



Efficacy of Dupilumab for Controlling Severe Atopic Dermatitis in a Patient with Hyper-IgE Syndrome

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To the Editor,

Autosomal dominant (AD) hyper-IgE syndrome (HIES) is caused by *STAT3* dominant-negative mutations, whereas loss-of-function mutations of *ZNF341*, which governs *STAT3* activity through transcriptional mechanisms, or *DOCK8* cause autosomal recessive (AR) HIES [1, 2]. HIES patients present early-onset allergy, including features of severe atopic dermatitis, thought to result at least in part from increased Th2 cytokines. Topical corticosteroids and calcineurin inhibitors associated with oral antihistamines are the main treatment, whereas immunosuppressive agents are not recommended given a higher risk of infection.

We report the successful treatment of severe atopic dermatitis in a 48-year-old patient with AR ZNF341 deficiency. This patient's major complaint was chronic, severe, intractable,

generalized pruritus. She had confluent papules on her shoulders, flank, abdomen, and thighs; multiple excoriated, achromic, and atrophic lesions, predominantly on her scalp, arms, legs, and abdomen; fissures and lichenification of the inner elbows; and atrophic scars due to life-long scratching (Fig. 1a–e, upper panels). She applied ultra-high potency class I topical corticosteroids daily and topical tacrolimus, which were ineffective. Standardized questionnaires revealed severe atopic dermatitis (SCORAD score of 85.5/103), with a profound effect on quality of life (DLQI score of 22/30).

Dupilumab, which blocks the alpha chain of the interleukin-4 receptor, was recently licensed for the treatment of severe atopic dermatitis in adults and in adolescents from the age of 12 years in most countries [3, 4]. Our patient received an initial dose of 600 mg dupilumab, followed by subcutaneous injections of 300 mg dupilumab at 2-week intervals. At each visit, she completed the DLQI and SCORAD questionnaires and gave a serum sample.

The patient reported rapid improvement after three injections, with strong decreases in DLQI and SCORAD scores (Fig. 1f, g). She stopped applying topical treatment after 3 months. Continuous treatment during 1 year led to complete response and was well tolerated. No further scratching-induced lesions were observed. The papulonodular lesions progressively disappeared, as did skin inflammation in previously excoriated areas (Fig. 1a–e, lower panels). This improvement was accompanied by a progressive decrease in total serum IgE and allergen-specific IgE (Fig. 1h, and Supplemental Fig. 1). Likewise, the serum concentrations of chemokines involved in leukocyte trafficking in the skin including Th2-driven chemokines like TARC and Eotaxin-3 and inflammatory cytokines normalized over time (Fig. 1i–k).

This observation suggests that Th2-mediated IL-4 and/or IL-13 signaling plays a central role in atopic dermatitis in HIES. Dupilumab should be considered for patients with AD *STAT3* or AR *ZNF341* deficiency, and possibly other primary immunodeficiencies in which Th2-mediated atopic

