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Rapid Skin Repigmentation on Oral Ruxolitinib in a Patient with Coexistent Vitiligo and Alopecia Areata

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TO THE EDITOR

Vitiligo and alopecia areata (AA) share a similar pathogenesis, as they are both IFN-γ-driven and dependent on $CD8^+$ T cells[1,2]. Here we report a case of rapid, but not durable, repigmentation and hair regrowth in a 35-year-old male with concurrent vitiligo and AA during treatment with oral ruxolitinib. His AA started at the age of 16 as patchy hair loss on his arms, trunk, and scalp. Several years later, he reported macular depigmentation on his face, trunk, and extremities, as well as notable overlap with alopecic lesions. He initially participated in a randomized, placebo-controlled trial at the University of Massachusetts to test the efficacy of oral simvastatin in the treatment of vitiligo. During six months of follow up while taking placebo he demonstrated no evidence of spontaneous repigmentation. Eighteen months later, he enrolled in a phase-2 open-label clinical trial at Columbia University to evaluate the efficacy of ruxolitinib (Jakafi®, Incyte, Wilmington, DE) in moderate to severe AA.

His baseline skin examination at that time revealed widespread, near-complete depigmentation of his face, as well as lesions on his trunk and extremities. He also had patches of non-scarring alopecia on his scalp and extremities. He began treatment with ruxolitinib 20mg orally twice daily for a total of twenty weeks. Four weeks after initiating

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The single center, proof-of-concept clinical trial entitled “An Open-Label Pilot Study to Evaluate the Efficacy of ruxolitinib in Moderate to Severe Alopecia Areata,” is registered at ClinicalTrials.gov identifier NCT01950780. The protocol for this intervention trial was reviewed and approved by the Institutional Review Board at Columbia University and conducted under the Declaration of Helsinki principles.

Conflict of Interest Disclosure: The authors have no conflict of interest to declare

treatment, he experienced some hair regrowth on his frontoparietal scalp, and after twelve weeks he had significant improvement (85% scalp hair compared to 63% at baseline). At that time he also began to note the appearance of pigmented macules, and at week 20 he exhibited a large amount of repigmentation on his face and other areas (51% facial pigmentation compared to 0.8% at baseline). Twelve weeks after discontinuing ruxolitinib, while his hair regrowth was maintained, much of the regained pigment had regressed (Figure 1).

Ruxolitinib is a potent small-molecule Janus kinase (JAK) inhibitor approved by the US Food and Drug Administration (FDA) for the treatment of intermediate- or high-risk myelofibrosis and polycythemia vera. It interferes with IFN-γ signaling by preferential inhibition of JAK1 and JAK2[3,4]. We previously demonstrated that ruxolitinib eliminated the IFN signature and effectively reversed hair loss in three patients and a mouse model of AA[2]. We also reported that CXCL10, an IFN-γ induced chemokine, is critical for autoreactive T cell recruitment to the skin during the progression and maintenance of vitiligo, and hypothesized that targeting the IFN-γ-CXCL10 cytokine axis might be an effective treatment by reducing the production of CXCL10[1]. Interestingly, measuring the patient's serum CXCL10 level by enzyme-linked immunosorbent assay (ELISA) revealed that it was initially elevated and stable for over 1 year, but was reduced after treatment with ruxolitinib (Figure 2).

There are currently no FDA-approved treatments for vitiligo, and standard off-label treatments are limited in efficacy. Recently, significant repigmentation was reported in a patient with vitiligo after treatment with tofacitinib, an oral JAK 1/3 inhibitor[5]. Additional studies will be needed to determine whether ruxolitinib, or other JAK inhibitors, are safe and effective long-term treatments for vitiligo.

