doi:10.36849/JDD.8381

Rapid Remission of Plaque Psoriasis With Bimekizumab Treatment

Rama Abdin BS,[a] Rola Gharib MD,[b,c] Christopher G. Bunick, MD PhD,[d] Naiem T. Issa MD PhD[e,f,g,h]

[a]Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, FL
[b]Dermatology Center for Skin Health, PLLC, Morgantown, WV
[c]West Virginia Research Institute, Morgantown, WV
[d]Department of Dermatology and Program in Translational Biomedicine, Yale University School of Medicine, New Haven, CT
[e]Forefront Dermatology, Vienna, VA
[f]Issa Research and Consulting, LLC, Springfield, VA
[g]University of Miami Miller School of Medicine Dr. Phillip Frost Department of Dermatology & Cutaneous Surgery, Miami, FL
[h]The George Washington University School of Medicine and Health Sciences, Washington, DC

ABSTRACT

Bimekizumab is a novel humanized bispecific monoclonal immunoglobulin G1 (IgG1) antibody that dually inhibits both IL-17A and IL-17F. Investigation of the pivotal role of IL-17A, and more recently, IL-17F, in the pathogenesis of psoriasis has underscored the utility of biologics targeting these cytokines in the treatment of the disease. Treatments include the anti-IL-17 biologics specifically targeted against IL-17A (secukinumab and ixekizumab) or its receptor (brodalumab). Recent clinical trials proved the efficacy and safety of bimekizumab in the treatment of moderate-to-severe plaque psoriasis and even showed it to be superior to other psoriasis biologic treatments in regards to efficacy and rapidity of response. These are important factors to consider when discussing treatment options with patients as psoriasis patients commonly desire fast-acting results. In this case, we describe clearance of moderate-to-severe plaque psoriasis within 72 hours of treatment with bimekizumab, one of the fastest reported clearance times in the medical literature.

J Drugs Dermatol. 2024;23(8):694-696. doi:10.36849/JDD.8381

INTRODUCTION

Some psoriatic disease topical treatments, such as coal tar and salicylic acid, have stood the test of time, being used consistently over the past century.[1] However, the landscape of systemic medications used to treat psoriasis has undergone significant evolution in a fraction of the time. Since their first approval by the US Food and Drug Administration (FDA) in 2003, biologics have transformed the treatment of moderate-to-severe psoriasis because of their high degree of efficacy.[1] These include T-cell targeted agents, tumor necrosis factor (TNF)-α inhibitors, interleukin (IL)-17 inhibitors, IL-12/23 inhibitors, and IL-23 inhibitors. The newest approved biologic in the United States is bimekizumab, a selective inhibitor of both IL-17A and IL-17F, which has shown significant, long-term clinical efficacy in randomized clinical trials.[2,3,4] In fact, it has even been shown to be superior to other psoriasis biologic treatments, including IL-17A, IL-12/23, and TNF-α inhibition.[5–7]

The choice of psoriatic disease therapy is patient-dependent and involves the consideration of many factors, including patient preference. When queried on what aspects of treatment they valued, many psoriasis patients value effectiveness, rapidity of response, and longevity of response the most.[8] As such, dermatologists should focus on providing patients with treatment options that are rapid acting, effective while safe, and long-lasting. Two studies investigating the rapidity of the response of biologic treatments for moderate-to-severe psoriasis found that IL-17 inhibitors brodalumab and ixekizumab yielded the overall fastest response rate.[9,10] Utilizing Bayesian and Frequentist network meta-analyses of phase 3, double-blind, randomized, controlled trials testing IL-17, IL-12/-23, IL-23, and TNF inhibitors for the treatment of moderate-to-severe psoriasis, Warren et al found more rapid therapeutic effects on Psoriasis Area and Severity Index (PASI) 75 and 90 response rates at weeks 2, 4, and 8 with ixekizumab and brodalumab.[9] Egeberg et al similarly found that brodalumab and ixekizumab yielded the shortest time to achieve PASI 90 in 25% and 50% of patients in their systematic review of phase 3 clinical trials of IL-17 and IL-23 inhibitors for moderate-to-severe psoriasis in adult patients.[10] However, it is important to note that these studies were performed prior to the approval of bimekizumab. Since then, bimekizumab has shown in head-to-head clinical trials to be more rapid-acting than other psoriasis treatments.[5-7] Herein, we describe a case of treatment naïve moderate-to-severe plaque psoriasis with significant clearance within 72 hours of treatment with bimekizumab.

