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CASE REPORT

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The Role of Simultaneous Janus Kinase Inhibitor and Biologic Therapy Use for Refractory Atopic Dermatitis

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INTRODUCTION

Atopic dermatitis (AD) is a common inflammatory skin disease that can significantly affect a patient's quality of life. The pathogenesis of AD is multifactorial and is associated with the dysregulation of type 2 helper T cells and increased production of interleukins 4, 13, and 31.[1] A recent study found that the global 1-year period AD prevalence rate and affected population were estimated to be 2.6% and 204.05 million people, respectively.[2] Common treatments for this condition include topical steroids, emollients, calcineurin inhibitors, narrowband UVB phototherapy, methotrexate, cyclosporine, biologic therapies, and Janus kinase inhibitors (JAKi), among others.[1,3] While combination biologic therapy with dupilumab and various JAKi has been utilized previously, we report a unique case of a patient treated with lebrikizumab in combination with upadacitinib after unsuccessful treatment with upadacitinib 30 mg monotherapy.

An 18-year-old male presented to our clinic with a two-year history of well-demarcated eczematous plaques throughout the chest, neck, and lateral arms. At the time, he was treated with dupilumab 300 mg injections every 2 weeks and desoximetasone cream as needed without adequate treatment response. After initiating upadacitinib 15 mg for one month, he experienced mild improvement of the eczematous plaques and was then started on upadacitinib 30 mg. While on upadacitinib 30 mg, the patient reported gradual clearing of his eczematous plaques throughout the chest, neck, and arms. Six months later, he experienced an AD flare resulting in eczematous patches throughout the trunk, upper extremities, and periorbital area that did not resolve with the upadacitinib 30 mg maintenance dose (Figures 1 and 2). His presentation was clinically consistent with an AD flare, and fungal cultures were taken from the chest and axilla to evaluate for tinea corporis, which were negative. Lebrikizumab was added at a loading dose of 500 mg at weeks 0 and 2 followed by the maintenance dose of 250 mg injection every two weeks. While on the combined regimen of upadacitinib and lebrikizumab, he reported significant improvement and clearance of the eczematous patches throughout his body. He continues to remain clear on the combination maintenance dose of lebrikizumab 250 mg and upadacitinib 30 mg (Figures 1 and 2).

FIGURE 1. Multiple eczematous patches on the upper L arm while on treatment with upadacitinib 30 mg (left). Significant clearance of eczematous patches on the upper L arm after initiation of lebrikizumab and continuation of upadacitinib 30 mg.

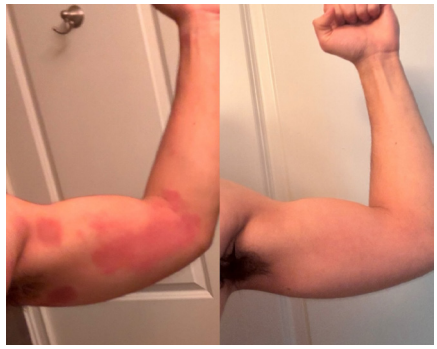
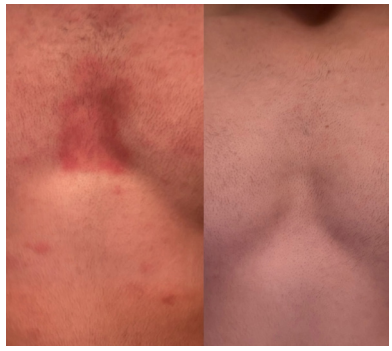


FIGURE 2. Eczematous patch on central chest while on treatment with upadacitinib 30 mg (left). Significant clearance of eczematous patches on the central chest after initiation of lebrikizumab and continuation of upadacitinib 30 mg.



