SKIN

BRIEF ARTICLE

Pityriasis Rubra Pilaris, Refractory to IL-17A Inhibition, with Rapid Improvement Following IL-17A/IL-17F Blockade by Bimekizumab

Jeremy Orloff, BA[1], Grayson Domzalski[1], Shivkar Amara, BS[1], Mark Lebwohl, MD[1]

[1] Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, New York, USA.

ABSTRACT

Introduction: Pityriasis rubra pilaris (PRP) is a rare inflammatory skin disorder which can severely affect patient quality of life. While there are no FDA-approved therapies for PRP, methotrexate and acitretin are often used as first line treatments. Recent analyses have implicated dysregulation of the IL23/IL17 axis in PRP pathogenesis and the use of biologics for severe cases have been reported in the literature.
Case Report: We report the case of a male in his thirties who presented with PRP refractory to a second course of secukinumab. Physical exam revealed diffuse salmon-colored hyperkeratotic patches coalescing to cover his entire body (BSA >95%). The patient was started on combination therapy with acitretin and bimekizumab. The patient recovered rapidly, with near total resolution of his skin findings four weeks after beginning treatment.
Discussion: Unlike earlier biologics targeting IL-17, bimekizumab has activity on IL-17F in addition to IL-17AF and IL-17A. The efficacy of bimekizumab in this case may signify an important role for IL-17F in PRP pathogenesis. Bimekizumab may offer improved efficacy for the treatment of pityriasis rubra pilaris (PRP) in patients who do not respond to other therapies.

INTRODUCTION

Pityriasis rubra pilaris (PRP) is a rare inflammatory papulosquamous inflammatory disorder thought to affect 1/5000 patients.[1] There are six clinical subtypes of the disease including HIV-associated PRP and a familial form associated with CARD14 mutations. Across all subtypes, patients most commonly present with palmoplantar keratoderma and coalescing, well-demarcated, scaly, red-orange plaques and patches that can cover most of the skin, resulting in an erythroderma with islands of sparing.[2] While there are no FDA-approved treatments for PRP, use of biologic therapies approved for psoriasis have been reported in the literature.[3]

We present a case of a patient with treatment-refractory PRP treated off-label with bimekizumab, a biologic medication. Bimekizumab is a biologic which selectively binds to Interleukin (IL)-17A, IL-17F and IL-17AF, inhibiting their interaction with the IL-17 receptor complex.[4]

CASE REPORT

A 34-year-old man presented with painful, erythematous rashes. Due to the pain, he

required a cane to ambulate. Family history was significant for atopic dermatitis in his mother and psoriasis in his sister.

The patient had been diagnosed eight years prior with PRP following two biopsies. He was initially treated with oral and injectable methotrexate, and his symptoms abated after one year. He relapsed after three years, and his symptoms were refractory to further methotrexate treatment. He was enrolled in a trial of secukinumab for patients with PRP (NCT03342573) (300mg weekly for four weeks, then every four weeks for six months) and was symptom free for approximately four years before relapsing. At that time, he was restarted on secukinumab.

On presentation, the patient's symptoms had minimally responded to this second course of secukinumab (receiving the full loading dose). Physical exam revealed diffuse salmon-colored hyperkeratotic patches coalescing to cover his entire body (BSA >95%) (**Figure 1**). His hands, which he had kept covered with surgical gloves since relapsing, were swollen, erythematous and cracked. No lymphadenopathy was appreciated on exam.

