

Dual efficacy of dupilumab in a patient with concomitant atopic dermatitis and alopecia areata

DOI: 10.1111/bjd.16711

DEAR EDITOR, Atopic dermatitis (AD) is a chronic itchy inflammatory skin condition associated with significant impact on quality of life. AD is a complex disease involving multiple combinatorial factors, including increased inflammation associated with a T helper (Th)2 immune response bias.¹ Recently, dupilumab, a human monoclonal antibody targeting the α -subunit of the interleukin (IL)-4 receptor, shared by the Th2-related cytokines IL-4 and IL-13, showed good results in AD, becoming the first biologic available for disease management.² AD is commonly associated with other chronic inflammatory conditions, including alopecia areata (AA), a chronic inflammatory non-scarring type of hair loss.³ Current therapies for AA are rather limited, typically involving topical, intralesional or systemic steroids, leading to poor clinical response with numerous side-effects and significant burden. However, recent insights into the mechanism of AA have suggested involvement of the Th2 immune response, emphasizing that targeting this immune pathway could potentially restore hair growth.

A 28-year-old man presented to our department of dermatology for the management of severe AD evolving since childhood associated with asthma. In addition to AD, he had a 1-year history of AA starting as focal well-circumscribed patches of hair loss with a positive pull test and the presence of exclamation points and yellow dots on dermoscopy. Then, AA progressed to complete hair loss. On physical examination, the patient had severe AD [total Scoring Atopic Dermatitis (SCORAD) 58.5; Eczema Area and Severity Index (EASI) 14.9], with major pruritus and lichenified or crusted lesions involving mainly the head, neck and flexural areas. Universal AA involved mainly the scalp [Severity of Alopecia Tool (SALT) score 87.4], eyebrows, eyelashes and beard. Biological investigations revealed elevated IgE levels ($11\,987\text{ kUI L}^{-1}$) together with a slight increase in eosinophil count ($0.54 \times 10^9\text{ cells L}^{-1}$), and no other abnormality.

The patient was previously under ciclosporin (5 mg kg^{-1} per day) for 8 months for AD, which led to only partial response with remaining flares. Ciclosporin was stopped and methotrexate 20 mg per week was initiated. However, during 7 months of treatment, AD was only moderately controlled and the treatment was associated with side-effects,

such as asthenia and nausea. AA did not improve under these two systemic therapies. It was then decided to start dupilumab therapy to treat AD, 600 mg subcutaneously at day 0, then 300 mg every 15 days, with no additional medication. At 3 months, the patient showed significant improvement of AD and of his quality of life, associated with a significant reduction of pruritus. At month 6, AD scores were significantly reduced (Δ total SCORAD -22 , Δ EASI -8.4) (Fig. 1).

In addition to this response of dupilumab on AD, the patient experienced hair regrowth starting at month 3 with almost full recovery at month 6 (Δ SALT -80.4) (Fig. 1). One remaining AA plaque was observed in the occipital area. Total serum IgE levels dropped to 2164 kUI L^{-1} and a slight increase in eosinophil count was observed ($0.77 \times 10^9\text{ cells L}^{-1}$). No important side-effects associated with the use of dupilumab were reported, with only slight conjunctivitis.

While dupilumab has shown great efficacy for the treatment of moderate-to-severe AD,² its efficacy on AA with a recovery of eyebrows and eyelashes (two areas characterized by slow-growing hair) confirms recent advances made in the understanding of the mechanism of this disease. Previous studies on AA pathophysiology were performed mainly on mouse models and focused on the role of Th1 immune response with elevated levels of interferon- γ , leading to the use of Janus kinase inhibitors in AA.⁴ However, it is now well known that AD can be associated with AA,³ and that both conditions share genetic predisposing factors, especially involving Th2 signalling.

Recently, IL-13 gene susceptibility was identified in a large genome-wide study in patients with AA, and an IL-4 polymorphism was also associated with an increased risk of AA.⁵ Moreover, transcriptomic analysis of AA skin biopsies revealed increased expression of genes associated with the Th2 immune response, and increased levels of IL-13 were found in patients' sera.⁶ Additionally, a significant reduction of the expression of Th2-related genes was shown following steroid injections in AA.⁷ Therefore, these recent data suggest a role of Th2-related cytokines in AA mechanisms, hence the interest in blocking their functions to induce the entry of hair follicles into the anagen phase. In contrast, one case report showed occurrence of AA after dupilumab therapy,⁸ supporting the need for further research into the clinical effect of dupilumab for AA.

