The use of dupilumab for the treatment of alopecia areata

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To the Editor:

Alopecia areata (AA) is a chronic, autoimmune-mediated skin condition affecting hair follicles, nails, and occasionally the retinal epithelium. Alopecia areata shows no sex predilection and can occur at any age, with an estimated prevalence of 6.7 million people in the United States and a lifetime risk of 2% [1]. In addition to the physical impact, AA also can pose numerous psychosocial challenges, with patients suffering from higher rates of anxiety, depression, and other comorbid psychological conditions [2]. The sudden nature of hair loss can lead to psychological distress, causing social withdrawal and a reduced quality of life. Additionally, the lack of a definitive treatment for AA exacerbates these challenges.

Current treatment for AA is largely dependent on the degree of disease involvement and a variety of topical and systemic options exist. Topical treatments include corticosteroids, tacrolimus, minoxidil, and retinoids, whereas azathioprine, cyclosporine, JAK inhibitors, and methotrexate are among those used as systemic treatments [3]. Among the systemic treatment options, JAK inhibitors are particularly effective at hair regrowth in those with AA and pose mild-to-moderate side effects [18]. Although these topical and systemic therapies can be effective in the treatment of AA, they often lose their efficacy after some time.

Dupilumab, an IL4 and IL13 receptor antagonist [7,9], has become a mainstay of treatment for atopic dermatitis (AD) and has shown great promise in other skin conditions including prurigo nodularis, chronic spontaneous urticaria, drug eruptions, and Netherton syndrome. Even more recently, case reports have described the potential application of dupilumab in the treatment of AA [5,10-17].

To better assess the use of dupilumab in the treatment of AA, a scoping review of all PubMed articles published from inception to January 1, 2024 was conducted for the terms "dupixent OR dupilumab AND alopecia areata." Data collection for the following variables was performed on each article that met criteria for inclusion: patient age, patient sex, comorbidities, duration of treatment, and treatment outcome (**Table 1**).

Dupilumab is the first biologic to reach late-phase trials for AD [6] and was FDA-approved for the treatment of AD in March of 2017, marking a significant breakthrough in eczema management. Notably, AD is a common concomitant condition associated with AA [4]; thus, clinicians have increasingly integrated dupilumab into the therapeutic regimen of AA. Nine of the case reports reviewed in this scoping review have demonstrated dupilumab's potential as an effective treatment for AA (**Table 1**). However, it should be noted that one case in those reviewed reported exacerbation of AA and new-onset AA with the use of dupilumab [11]. As such, further exploration into dupilumab's mechanism of action in relation to the immune

Table 1. *Case reports of the use of dupilumab for the treatment of alopecia areata.*

Author	Year	Journal	Age	Sex	Atopic comorbidities	Time between onset of AA and initiation of dupilumab	Duration of treatment with dupilumab	Treatment outcome
Kulkarni et al. [5]	2022	*American Journal of Case Reports*	16	M	Atopic dermatitis	8 months	3 years	Complete regrowth of hair, no evidence of recurrence
Cai et al. [10]	2023	*Frontiers in Medicine*	4	M	Allergic rhinitis	3 years	10 months	Complete regrowth of eyebrows and eyelashes, negative hair pull test, SALT85
Chung et al. [11]	2019	*JAAD Case Reports*	51	F	Atopic dermatitis, asthma, allergic rhinitis	Unknown	44 months	90% scalp regrowth
Chung et al. [11]	2019	*JAAD Case Reports*	25	M	Atopic dermatitis, asthma, seasonal allergies	4 years	6-8 weeks	Initial improvement in his AD, but complete loss of his few remaining patches of hair by his fifth dose of dupilumab
Penzi et al. [12]	2018	*JAMA Dermatology*	13	F	Atopic dermatitis	2 years	11 months	Terminal hair growth noted on almost the entire scalp
Darrigade et al. [13]	2018	*British Journal of Dermatology*	28	M	Atopic dermatitis, asthma	1 year	6 months	Almost full hair recovery, one remaining AA plaque in the occipital area, SALT score=−80.4
Alniemi and McGevna [14]	2019	*JAAD Case Reports*	49	F	Atopic dermatitis	6 years	8 months	Full scalp hair regrowth with some regrowth of eyebrows
Smogorzewski et al. [15]	2019	*JAAD Case Reports*	35	F	Atopic dermatitis, chronic urticaria	5 years	12 months	Full, thick regrowth of terminal hairs on entire scalp and eyebrow, axillary, and pubic hair growth
Uchida et al. [16]	2019	*Acta Dermato-Venereologica*	44	M	Atopic dermatitis	8 years	3 months	Significant hair regrowth, SALT score decreased to 8
Magdaleno-Tapial et al. [17]	2019	*Australasian Journal of Dermatology*	49	M	Atopic dermatitis	4 years	3 months	Full hair regrowth on scalp

AD, atopic dermatitis; F, female; JAAD, Journal of the American Academy of Dermatology; JAMA, Journal of the American Medical Association; M, male; SALT, Severity of Alopecia Tool.

pathways involved in AA is needed to improve its targeted therapeutic approach.

