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Dual Therapy for Atopic Dermatitis: Lebrikizumab and JAK Inhibitors Used in Tandem for Treatment-Resistant Cases

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INTRODUCTION

Atopic dermatitis (AD) is an inflammatory skin disease marked by intense pruritus, impaired skin barrier function, and recurrent flares.[1] Its prevalence in the United States is estimated to range from 8.7% to 18.1%, and an estimated 2.6% of individuals are affected by AD globally.[2,3] Disease burden can manifest in various ways, including lower quality-of-life scores, reduced sleep quality, and increased workplace absenteeism.[4,5]

There are now many FDA-approved treatments for moderate-to-severe AD, including biologic medications like dupilumab, tralokinumab, nemolizumab, and lebrikizumab, and oral agents such as the JAK inhibitors upadacitinib and abrocitinib. While biologics and JAK inhibitors show robust efficacy as monotherapy in clinical trials, in real-world practice, cases of recalcitrant AD often remain inadequately controlled on monotherapy alone. To date, little is known about the use of dual therapy with lebrikizumab and JAK inhibitor therapy.

We present a small cohort of patients treated with dual therapy, lebrikizumab and either upadacitinib or abrocitinib for moderate-to-severe recalcitrant AD inadequately controlled on monotherapy alone. This study aims to provide real-world evidence on the efficacy and safety of lebrikizumab combined with JAK inhibitors, a regimen not yet formally evaluated in published literature.

MATERIALS AND METHODS

We performed a retrospective chart review of patients who received lebrikizumab and a JAK inhibitor therapy simultaneously for the treatment of atopic dermatitis at Mount Sinai Dermatology from September 2024 to September 2025. Variables extracted included demographic data, physical exam description, comorbidities, therapeutic regimen, dosing, and temporal data regarding treatment. Descriptive statistics were reported as n (%), mean ± SD, and median (IQR).

Body surface area (BSA) was used as the primary indicator of treatment response. When BSA was available, improvement was considered a decrease in BSA between the initiation of dual therapy and one-month follow up, four-month follow up, or both. If BSA data were not available, physician assessment from clinical notes was utilized to determine response.

RESULTS

There were 9 patients with an average age of 28.11 ± 10.55 years. The cohort was predominantly female (78%, n=7) and Caucasian (56%, n=5). The median duration of monotherapy was 413 days (IQR: 273-549 days), with a range from 178 to 1225 days (mean: 509.44 ± 360.5). The median duration of dual therapy was 232 days (IQR: 64-264 days), with a range of 30 to 325 days (mean: 180 days ± 107.27). Of the 9 patients on dual therapy, at the last follow up 44% (n=4) continued treatment and 33% discontinued (n=3), while two patients transitioned from upadacitinib and lebrikizumab to abrocitinib and lebrikizumab (Table 1).

Of the three patients who discontinued dual therapy, 2 were due to insurance coverage issues, and only one was due to insufficient response to the medication regimen. It is also important to note that of the 2 patients who discontinued treatment for alternative reasons (insurance), one saw improvement while on dual therapy.

Two patients were placed on an alternative combination of lebrikizumab and a JAK inhibitor. Both started with upadacitinib/lebrikizumab. One was switched directly to abrocitinib/lebrikizumab, and the other started this regimen after a long period of lebrikizumab monotherapy (186 days). Notably, the patient who had a period of monotherapy between dual lebrikizumab/JAK inhibitor combinations initially discontinued upadacitinib/lebrikizumab due to JAK-induced acne despite a positive clinical response (Subject 4). This patient went on to experience significant flaring on lebrikizumab alone, and therefore abrocitinib was added to lebrikizumab therapy with the goal of controlling the acute state.

Positive treatment response was seen in most of the cohort as a result of dual therapy (n=6/9, 67%). Of those who did not see a positive response (n=3), one had a worsening BSA, another saw a plateau in response, leading them to switch to a different combination of lebrikizumab/JAK inhibitor, and the third had an inadequate response to treatment.

Adverse events were limited and included known side effects of medications used, such as nausea or JAK inhibitor-induced acne. In only one instance did side effects contribute to the decision to discontinue dual regimen, otherwise the cohort had adequate tolerability of the treatment. No severe adverse events were seen.

TABLE 1.

