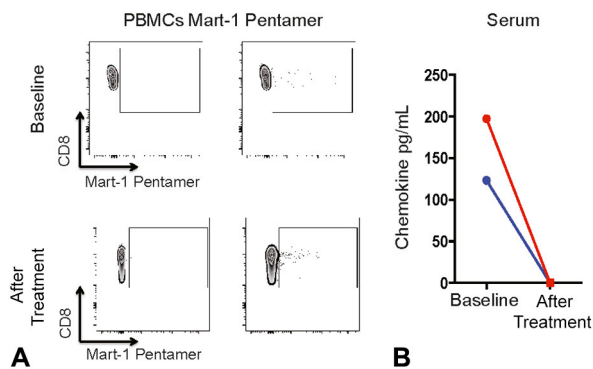
Treatment with JAK inhibitors together with light exposure may be an effective targeted treatment for vitiligo. In this series, JAK inhibitor monotherapy did not appear to be efficacious, but JAK inhibitor in combination with either low-dose nbUVB phototherapy or sun exposure led to repigmentation. Prospective clinical trials are needed to further assess JAK inhibitor treatment of vitiligo.

Drs Harris and King acknowledge the efforts of the patient who volunteered for suction blister sampling. Flow cytometry equipment was maintained by the University of Massachusetts Medical School Flow Cytometry Core Facility.

REFERENCES

1. Alikhan A, Felsten LM, Daly M, Petronic-Rosic V. Vitiligo: a comprehensive overview. Part I. Introduction, epidemiology, quality of life, diagnosis, differential diagnosis, associations, histopathology, etiology, and work-up. *J Am Acad Dermatol*. 2011;65:473-491.
2. Linthorst Homan MW, Spuls PI, de Korte J, Bos JD, Sprangers MA, van der Veen JP. The burden of vitiligo: patient characteristics associated with quality of life. *J Am Acad Dermatol*. 2009;61:411-420.
3. Bonotis K, Pantelis K, Karaoulanis S, et al. Investigation of factors associated with health-related quality of life and psychological distress in vitiligo. *J Dtsch Dermatol Ges*. 2016;14:45-49.
4. Porter J, Beuf AH, Nordlund JJ, Lerner AB. Psychological reaction to chronic skin disorders: a study of patients with vitiligo. *Gen Hosp Psychiatry*. 1979;1:73-77.
5. Anbar TS, Westerhof W, Abdel-Rahman AT, El-Khayyat MA. Evaluation of the effects of NB-UVB in both segmental and non-segmental vitiligo affecting different body sites. *Photo-dermat Photoimmunol Photomed*. 2006;22:157-163.
6. Koga M. Vitiligo: a new classification and therapy. *Br J Dermatol*. 1977;97:255-261.
7. Grimes PE. New insights and new therapies in vitiligo. *JAMA*. 2005;293:730-735.
8. Bae JM, Yoo HJ, Kim H, Lee JH, Kim GM. Combination therapy with 308-nm excimer laser, topical tacrolimus, and short-term systemic corticosteroids for segmental vitiligo: a retrospective study of 159 patients. *J Am Acad Dermatol*. 2015;73:76-82.
9. Mohammad TF, Al-Jamal M, Hamzavi IH, et al. The Vitiligo Working Group recommendations for narrowband ultraviolet B light phototherapy treatment of vitiligo. *J Am Acad Dermatol*. 2017;76:879-888.
10. Li R, Qiao M, Wang X, Zhao X, Sun Q. Effect of narrow band ultraviolet B phototherapy as monotherapy or combination therapy for vitiligo: a meta-analysis. *Photodermat Photoimmunol Photomed*. 2017;33:22-31.
11. Guerra L, Dellambra E, Brescia S, Raskovic D. Vitiligo: pathogenetic hypotheses and targets for current therapies. *Curr Drug Metab*. 2010;11:451-467.
12. Spritz RA. Six decades of vitiligo genetics: genome-wide studies provide insights into autoimmune pathogenesis. *J Invest Dermatol*. 2012;132:268-273.
13. Rashighi M, Agarwal P, Richmond JM, et al. CXCL10 is critical for the progression and maintenance of depigmentation in a mouse model of vitiligo. *Sci Transl Med*. 2014;6:223ra23.
14. Lang KS, Caroli CC, Muhm A, et al. HLA-A2 restricted, melanocyte-specific CD8(+) T lymphocytes detected in vitiligo patients are related to disease activity and are predominantly directed against MelanA/MART1. *J Invest Dermatol*. 2001;116:891-897.
15. Strassner JP, Rashighi M, Ahmed Refat M, Richmond JM, Harris JE. Suction blistering the lesional skin of vitiligo patients reveals useful biomarkers of disease activity. *J Am Acad Dermatol*. 2017;76:847-855.
16. Rashighi M, Harris JE. Interfering with the IFN-gamma/CXCL10 pathway to develop new targeted treatments for vitiligo. *Ann Transl Med*. 2015;3:343.
17. Xing L, Dai Z, Jabbari A, et al. Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition. *Nat Med*. 2014;20:1043-1049.
18. Harris JE. Vitiligo and alopecia areata: apples and oranges? *Exp Dermatol*. 2013;22:785-789.
19. Craiglow BG, King BA. Tofacitinib citrate for the treatment of vitiligo: a pathogenesis-directed therapy. *JAMA Dermatol*. 2015;151:1110-1112.
20. Harris JE, Rashighi M, Nguyen N, et al. Rapid skin repigmentation on oral ruxolitinib in a patient with coexistent vitiligo and alopecia areata (AA). *J Am Acad Dermatol*. 2016;74:370-371.
21. Rothstein B, Joshupura D, Saraiya A, et al. Treatment of vitiligo with the topical Janus kinase inhibitor ruxolitinib. *J Am Acad Dermatol*. 2017;76:1054-1060.
22. Sosa JJ, Currimbhoy SD, Ukoha U, et al. Confetti-like depigmentation: a potential sign of rapidly progressing vitiligo. *J Am Acad Dermatol*. 2015;73:272-275.

23. Richmond JM, Bangari DS, Essien KI, et al. Keratinocyte-derived chemokines orchestrate T-cell positioning in the epidermis during vitiligo and may serve as biomarkers of disease. *J Invest Dermatol.* 2017;137:350-358.
24. Craiglow BG, Liu LY, King BA. Tofacitinib for the treatment of alopecia areata and variants in adolescents. *J Am Acad Dermatol.* 2017;76:29-32.
25. Kennedy Crispin M, Ko JM, Craiglow BG, et al. Safety and efficacy of the JAK inhibitor tofacitinib citrate in patients with alopecia areata. *JCI Insight.* 2016;1:e89776.
26. Liu LY, Craiglow BG, Dai F, King BA. Tofacitinib for the treatment of severe alopecia areata and variants: A study of 90 patients. *J Am Acad Dermatol.* 2017;76: 22-28.



Supplemental Fig 1. **A**, Mart-1 pentamer-positive CD8⁺ T cells in the peripheral blood mononuclear cells (PBMCs) are shown before and after treatment. Fluorescent minus 1 samples comprise the left panels, and the full staining comprises the right panels. **B**, C-X-C motif chemokine ligand 9 (*red*) and C-X-C motif chemokine ligand 10 (*blue*) chemokine levels in the serum at baseline and after treatment.