Case Description

A 38-year-old skin of color male presented with a 2-year history of treatment naïve plaque psoriasis. He reported moderate pruritus of the affected areas which interfered with his daily activities and quality of life. On physical exam, he had 20% body surface area involvement, including the trunk, bilateral lower extremities (Figure 1A), upper extremities (Figure 2A), and forehead (Figure 3A). The patient shared his desire for an effective systemic treatment and did not want to pursue topical therapy. Bimekizumab treatment was initiated. He reported his itch to be negligible approximately 6 to 12 hours after the injection. Within 72 hours after the initial dose (given as two subcutaneous syringes of 160 mg each, both injected into the arms), the patient experienced a remarkable clearance of his psoriasis (PASI 90) (Figure 1B, 2B, and 3B). He achieved PASI 100 at day 7 (1 week) and rated his itch score as 0 with only post-inflammatory hyperpigmentation remaining (Figure 1C, 2C, and 3C).

FIGURE 1. Psoriasis of the lower extremities at (A) day 0 (B) day 3 (72 hours after treatment with two subcutaneous injections of 160 mg bimekizumab into the arms), and (C) day 7.

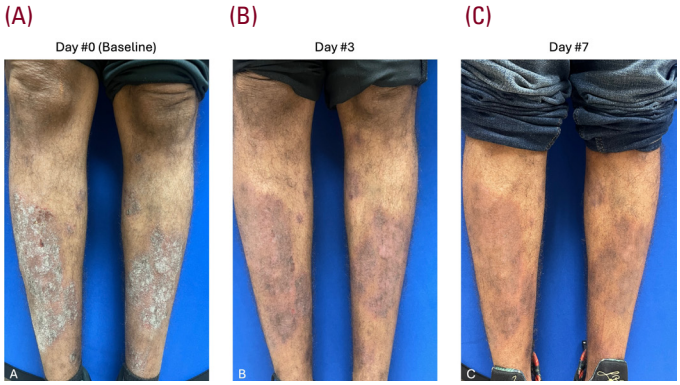


FIGURE 2. Psoriasis of the left forearm at (A) day 0 (B) day 3 (72 hours after treatment with two subcutaneous injections of 160 mg bimekizumab into the arms), and (C) day 7.

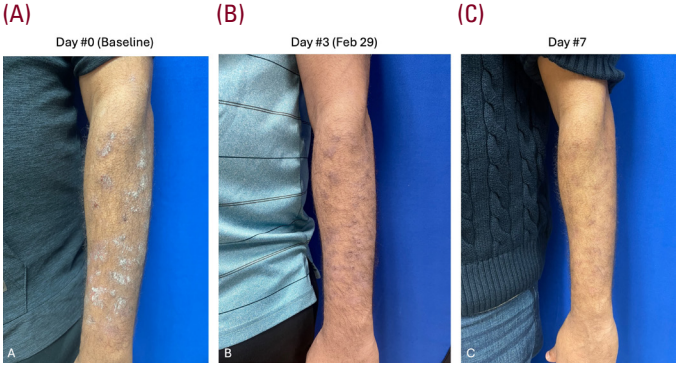
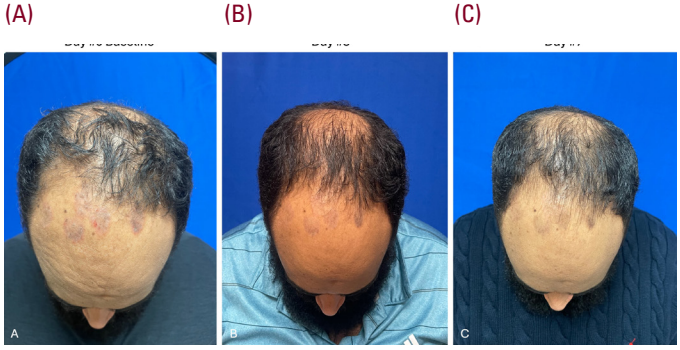


FIGURE 3. Psoriasis of the forehead at (A) day 0 (B) day 3 (72 hours after treatment with two subcutaneous injections of 160 mg bimekizumab into the arms), and (C) day 7.