Dual Therapy Patients Characteristics

#	Age at Start of dual therapy	Sex	Dual Regimen Doses/Frequency	Previously Attempted Therapies	Duration of dual therapy (days)	Clinical Response			Response	Adverse Events	Continues Presently?	If discontinued, reason for dis-continuation?	If discontinued, new medication prescribed?
						BSA at 1st therapy start	BSA at 2nd therapy start	BSA at follow-up					
1	27	F	200 mg Abrocitinib Lebrikizumab q 2 weeks	Topical steroids, crisaborole, dupilumab, ruxolitinib	246	30%	10%	<5%	+	JAK-induced acne	Y	--	--
2	17	F	30 mg Upadacitinib Lebrikizumab q 2 weeks	dupilumab topical steroids, upadacitinib 15 mg, anti-histamines, tacrolimus ointment	228	>70%	NA	0%	++*	None	Y	--	--
3	53	M	100 mg Abrocitinib Lebrikizumab q 2 weeks	tacrolimus ointment, topical steroids, dupilumab, roflumilast, tacrolimus ointment	232	NA	5%	NA	-**	None	N	Insufficient re-sponse, "BSA worsening" ac-cording to rec-ords	Abroctinib + Tralokinumab
4	29	F	Upadacitinib alternating 30 mg and 15 mg daily Lebrikizumab q 2 weeks Abrocitinib 200 mg Lebrikizumab q 10 days	Tacrolimus ointment, dupilumab, antihistamines, topical steroids	48	10%	10%	4%	+	JAK-induced acne	Switched to different JAK/ lebrikizumab combination	To help decrease JAK-induced acne To taper off d/t positive clinic response	Abrocitinib+ Lebrikizumab
5	23	F	Upadacitinib 15 mg every other day, every 2 days, every 3 days, weekly Lebrikizumab q 4 weeks	Dupilumab, topical steroids	325	NA	4%	<1%	+	None	Y	--	--
6	27	F	Abrocitinib 200 mg Lebrikizumab q 2 weeks	Dupilumab, lebrikizumab	30	>30%	30%	5%	+	None	N	Lebrikizumab not covered by insurance Patient had achieved good control even when D/C	Abrocitinib
7	18	M	Upadacitinib 30 mg Lebrikizumab q 2 weeks	Lebrikizumab, rofluilast, dupilumab, topical steroids	155	NA	30%	30%	¥***	None	N	Upadacitinib would not be covered when combined with Lebrikizumab	dupilimab + upadacitinib
8	27	F	Abrocitinib 200 mg Lebrikizumab q 2 weeks	oral steroids, elidel, topical steroids, tralokinumab dupilumab, upadacitinib, mycophenolate	246	NA	10%	1%	+	JAK-induced acne, nausea	Y	--	--
9	32	F	Upadacitinib 30 mg Lebrikizumab q 2 weeks Abrocitinib 200 mg Lebrikizumab q 2 weeks	Dupilumab, cyclosporine	80	35%	10%	15%	=****	None	Switched to different JAK/ lebrikizumab combination	Patient reached plateau in response	Abrocitinib + Lebrikizumab

(++), clear; (+), improved; (=), plateau; (-), worsened; (¥), inadequate response
*Medical documentation indicated "skin clear today". Clinical response determined to be "clear" in deferring to medical documentation in the absence of BSA data.
**Medical documentation indicated that BSA was "worsening" despite no documentation of BSA at follow up. Clinical response determined to be "worsened" in deferring to medical documentation in the absence of BSA data.
***Medical documentation indicated that skin had "improved," but skin disease was still "severe". Clinical response determined to be "inadequate response" according to lack of change in BSA and disease categorized as "severe".
****Medical documentation indicated that the patient had seen a "plateau" in response; BSA showed worsening from 10% to 15%, and EASI showed improvement from 16 to 12. Clinical response determined to be categorized as "plateau."
Discontinued (D/C)

DISCUSSION

These data demonstrate the successful use of a relatively unexplored option for difficult-to-treat atopic dermatitis. This small cohort provides real-world evidence of adequate tolerability and encouraging efficacy, supporting further exploration of dual therapy with JAK inhibitors and lebrikizumab for recalcitrant AD. The adverse events observed were mild and consistent with the known safety profiles of these agents when used as monotherapy.

There are limited studies evaluating the use of combined oral systemic and biologic therapies for skin diseases. One small cohort study investigating dual treatment with a biologic and a JAK inhibitor in patients with psoriasis and psoriatic arthritis has demonstrated a potentially additive therapeutic effect, serving as a model for combination systemic strategies in dermatologic conditions.[6]

Limitations such as the retrospective and single-center nature of this study, combined with the small sample size, limit the generalizability of results. Of note, reliance on clinical documentation is a limitation of this study, given the subjectivity in describing the response to therapeutics. Finally, the follow-up duration was limited, precluding a comprehensive understanding of long-term safety and efficacy.

Overall, these findings contribute to the growing body of evidence supporting combination systemic therapy in dermatology and warrant prospective studies with larger, more diverse populations to validate and expand upon these initial observations.

CONCLUSION

Dual therapy with lebrikizumab and JAK inhibitors demonstrated promising efficacy and tolerability in this small cohort of patients with treatment-resistant AD. While insurance coverage and cost remain significant barriers, these findings support further investigation of this combination in larger, prospective studies.

DISCLOSURES

Dr Saakshi Khattri is an employee of Mount Sinai and receives research funds from Leo Pharma, AbbVie, Bristol Myers Squibb, Pfizer, Celgene, and Acelyrin. Dr Khattri is also a consultant for Leo, AbbVie, Eli Lilly, Janssen, Regeneron, Sanofi, and UCB.

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