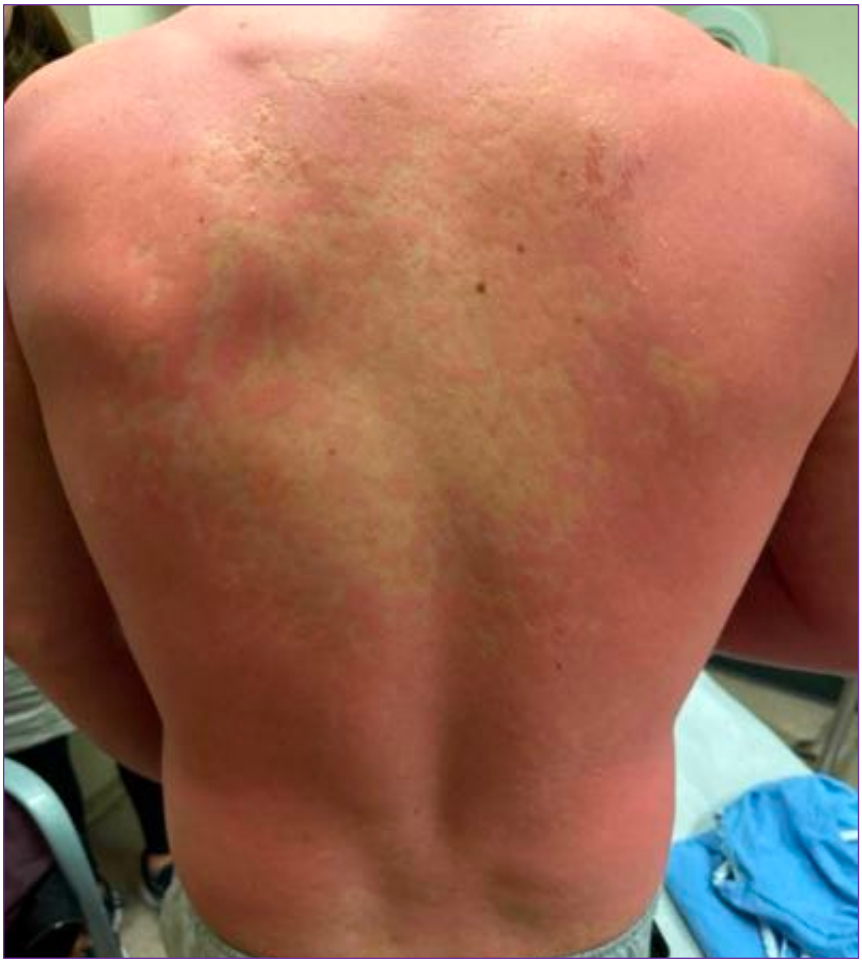

Figure 1. Pre-bimekizumab clinical photo

Given his lack of response to secukinumab and diffuse erythroderma, his pre-visit workup included flow cytometry to rule out Sezary syndrome the results of which were

unremarkable. He was prescribed acitretin (25mg daily) and received a loading dose of 320mg of bimekizumab.

He presented to the emergency department four days later with diffuse weakness, body aches, blurry vision and dizziness. A workup for cardiac and neurologic etiology was negative. Dermatology was consulted and, after assessment, his symptoms were attributed to a flare of his underlying chronic PRP, exacerbated by significant dehydration. He was discharged with out-patient pain management follow-up and at-home intravenous fluid supplementation.

At his one-month follow-up visit the patient was significantly improved and no longer in physical pain. He was able to walk unassisted, without the use of a cane. On physical exam his skin was clear of any salmon-colored hyperkeratotic patches (**Figures 2A and 2B**). His palms were significantly clear of cracking and desquamation. His scalp, which had been painful, erythematous and flaky on initial presentation (**Figure 3A**) was completely clear (**Figure 3B**). He reported increasing strength and improving exercise tolerance as well as persistent temperature dysregulation.