To the best of our knowledge this is the first report showing efficacy of dupilumab in AA. Therefore, clinical trials are needed to address more systematically the safety and efficacy

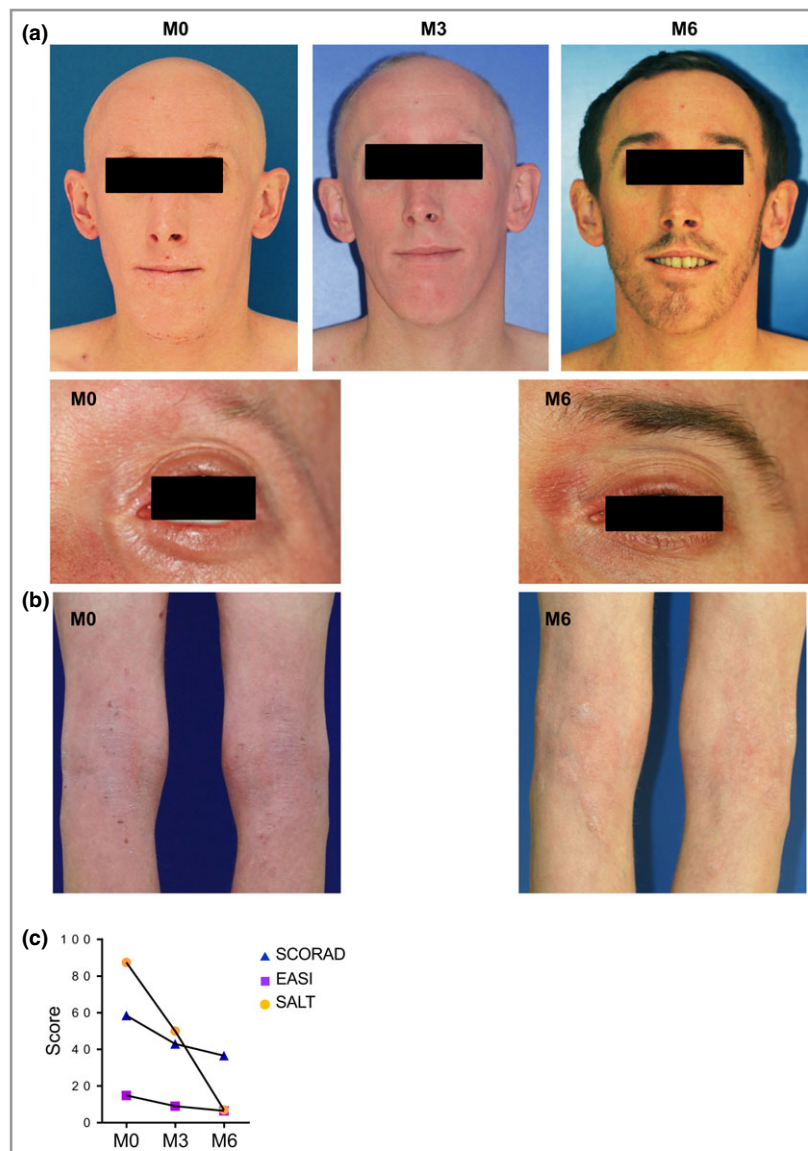


Fig 1. Representative photographs and clinical scores of a patient with concomitant atopic dermatitis (AD) and alopecia areata (AA). (a) The patient with universal AA involving the scalp, eyebrows, eyelashes and beard at months 0, 3 and 6 after dupilumab therapy. (b) Improvement of AD from month 0 to month 6. (c) Clinical AD scores (total SCORAD and EASI scores) and AA score (SALT score) at months 0, 3 and 6 after dupilumab therapy. SCORAD, Scoring Atopic Dermatitis; EASI, Eczema Area and Severity Index; SALT, Severity of Alopecia Tool.

of dupilumab in this disease in the context of the currently limited therapeutic options.

¹Department of Dermatology, National Reference Center for Rare Skin Diseases, Bordeaux University Hospitals, Bordeaux, France

²INSERM U1035, BMGIC, Immuno-Dermatology, ATIP-AVENIR, Bordeaux University, Bordeaux, France

Correspondence: Julien Seneschal.

E-mail: julien.seneschal@chu-bordeaux.fr

A.-S. DARRIGADE^{1,2}

A. LEGRAND¹

N. ANDREU¹

C. JACQUEMIN²

K. BONIFACE²

A. TAÏEB¹

J. SENESCHAL^{1,2}

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Funding sources: none.

Conflicts of interest: none to declare.