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Abbreviations

AA	Alopecia areata
JAK	Janus kinase
FDA	Food and Drug Administration
ELISA	enzyme-linked immunosorbent assay

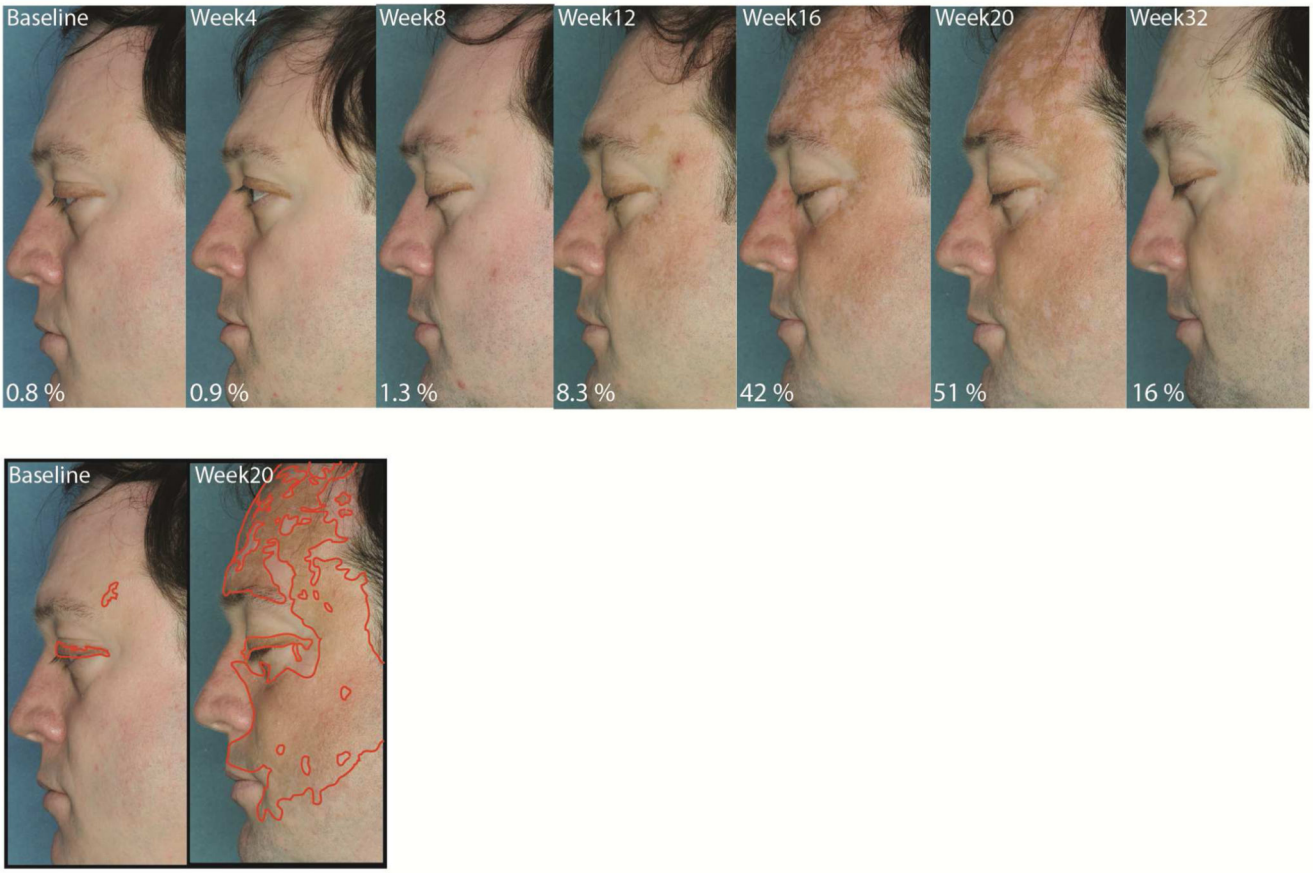

Figure 1. Vitiligo repigmentation during treatment with ruxolitinib

Screening skin examination reveals near-complete depigmentation of the patient's face at baseline. The first evidence of skin repigmentation appeared after 12 weeks of therapy, which continued until week 20, when ruxolitinib was discontinued. Follow up visit 12 weeks after stopping the treatment shows recurrent depigmentation in the majority of previously repigmented areas. Pigmented areas of the face were outlined using the free-hand selection tool followed by calculation of the % selected area using ImageJ software.