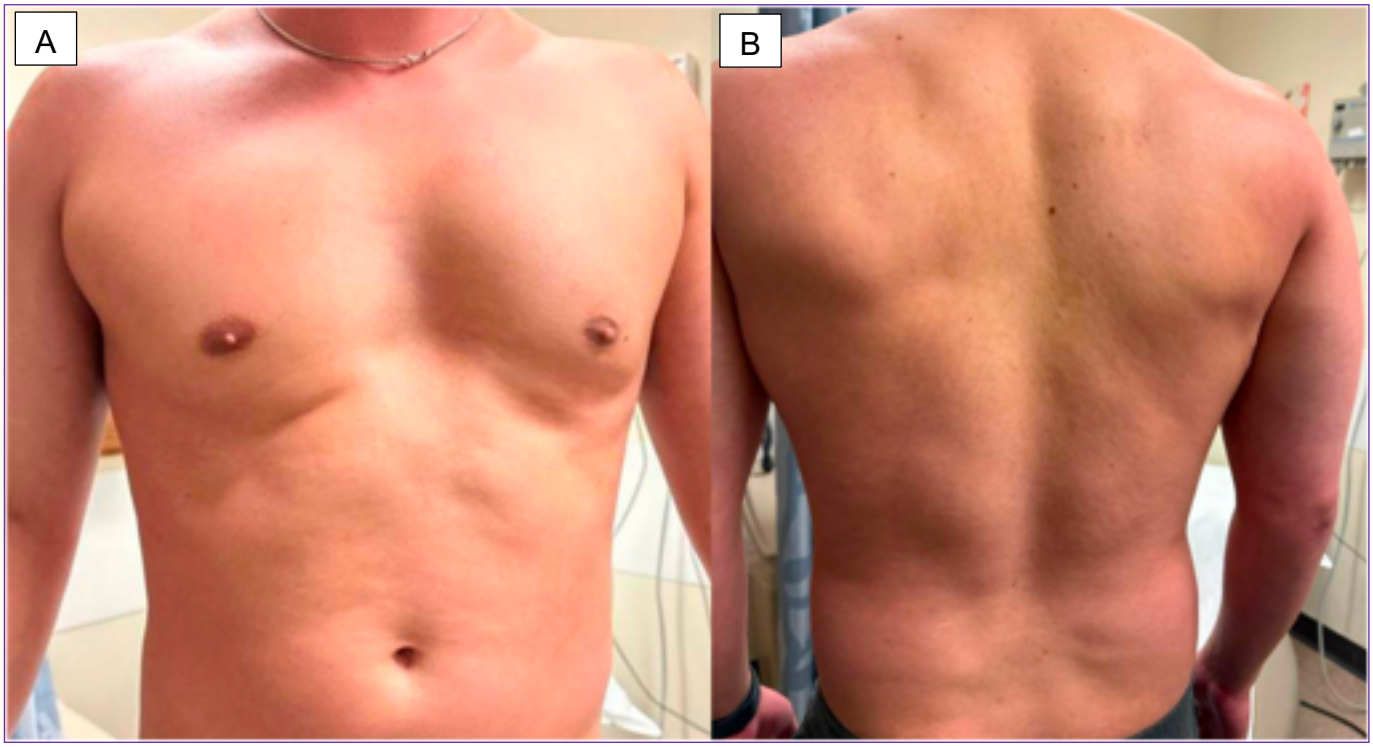

Figure 2. Resolution of pityriasis rubra pilaris at 4 weeks on bimekizumab. Clinical photos showing (A) chest and (B) back.

Despite the improvement in his skin symptoms, the patient remained anxious and fearful of panic attacks. He endorsed persistent sleep-cycle disturbance. The patient was agreeable to continuing bimekizumab monthly for another four months, and every other month thereafter.

DISCUSSION

In adult-onset PRP, approximately half of all patients achieve spontaneous resolution after three years on average while others can have life-long disease. PRP is associated

