

LETTER TO THE EDITOR

Severe atopic dermatitis effectively treated with dupilumab changed from interleukin-5 inhibitors for concomitant severe bronchial asthma

Dear Editor,

The anti-interleukin (IL)-4 receptor- α antibody dupilumab was launched for patients with refractory atopic dermatitis in April 2018 and also became available for patients with intractable bronchial asthma in March 2019.^{1,2} The IL-5 inhibitors mepolizumab and benralizumab were launched for patients with refractory bronchial asthma in June 2016 and April 2018, respectively.³ To the best of our knowledge, this is the first case report of severe atopic dermatitis effectively treated with dupilumab, which was changed from IL-5 inhibitors for concomitant severe bronchial asthma.

A 57-year-old Japanese woman who had been treated for atopic dermatitis and bronchial asthma for 56 and 51 years, respectively, was referred to us in July 2018. She had not suffered from allergic rhinitis or conjunctivitis. Her atopic dermatitis had been treated with topical corticosteroids with limited effect. Her bronchial asthma had been treated with anti-asthmatics, including mepolizumab, since June 2016

(eosinophils, 242/ μ L) and benralizumab since April 2018 (eosinophils, 169/ μ L), with good effects, but without effects for atopic dermatitis. Physical examination revealed erythema, papules, excoriation and lichenification on the back (Fig. 1a), chest, abdomen and extremities with severe itching. The Eczema Area and Severity Index (EASI) score was 45. Abnormal laboratory findings were as follows: lactate dehydrogenase (LDH), 378 U/L (normal, 124–222); immunoglobulin E (IgE), 65 866 IU/mL (normal, <170); and thymus- and activation-regulated chemokine (TARC), 17 987 pg/mL (normal, <450). Cyclosporin 150 mg/day was administered for 1 month with some effect, and it was continued every other day thereafter. Because the skin lesions had become worse again, a respiratory physician was consulted on whether it was possible to change the drug from benralizumab to dupilumab in May 2019. He changed the drug in July 2019 (eosinophils, 0/ μ L), and thereafter the skin lesions gradually improved. One year after the initiation of dupilumab, the EASI score became 10.2

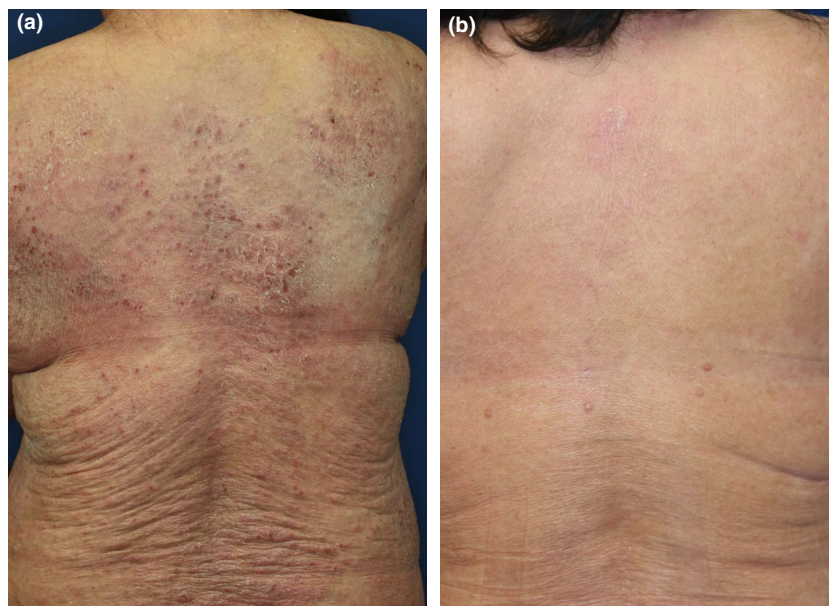


Figure 1. Clinical features, treatments and laboratory tests on (a) the first medical examination and (b) 1 year after the initiation of the treatment with dupilumab. EASI, Eczema Area and Severity Index; IgE, immunoglobulin E; LDH, lactate dehydrogenase; TARC, thymus- and activation-regulated chemokine.

Correspondence: Hidehisa Saeki, M.D., Department of Dermatology, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan.
Email: h-saeki@nms.ac.jp

(Fig. 1b) and the number of asthma attacks decreased further. LDH, IgE, TARC and eosinophils became 271 U/L, 14 707 IU/mL, 2214 pg/mL and 891/ μ L, respectively.

Dupilumab blocks both IL-4 and IL-13, which are the key cytokines involved in the pathogenesis of atopic dermatitis and bronchial asthma. Because IL-4 is the key cytokine for T-helper 2 polarization, dupilumab decreases markers of airway inflammation including IgE, eosinophilic lung inflammation and the fraction of exhaled nitric oxide. Ando *et al.*⁴ conducted an indirect treatment comparison to estimate the differences in efficacy between dupilumab and benralizumab for inadequately controlled asthma. The results demonstrated that there was no significant difference in the annual exacerbation rate (AER) between these drugs in patients overall or in the subgroup with a blood eosinophil count of less than 150/ μ L. However, the AER was significantly lower in the dupilumab group than in the benralizumab group in the subgroup with a blood eosinophil count of more than 150/ μ L. Now that dupilumab is available for both patients with intractable atopic dermatitis and bronchial asthma, it is desirable to use dupilumab for patients with refractory atopic dermatitis concomitant with severe bronchial asthma, especially for the patients with higher blood eosinophil counts at baseline.

CONFLICT OF INTEREST: None declared.

Susumu ICHIYAMA,¹  Michiko ITO,¹ Toshihiko HOASHI,¹ Naoko KANDA,²  Toyoki NATSUNO,³ Hidehisa SAEKI¹ 

¹Department of Dermatology, Nippon Medical School, Tokyo, ²Department of Dermatology, Nippon Medical School Chiba Hokusoh Hospital, Chiba and ³Natsunoiin, Tokyo, Japan

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REFERENCES

- 1 Blauvelt A, de Bruin-Weller M, Gooderham M *et al.* Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. *Lancet* 2017; **389**: 2287–2303.
- 2 Castro M, Corren J, Pavord ID *et al.* Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. *N Engl J Med* 2018; **378**: 2486–2496.
- 3 Agache I, Beltran J, Akdis C *et al.* Efficacy and safety of treatment with biologicals (benralizumab, dupilumab, mepolizumab, omalizumab and reslizumab) for severe eosinophilic asthma. A systematic review for the EAACI Guidelines - recommendations on the use of biologicals in severe asthma. *Allergy* 2020; **75**: 1023–1042.
- 4 Ando K, Tanaka A, Sagara H. Comparative efficacy and safety of dupilumab and benralizumab in patients with inadequately controlled asthma: a systematic review. *Int J Mol Sci* 2020; **21**: E889.