As standalone therapies for AD, lebrikizumab, and upadacitinib demonstrate robust treatment responses against AD. Lebrikizumab is an IgG4 monoclonal antibody that targets and binds interleukin-13, a key cytokine involved in the pathogenesis of AD.[1] The ADvocate1 and ADvocate 2 trials demonstrated a significantly greater number of lebrikizumab-treated patients achieving an IGA score of 0 or 1 with a reduction of ≥2 points

from baseline compared to placebo.[1] EASI-75 and EASI-90 were evaluated at week 16 within these trials. A greater percentage of patients treated with placebo compared to lebrikizumab (500 mg loading dose at week 0 and 2, followed by 250 mg maintenance dose) failed to achieve EASI-75 at week 16 in trials 1 and 2; 83.8% vs 41.2% in trial 1 and 81.9% vs 47.9% in trial 2.[1] A similar trend was observed for EASI-90 at week 16, with a higher proportion failing to achieve EASI-90 in the placebo-treated group compared to the lebrikizumab-treated group: 91% vs 61.7% in trial 1 and 90.5% vs 69.3% in trial 2.[1]

Furthermore, upadacitinib is a JAKi that selectively targets the JAK1 pathway with strong data supporting its efficacy in achieving EASI-75 by week 16.[4] A network meta-analysis found that among the various JAKi, the odds for achieving EASI-75 compared to placebo was the highest with upadacitinib 30 mg monotherapy (OR) = 18.90 [95% confidence interval (CI): 13.94–25.62].[4] Pivotal data from the Measure Up 1 trial demonstrated that a greater percentage of patients treated with placebo failed to achieve EASI-75 and EASI-90 compared to those treated with upadacitinib.[5] In Measure Up 1, the percentage of patients treated with upadacitinib 15 mg, 30 mg, and placebo who failed to achieve the EASI-75 endpoint by week 16 was 30%, 20%, 84%, respectively.[5] For the same treatment cohorts failing to achieve EASI-90 endpoint at week 16, the percentages were 46.9%, 34.2%, and 91.9%, respectively.[5]

Existing literature has highlighted the utility of combination JAKi and biologic therapy for AD. A systematic review found that dupilumab has been commonly used in conjunction with tofacitinib and baricitinib to treat AD and secondary diseases, including psoriasis and urticaria.[6] Of the 25 patients in the dual JAKi and biologic therapy cohort, 96% improved after treatment.[6] Although this study did not differentiate between adverse events experienced by the dual biologic-treated group and the biologic/JAKi-treated group, the overall rates of adverse events were low. Another case series of 6 patients highlighted the utility of JAKi as a rescue therapy for dupilumab-treated patients experiencing a breakthrough AD flare.[7] All 6 patients were treated with either upadacitinib or tofacitinib, resulting in significantly reduced IGA scores and BSA involvement after the addition of JAKi. Additionally, none of the 6 patients included in the cohort experienced any adverse events from concomitant biologic and JAKi treatment. One case report describes a patient with refractory AD who failed multiple therapeutic regimens, including cyclosporine, methotrexate, tralokinumab monotherapy, dupilumab monotherapy, and upadacitinib monotherapy.[8] While the patient experienced moderate but inconsistent improvement on the upadacitinib 30 mg monotherapy, he demonstrated sustained improvement when treated concomitantly with upadacitinib 30 mg and tralokinumab injections.[8]

Although JAKi such as upadacitinib have great efficacy in treating AD, they are associated with various adverse events and include warnings for infection, malignancy, thrombosis, or major adverse cardiovascular events.[8] Within the medication package inserts for these JAKi, the manufacturer specifically advises against their concomitant use with biologic therapies.[9] This is largely due to the theoretical concern for increased risk of immunosuppression given their dual immunomodulatory effects.[10] However, in previous case series and reports, patients treated concurrently with both biologics and JAK inhibitors did not experience many adverse events, if any.[6,7] Furthermore, our patient continues to remain clear on both upadacitnib and lebrikizumab, without experiencing any adverse events. Notably, the package inserts for JAKis specifically state that they can be used in combination with methotrexate despite it being associated with many side effects, including reactivation of latent tuberculosis and development of lymphomas[11] compared to biologic therapies. The combination of therapies is presumably allowed because JAKis were tested in conjunction with methotrexate instead of biologics for inflammatory arthritis.