DISCUSSION

Bimekizumab is a novel humanized bispecific monoclonal immunoglobulin G1 (IgG1) antibody that dually inhibits IL-17A and IL-17F.[2,11] Historically, the role of IL-17A in the pathogenesis and treatment of psoriasis has been the point of focus; as such, prior to the approval of bimekizumab, the anti-IL-17 biologics specifically targeted only IL-17A (secukinumab and ixekizumab) or its receptor (brodalumab).[2,11] However, there has been recent interest in the role of IL-17F in the pathogenesis and treatment of the disease given its structural homology with IL-17A. Indeed, both IL-17 isomers bind to the same complex of IL-17RA and IL-17RC.[11] Although IL-17F has been regarded as less biologically active than IL-17A, given its decreased binding affinity for the IL-17RA/RC complex, it is ~30-fold more abundant than IL-17A in the skin and its role in the pathogenesis of psoriasis has been described.[11,12] Therefore, it is not surprising that the dual inhibition of IL-17A and IL-17F offered by bimekizumab provides more effective and rapid-acting clinical results than its biologic comparators. The molecular and structural basis for bimekizumab inhibition of IL-17A and IL-17F was also recently reported.[13]

Regarding the specific studies on bimekizumab, BE ABLE 1 (NCT02905006) is a 12-week multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-ranging, phase IIb study investigating the efficacy of bimekizumab compared to placebo in patients with moderate-to-severe psoriasis. Patients were randomized to receive bimekizumab every 4 weeks at doses of 64 mg, 160 mg, 160 mg (with 320 mg loading dose at baseline), 320 mg, 480 mg, or placebo over 12 weeks. A statistically significant dose-response was noted in regards to PASI 90 response at week 12 (primary endpoint), and this was achieved by significantly more bimekizumab-treated patients compared to placebo-treated patients (46.2% to 79.1% vs 0%, $P<0.0001$ for all dose comparisons).[2] Given its proven clinical efficacy, the next question was how bimekizumab fared compared to other IL-17 inhibitors. BE RADIANT (NCT03536884) is a 48-week multicenter, randomized, double-blind, secukinumab-controlled, parallel-group, phase IIIb study comparing the efficacy of bimekizumab versus secukinumab in

the treatment of moderate-to-severe plaque psoriasis.[6] Patients were randomized to receive bimekizumab 320 mg every 4 weeks or secukinumab 300 mg weekly to week 4 followed by once every 4 weeks. At week 16, patients in the bimekizumab group underwent rerandomization to receive a maintenance dose of bimekizumab (320 mg) either once every 4 weeks or once every 8 weeks to week 48; patients in the secukinumab group continued to receive secukinumab to week 48. By week 16, 61.7% of patients treated with bimekizumab achieved PASI 100 response (the primary endpoint) compared to 48.9% of those treated with secukinumab (adjusted risk difference, 12.7 percentage points; 95% confidence interval (CI), 5.8 to 19.6, $P<0.001$ for noninferiority and superiority). In addition, after just one dose of bimekizumab (week 4), 71.0% of patients achieved a PASI 75 response compared to 47.3% of secukinumab-treated patients at this time point (adjusted risk difference, 23.7 percentage points; 95% CI, 17.0 to 30.4, $P<0.001$). The superiority and noninferiority of bimekizumab compared to control was maintained through the period of 48 weeks. The authors postulate two theories as to why better response rates were observed. One theory suggests a higher binding affinity of bimekizumab for IL-17A than secukinumab in vitro. The second theory is that dual inhibition of IL-17A and IL-17F is superior to IL-17A inhibition alone. Either one of these two theories is plausible, but likely it is a combination of the two that explains the observed differences in response.[6] Treatment with bimekizumab in clinical trials was associated with oral candidiasis; however, our patient has not experienced candidiasis to date.[2,6]

CONCLUSION

In conclusion, our case presents one of the fastest documented clearances of moderate-to-severe plaque psoriasis in the medical literature. Our patient received bimekizumab loading doses and achieved PASI 90 and PASI 100 at 72 hours and 1 week, respectively, with associated itch resolution. One other report highlights rapid clearance albeit at two weeks.[14] These findings have real-world implications, as our patient's quality of life benefited immensely in the clearance of his disease and associated symptoms after the initial dose of bimekizumab. Notably, there is no formally reported data on PASI scores with any biologic at time points less than 1 week. Given the dramatically effective and rapid clearance in our treatment-naïve patient, we encourage other investigators to report their experience with bimekizumab as a rapidly effective treatment for moderate-to-severe plaque psoriasis.

DISCLOSURES

NTI has received funding from the following entities either as a speaker, consultant, advisor, or investigator: Abbvie, Bristol Myers Squibb, Castle Biosciences, Dermavant Sciences, DermTech, Galderma, Incyte, Journey, LEO Pharma, Lilly, National Eczema Association, Ortho Dermatologics, Pfizer, RBC Consultants, Verrica Pharmaceuticals, and WebMD. CGB has served as an investigator for AbbVie, Almirall, Daiichi Sankyo, LEO Pharma, Ortho Dermatologics, Sun Pharma, Timber, and Palvella; a consultant for AbbVie, Almirall, Apogee, Arcutis, Eli Lilly, EPI Health/Novan, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Sanofi-Regeneron, and UCB; and a speaker for and received honoraria from Allergan, Almirall, LEO Pharma, and UCB. RG discloses consulting, speaking, and clinical trials for Abbvie, Amgen, Pfizer, Mindera, Sanofi, Regeneron, Cara Therapeutics, Argenx, BMS, Galderma, Arcutis, AstraZeneca, Leo, Lilly, UCB, and Incyte.