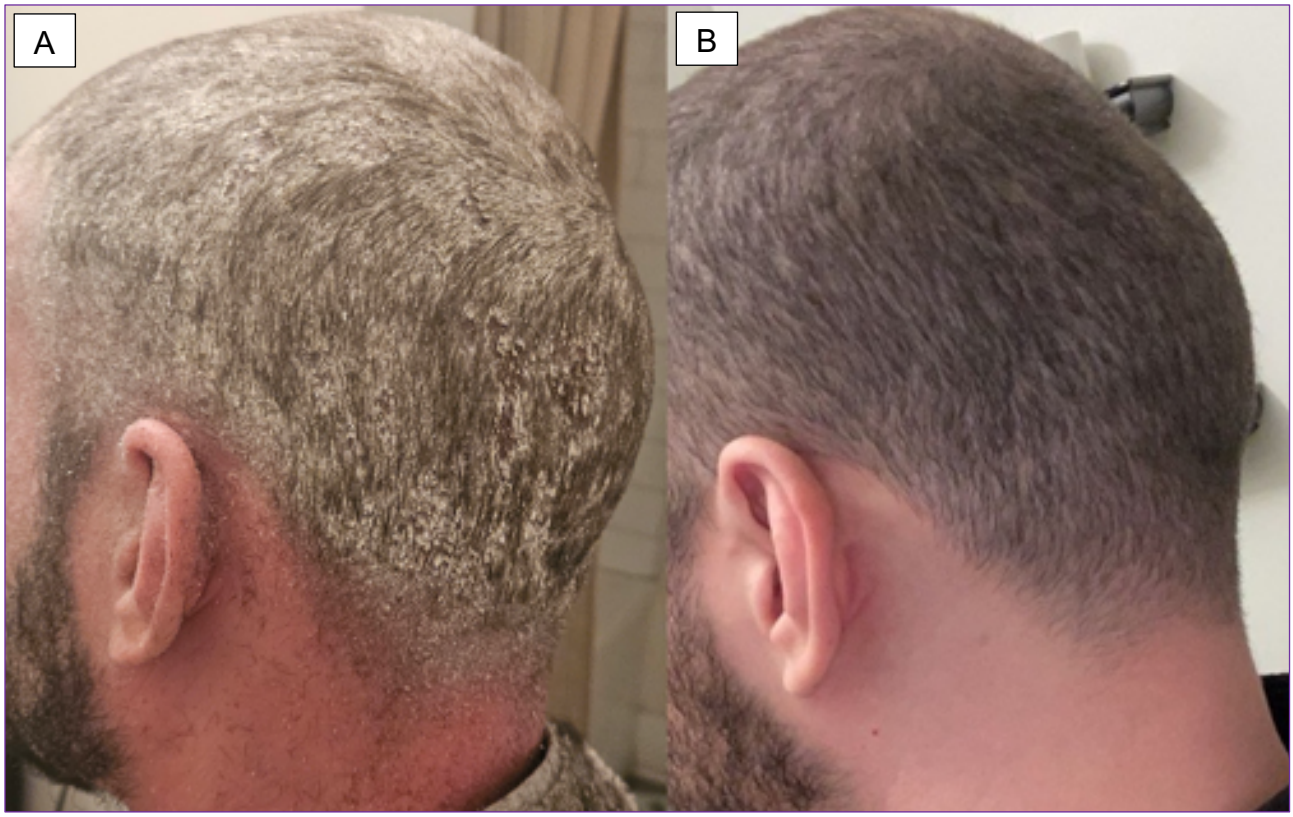

Figure 3. Clinical photo showing the condition of the patient's temporal/posterior scalp (A) prior to starting bimekizumab and (B) improved condition at 4 weeks on bimekizumab.

with severe itch and pain and severely impacts quality of life, with increased rates of depression and suicidal ideation. Plantar involvement can lead to difficulty walking as seen in this patient and widespread involvement can severely impact temperature regulation and is associated with skin dysesthesia.[2]

Methotrexate and acitretin are often used as first line treatments for PRP. More recent analyses have implicated dysregulation of the IL23/IL17 axis in PRP pathogenesis, and the efficacy of IL-17 and IL23 inhibitors in treatment supports this conclusion.[5] Unlike earlier biologics targeting IL-17, bimekizumab has activity on IL-17F in addition to IL-17AF and IL-17A.

In addition to the rapidity of improvement observed, this case is notable as the first published observation of PRP refractory to secukinumab, responsive to treatment with bimekizumab and acitretin.

To the authors knowledge, three cases of PRP treated with bimekizumab have been published. Although the Psoriasis Area and Severity Index (PASI) score tool is not validated for PRP, it is often used in the literature for this psoriasis-like disease. Kromer et al. describe a patient with PRP refractory to conventional, non-biologic, treatment. In that case, the patient achieved a PASI of 15 after 4 weeks and a PASI <5 after 24 weeks.[6] The second case, by Saad et al., reported erythrodermic PRP following SARS-CoV-2 vaccination. The patient failed to respond to treatment with oral and topical steroids or cyclosporine. After initiating bimekizumab, the patient achieved near total improvement after 8 months of treatment.[7]

The most recently reported case describes a patient who relapsed after initially successful treatment with topical glucocorticoids and acitretin. Four months after starting bimekizumab, the patient's skin was almost entirely clear.[8]

In light of the success of bimekizumab to treat PRP, we must reassess earlier reports of PRP treated with brodalumab[9-10], which targets IL-17RA the common receptor for both 17A and 17F. In their review of IL-17C and CCl20 protein levels in PRP response to IL-17A inhibition, Strunck et al. posited that treatment success with brodalumab raised the possibility of Il-17F's importance in PRP pathogenesis.[5] We believe that the efficacy of bimekizumab only further implicates IL-17F as a critical cytokine in PRP pathogenesis, particularly for patients who relapse after treatment with IL-17A inhibitors.