The etiology of AA is believed to be multifactorial and may involve dysregulation of multiple immune pathways. In patients with AA, there is an observed commonality involving the upregulation of cytokines, which leads to the release of inflammatory factors such as IL4, TNF, IL12, and IL13 [9]. As previously mentioned, dupilumab antagonizes IL4 and IL13, which suppress the activation of some inflammatory pathways that may be involved in both AD and AA [7].

Apart from AD, AA also commonly occurs with psychiatric disorders, including anxiety and

depression, which occur at a significantly higher rate in patients with AA than those in the general population [2]. The limited efficacy of current treatments for AA further augment symptoms of anxiety, depression, and social withdrawal among this population. The cases discussed show promising steps towards creating broader treatment options for AA, with the potential to improve overall quality of life by addressing the physical symptoms, and also enhancing mental wellbeing of patients.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Pratt CH, King LE Jr, Messenger AG, Christiano AM, Sundberg JP. Alopecia areata. *Nat Rev Dis Primers*. 2017;3:17011. [PMID: 28300084].
2. Villasante Fricke AC, Miteva M. Epidemiology and burden of alopecia areata: a systematic review. *Clin Cosmet Investig Dermatol*. 2015;8:397-403. [PMID: 26244028].
3. Malhotra K, Madke B. An updated review on current treatment of alopecia areata and newer therapeutic options. *Int J Trichology*. 2023;15:3-12. [PMID: 37305188].
4. Fukuyama M, Kinoshita-Ise M, Mizukawa Y, Ohyama M. Two-sided influence of dupilumab on alopecia areata co-existing with severe atopic dermatitis: A case series and literature review. *J. Cutan. Immunol. Allergy*. 2023;6:13-17. [DOI: 10.1002/cia2.12289].
5. Kulkarni M, Rohan CA, Travers JB, Serrao R. Long-term efficacy of dupilumab in alopecia areata. *Am J Case Rep.* 2022;23:e936488. [PMID: 35726185].
6. Hamilton JD, Ungar B, Guttman-Yassky E. Drug evaluation review: dupilumab in atopic dermatitis. *Immunotherapy*. 2015;7:1043-1058. [PMID: 26598956].
7. Olbrich H, Sadik CD, Ludwig RJ, Thaçi D, Boch K. Dupilumab in inflammatory skin diseases: a systematic review. *Biomolecules*. 2023;13:634. [PMID: 37189381].
8. Paller AS, Silverberg JI, Cork MJ, et al. Efficacy and safety of dupilumab in patients with erythrodermic atopic dermatitis: a post hoc analysis of 6 randomized clinical trials. *JAMA Dermatol*. 2023;159:255-266. [PMID: 36723913].
9. Sibbald C. Alopecia Areata: an updated review for 2023. *J Cutan Med Surg*. 2023;27:241-259. [PMID: 37340563].
10. Cai L, Wei Y, Zhao M, Zhuo J, Tao X, Lin M. Case report: Dupilumab therapy for alopecia areata in a 4-year-old patient resistant to baricitinib. *Front Med (Lausanne)*. 2023;10:1253795. [PMID: 37877023].
11. Chung J, Slaught CL, Simpson EL. Alopecia areata in two patients treated with dupilumab: New onset and worsening. *JAAD Case Rep*. 2019;5:643-645. [PMID: 31388527].
12. Penzi LR, Yasuda M, Manatis-Lornell A, Hagigeorges D, Senna MM. Hair regrowth in a patient with long-standing alopecia totalis and atopic dermatitis treated with dupilumab. *JAMA Dermatol*. 2018;154:1358-1360. [PMID: 30304403].
13. Darrigade AS, Legrand A, Andreu N, et al. Dual efficacy of dupilumab in a patient with concomitant atopic dermatitis and alopecia areata. *Br J Dermatol*. 2018;179:534-536. [PMID: 29710431].
14. Alniemi DT, McGevna L. Dupilumab treatment for atopic dermatitis leading to unexpected treatment for alopecia universalis. *JAAD Case Rep*. 2019;5:111-112. [PMID: 30671522].
15. Smogorzewski J, Sierro T, Compoginis G, Kim G. Remission of alopecia universalis in a patient with atopic dermatitis treated with dupilumab. *JAAD Case Rep.* 2019;5:116-117. [PMID: 30671524].
16. Uchida H, Kamata M, Watanabe A, et al. Dupilumab Improved Alopecia Areata in a Patient with Atopic Dermatitis: A Case Report. *Acta Derm Venereol*. 2019;99:675-676. [PMID: 30938821].
17. Magdaleno-Tapial J, Valenzuela-Oñate C, García-Legaz-Martínez M, Martínez-Domenech Á, Pérez-Ferriols A. Improvement of alopecia areata with Dupilumab in a patient with severe atopic dermatitis and review the literature. *Australas J Dermatol*. 2020;61:e223-e225. [PMID: 31766073].
18. Sardana, K., Bathula, S., & Khurana, A. Which is the ideal JAK inhibitor for alopecia areata - baricitinib, tofacitinib, ritlecitinib or ifidancitinib - revisiting the immunomechanisms of the JAK pathway. *Indian Dermatol Online J*. 2023; 14: 465–474. [PMID: 37521227].