REFERENCES

1. Reid C, Griffiths CEM. Psoriasis and treatment: past, present and future aspects. *Acta Derm Venereol.* 2020;100(3):adv00032. doi:10.2340/00015555-3386
2. Papp KA, Merola JF, Gottlieb AB, et al. Dual neutralization of both interleukin 17A and interleukin 17F with bimekizumab in patients with psoriasis: results from BE ABLE 1, a 12-week randomized, double-blinded, placebo-controlled phase 2b trial. *J Am Acad Dermatol.* 2018;79(2):277-286.e10. doi:10.1016/j.jaad.2018.03.037
3. Blauvelt A, Papp KA, Merola JF, et al. Bimekizumab for patients with moderate to severe plaque psoriasis: 60-week results from BE ABLE 2, a randomized, double-blinded, placebo-controlled, phase 2b extension study. *J Am Acad Dermatol.* 2020;83(5):1367-1374. doi:10.1016/j.jaad.2020.05.105
4. Gordon KB, Foley P, Krueger JG, et al. Bimekizumab efficacy and safety in moderate to severe plaque psoriasis (BE READY): a multicentre, double-blind, placebo-controlled, randomised withdrawal phase 3 trial. *Lancet.* 2021;397(10273):475-486. doi:10.1016/S0140-6736(21)00126-4
5. Reich K, Papp KA, Blauvelt A, et al. Bimekizumab versus ustekinumab for the treatment of moderate to severe plaque psoriasis (BE VIVID): efficacy and safety from a 52-week, multicentre, double-blind, active comparator and placebo controlled phase 3 trial. *Lancet.* 2021;397(10273):487-498. doi:10.1016/S0140-6736(21)00125-2
6. Reich K, Warren RB, Lebwohl M, et al. Bimekizumab versus secukinumab in plaque psoriasis. *N Engl J Med.* 2021;385(2):142-152. doi:10.1056/NEJMoa2102383
7. Warren RB, Blauvelt A, Bagel J, et al. Bimekizumab versus adalimumab in plaque psoriasis. *N Engl J Med.* 2021;385(2):130-141. doi:10.1056/NEJMoa2102388
8. Gorelick J, Shrom D, Sikand K, et al. Understanding treatment preferences in patients with moderate to severe plaque psoriasis in the USA: results from a cross-sectional patient survey. *Dermatol Ther (Heidelb).* 2019;9(4):785-797. doi:10.1007/s13555-019-00334-1
9. Warren RB, See K, Burge R, et al. Rapid response of biologic treatments of moderate-to-severe plaque psoriasis: a comprehensive investigation using Bayesian and frequentist network meta-analyses. *Dermatol Ther (Heidelb).* 2020;10(1):73-86. doi:10.1007/s13555-019-00337-y
10. Egeberg A, Andersen YMF, Halling-Overgaard AS, et al. Systematic review on rapidity of onset of action for interleukin-17 and interleukin-23 inhibitors for psoriasis. *J Eur Acad Dermatol Venereol.* 2020;34(1):39-46. doi:10.1111/jdv.15920
11. Iznardo H, Puig L. Dual inhibition of IL-17A and IL-17F in psoriatic disease. *Ther Adv Chronic Dis.* 2021;12:20406223211037846. doi:10.1177/20406223211037846
12. Kolbinger F, Loesche C, Valentin MA, et al. β-Defensin 2 is a responsive biomarker of IL-17A-driven skin pathology in patients with psoriasis. *J Allergy Clin Immunol.* 2017;139(3):923-932.e8. doi:10.1016/j.jaci.2016.06.038
13. Adams R, Bunick C, Lawson A, et al. Crystal structure of bimekizumab fab fragment in complex with IL-17F provides molecular basis for dual IL-17A and IL-17F inhibition. *Journal of Investigative Dermatology.* Published online 2024.
14. Vender R. Dermsquared. Rapid and sustained clearance of severe psoriasis with dual inhibition of IL-17A and IL-17F. Available at: https://dermsquared.com/case-studies/rash-decisions-rapid-sustained-clearance-severe-psoriasis-il-17-inhibition. Accessed April 6, 2024.

AUTHOR CORRESPONDENCE

Naiem T. Issa MD PhD

E-mail:..... drnaiemissa@gmail.com