CONCLUSION

In conclusion, this case further highlights the safety and efficacy of biologic and JAKi therapy for AD refractory to monotherapy treatments. Notably, our patient had an inadequate response to upadacitinib monotherapy and was subsequently started on lebrikizumab, unlike most existing reports of patients failing a biologic monotherapy prior to the initiation of JAKi rescue therapy. Additionally, larger cohort studies are warranted to further investigate the safety and efficacy of dual biologic and small-molecule therapy.

DISCLOSURES

Lau has no conflicts of interest to disclose. Golant is an employee of Mount Sinai and reports personal fees from Abbvie, Amgen, Arcutis, Bristol Meyers Squibb, Dermavant, Galderma, Incyte, Janssen, Eli Lilly and Company, Ortho Dermatologics, Pfizer, Regeneron, and Sanofi. 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 Aikium, Almirall, AltruBio Inc., Amgen, 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, Goodrx-Mayne, Meiji Seika Pharma, Mindera, Mirium Pharmaceuticals, Oruka, Pfizer,Sanofi-Regeneron, Revolo, Seanergy, Strata, Sunpharma,Takeda,Trevi, and Verrica.

REFERENCES

1. Silverberg JI, Guttman-Yassky E, Thaçi D, et al. Two phase 3 trials of lebrikizumab for moderate-to-severe atopic dermatitis. *N Engl J Med.* 2023;388(12):1080-1091. doi:10.1056/NEJMOA2206714
2. Tian J, Zhang D, Yang Y, et al. Global epidemiology of atopic dermatitis: a comprehensive systematic analysis and modelling study. *Br J Dermatol.* 2023;190(1):55-61. doi:10.1093/BJD/LJAD339.
3. Guttman-Yassky E, Renert-Yuval Y, Brunner PM. Atopic dermatitis. *Lancet.* 2025;405(10478):583-596. doi:10.1016/S0140-6736(24)02519-4
4. Müller S, Maintz L, Bieber T. Treatment of atopic dermatitis: recently approved drugs and advanced clinical development programs. *Allergy.* 2024;79(6):1501-1515. doi:10.1111/ALL.16009.
5. Guttman-Yassky E, Teixeira HD, Simpson EL, et al. Once-daily upadacitinib versus placebo in adolescents and adults with moderate-to-severe atopic dermatitis (Measure Up 1 and Measure Up 2): results from two replicate double-blind, randomised controlled phase 3 trials. *Lancet.* 2021;397(10290):2151–2168. doi:10.1016/S0140-6736(21)00588-2.
6. Metko D, Mehta S, McMullen E, Lam M, Croitoru D. Dual biologic or small-molecule therapy in patients with atopic dermatitis: a systematic review. *Clin Exp Dermatol.* 2024;50(1):155-156. doi:10.1093/CED/LLAE308.
7. Shahriari N, Strober B, Shahriari M. JAK-inhibitors as rescue therapy in dupilumab-refractory severe atopic dermatitis: a case series of 6 patients. *JAAD Case Rep.* 2023;33:81. doi:10.1016/J.JDCR.2023.01.020.
8. Lansang RP, Zhao IX, Lansang P. Atopic dermatitis treated with tralokinumab and upadacitinib combination therapy: a case report. *SAGE Open Med Case Rep.* 2023;11. doi:10.1177/2050313X231180766.
9. RINVOQ. RINVOQ® (upadacitinib) safety data. Available at: https://www.rinvoqhcp.com/dermatology/safety#patient-types. Accessed April 5, 2025.
10. Davis JS, Ferreira D, Paige E, et al. Infectious complications of biological and small molecule targeted immunomodulatory therapies. *Clin Microbiol Rev.* 2020;33(3):1–117. doi:10.1128/CMR.00035-19
11. Methotrexate. In: StatPearls [Internet]. National Center for Biotechnology Information (US); 2025. Available at: https://www.ncbi.nlm.nih.gov/books/NBK556114/. Accessed April 7, 2025.

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