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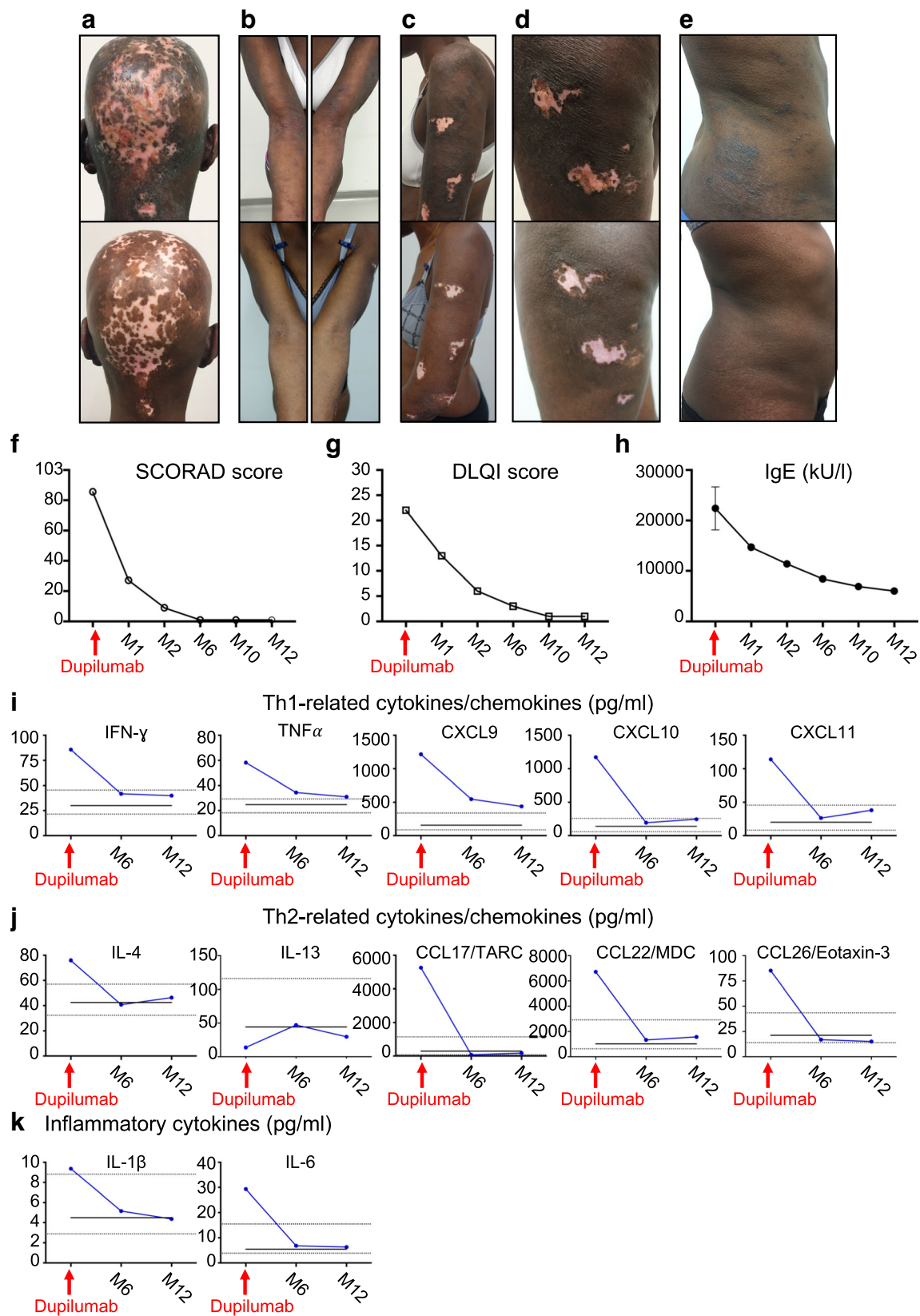
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◀ **Fig. 1** a–e Comparative photographs of the patient's skin lesions, taken before dupilumab initiation (upper panels) and after 1 year of treatment (lower panels). From left to right, photographs of the patient's head, forearms, left shoulder, left thigh, and right flank. f, g Standardized SCORAD (Scoring Atopic Dermatitis) and DLQI (Dermatology Life Quality Index) scores at dupilumab initiation and at multiple time points on treatment. h Serum IgE levels before dupilumab initiation (mean of 7 separate samples) and at multiple time points on treatment. i–k Levels of cytokines and chemokines in the patient's serum, determined by LUMINEX methods, at dupilumab initiation and after 6 and 12 months on treatment. The black line represents the mean value for 10 healthy non-atopic individuals tested in parallel at a single time point. The dot lines represent the range of the values obtained for the 10 healthy individuals. The values are given in pg/ml. TARC, Thymus- and activation-regulated chemokine; MDC, macrophage-derived chemokine

disorders are suspected or have been demonstrated, such as AR DOCK8 deficiency and X-linked WAS deficiency [5].

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval Informed consent was obtained from the patient to participate in this study, in accordance with the World Medical Association rules, the Helsinki Declaration, and EU directives.

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Supplemental figure 1.