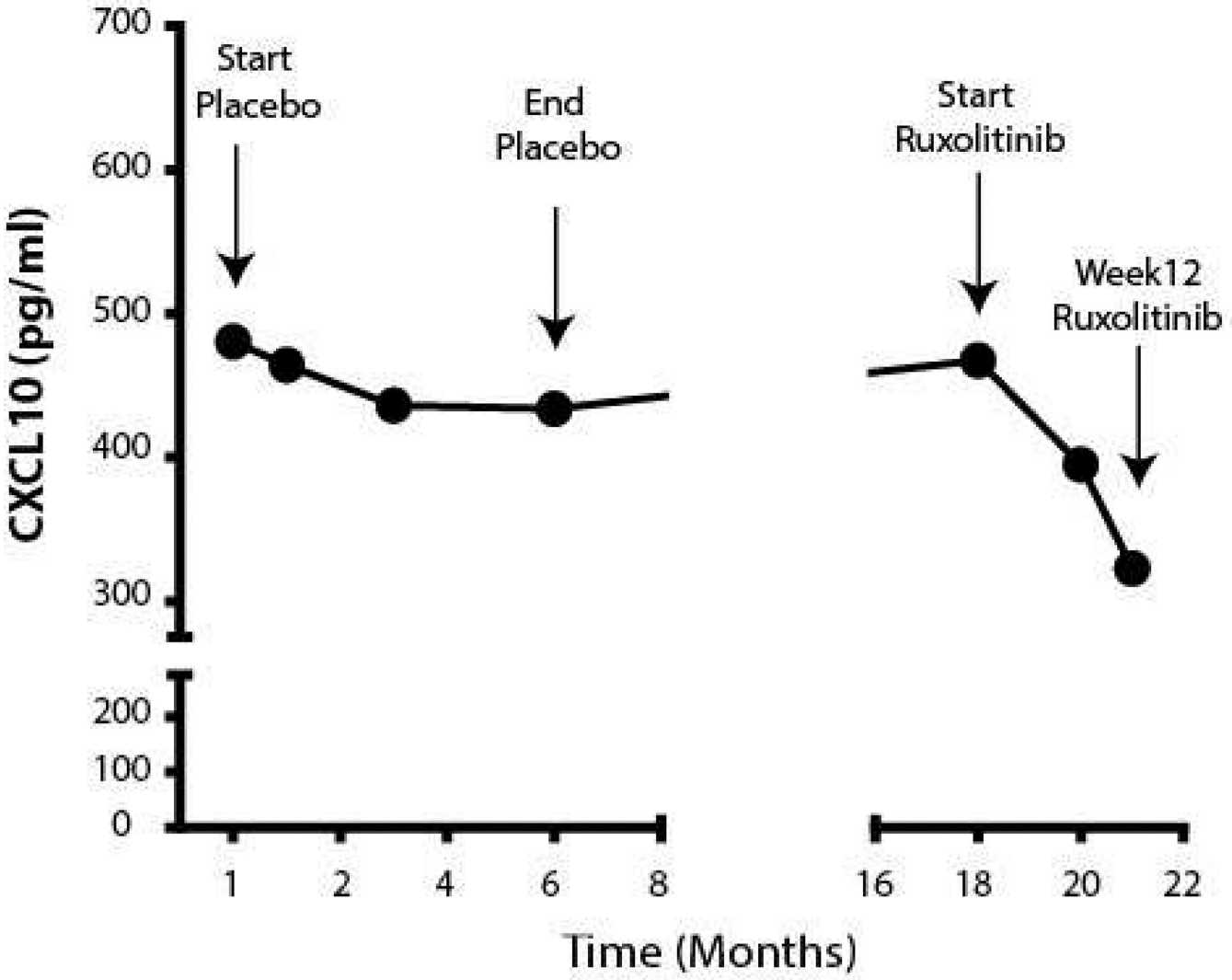

Figure 2. Decrease in serum CXCL10 after initiating treatment with ruxolitinib

Serum samples were analyzed by enzyme-linked immunosorbent assay (ELISA). CXCL10 level was elevated and remained stable while the patient was taking placebo in the first trial, but decreased after initiating treatment with ruxolitinib.