CONCLUSION

The psychosocial impact of PRP is highlighted by this case. Cases of PRP, especially those that are refractory to both conventional and second-line therapies, necessitate an interdisciplinary approach, often including psychiatric support. Taken collectively with earlier reports of bimekizumab's efficacy, it appears that dual inhibition of both IL-17a and IL-17F may be an effective means of controlling PRP. Further controlled studies are needed to better guide treatment for this challenging disease.

Conflict of Interest Disclosures: JO: No conflicts of interest to disclose. GD: No conflicts of interest to disclose. SA: No conflicts of interest to disclose. ML: Mark Lebwohl is an employee of Mount Sinai and receives research funds from: Abbvie, Arcutis, Avotres, Boehringer Ingelheim, Cara therapeutics, Clexio, Dermavant Sciences, Eli Lilly, Incyte, Inozyme, Janssen, Pfizer, Sanofi-Regeneron, and UCB, and is a consultant for Almirall, AltruBio Inc., Apogee, Arcutis, Inc., AstraZeneca, Atomwise, Avotres Therapeutics, Boehringer-Ingelheim, Bristol-Myers Squibb, Castle Biosciences, Celltrion, Corevitas, Dermavant Sciences, Dermsquared, Evommune, Inc., Facilitation of International Dermatology Education,Forte biosciences, Galderma, Genentech, Incyte, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer,Sanofi-Regeneron, Seanergy, Strata, Takeda,Trevi, and Verrica.

Funding: None

Corresponding Author:
Jeremy Orloff
5 East 98th St, 5th Floor,
New York, NY 10029
Email: jeremy.orloff@mountsinai.org

References:

1. Wang D, Chong VC, Chong WS, Oon HH. A Review on Pityriasis Rubra Pilaris. *Am J Clin Dermatol.* 2018;19(3):377-390.
2. Greiling TM, Brown F, Syed HA. Pityriasis Rubra Pilaris. StatPearls Publishing. StatPearls Web site. https://www.ncbi.nlm.nih.gov/books/NBK482436/. Published 2024. Updated April 2024. Accessed June 7, 2024.
3. Sood S, Akuffo-Addo E, Yeung J, Mufti A. Biologic treatment options for pityriasis rubra pilaris: An evidence-based systematic review. *J Am Acad Dermatol.* 2023;89(6):1306-1308.
4. BIMZELX (bimekizumab-bkzx) injection, for subcutaneous use [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761151s000lbl.pdf. Updated October 2023. Accessed June 6, 2024.
5. Strunck JL, Cutler B, Rajpal B, et al. Pityriasis Rubra Pilaris Response to IL-17A Inhibition Is Associated with IL-17C and CCL20 Protein Levels. *J Invest Dermatol.* 2022;142(1):235-239.e231.
6. Kromer C, Schön MP, Mössner R. Bimekizumab in refractory pityriasis rubra pilaris. *J Dtsch Dermatol Ges.* 2024;22(1):102-104.
7. Saad M, Bose R. Erythrodermic pityriasis rubra pilaris following SARS-CoV-2 vaccination treated with bimekizumab. *JAAD Case Rep.* 2023;42:7-11.
8. Rak K, Goebeler M, Kerstan A. Rapid improvement of severe pityriasis rubra pilaris

upon treatment with bimekizumab. *Int J Dermatol.* 2024.
9. De Rosa A, Gambardella A, Licata G, Alfano R, Argenziano G. Successful treatment of Pityriasis rubra pilaris with brodalumab. *Australas J Dermatol.* 2020;61(2):e249-e251.
10. Khan U, Shihab, N., Phelps, R. G., & Lebwohl, M. Successful Treatment of Pityriasis Rubra Pilaris with Brodalumab. *SKIN The Journal of Cutaneous Medicine.* 2020;4(2):139-142.