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Real-world effectiveness and safety of dupilumab for the treatment of atopic dermatitis in Japanese patients: A single-centre retrospective study

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Accepted Article

Recently, dupilumab, an anti-interleukin-4 receptor α antibody, became available for the treatment of atopic dermatitis (AD) and showed high efficacy and tolerable safety in clinical trials¹⁻³. Since clinical trials have many limitations due to limited inclusion criteria and many exclusion criteria, the real-world data are sometimes different from clinical trials' data. We experienced 22 Japanese adult AD patients treated with dupilumab, and herein report our real-life data on dupilumab.

All moderate-to-severe adult AD patients treated with dupilumab who visited our hospital from June 2018 to December 2018 were included in this study. Under the insurance system in Japan, dupilumab is indicated only for patients over 15 years old with “more than 16 of total Eczema Area and Severity Index (EASI) score or more than 2.4 of head and neck EASI score”, “more than 3 of Investigator's Global Assessment (IGA)”, and “more than 10% of affected body surface area (BSA)” who have been refractory to topical corticosteroid and/or tacrolimus for more than six months or cannot use it due to its adverse effect. All data were collected retrospectively from their charts. All patients received a 600 mg loading dose of dupilumab once; then, starting two weeks later, 300 mg of dupilumab was administered subcutaneously every two weeks, in addition to treatment with topical corticosteroid and/or tacrolimus. This study was approved by the ethics committee of Teikyo University.

Data on 22 Japanese patients (20 men and two women) with moderate-to-severe AD were analyzed. The mean age was 41.4 years (range, 23-56 years), and the mean duration of AD at

initiation of dupilumab was 31.7 ± 14.3 years (mean $\pm$ standard deviation). Ten patients (45.5%) had asthma or a history of asthma.

In all patients, skin eruption improved greatly after receiving dupilumab. Erythema tended to disappear or be alleviated relatively rapidly, whereas it seemed that prurigo nodularis took about two to three months to improve. IGA scores and affected BSA significantly decreased at one month after starting dupilumab (Figure 1A, B). The EASI score significantly decreased by 43.5% on average at one month and by 69.2% at three months; however, no significant decrease in the EASI scores of the head and neck was found at one month after starting dupilumab (Figure 1C, D). Individual data on the changes in EASI score are shown in Figure 1E. In some patients, skin manifestations on the trunk and limbs improved, while skin manifestation on the face was refractory to treatment with dupilumab. The EASI score of the head and neck significantly decreased three months after starting dupilumab. Dermatology Life Quality Index scores, Patient-Oriented Eczema Measure scores and Visual Analogue Scale of pruritus significantly decreased at one month after starting dupilumab (Figure 1F-H). The serum levels of thymus and activation-regulated chemokine and LDH significantly decreased at one month (Figure 1I, J). The serum IgE level decreased at three months as shown in Figure 1K (it was not measured at one month). The number of circulating eosinophils tended to slightly increase after initiation of dupilumab, although there was no statistically significant difference (Figure 1L).

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As for safety of dupilumab, conjunctivitis was observed in eight patients (36.4%), three of whom had a history of allergic conjunctivitis. The adverse event of conjunctivitis occurred two to six weeks after starting dupilumab. Seven of the eight patients showed a good response to anti-histamine and corticosteroid eye drops prescribed by ophthalmologists. One patient had to continue to use anti-histamine eye drops even six months after starting dupilumab, although the symptoms were not severe. There seemed to be no relationship of conjunctivitis with a history of asthma, since four out of eight patients with conjunctivitis (50%) had asthma while six out of 14 patients without conjunctivitis (42.9%) had it. We observed a mild injection-site reaction in one patient and hair regrowth in another patient with alopecia areata, the latter of whom we previously reported⁴. No patients have discontinued dupilumab as of March 1st, 2019.

We observed significant improvement and tolerable safety of dupilumab in AD patients in real life as clinical trials showed^{1,2}. However, our data revealed in the real world that some patients showed poor improvement on the head and neck while obtaining good response on the trunk and the limbs to dupilumab, and that conjunctivitis was more common as an adverse event than in the clinical trials, which was controllable in most patients. Those issues our study suggested might be race-specific. Further accumulation is needed to clarify those issues.

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Figure legends

Figure 1

(A-E) Changes in clinical data before and one and three months after starting dupilumab treatment. (A) Investigator's Global Assessment (IGA) score. (B) Affected body surface area (BSA). (C) Eczema Area and Severity Index (EASI) score. (D) EASI score in head and neck. (E) Individual data on the changes in EASI score before and one and three months after starting treatment with dupilumab. Left panel, total EASI score. Right panel, EASI score of head and neck. (F-H) Changes in parameters related to quality of life before and one and three months after starting dupilumab treatment. (F) Dermatology Life Quality Index (DLQI). (G) Patient-Oriented Eczema Measure (POEM). (H) Visual Analogue Scale (VAS) of pruritus. (I-L) Changes in laboratory data before and one and three months after starting dupilumab treatment. (I) Serum level of thymus and activation-regulated chemokine (TARC). (J) Serum level of LDH. (K) Serum level of IgE. (L) Number of circulating eosinophils. Mean values are shown. * $p < 0.05$ compared with the respective baseline value.

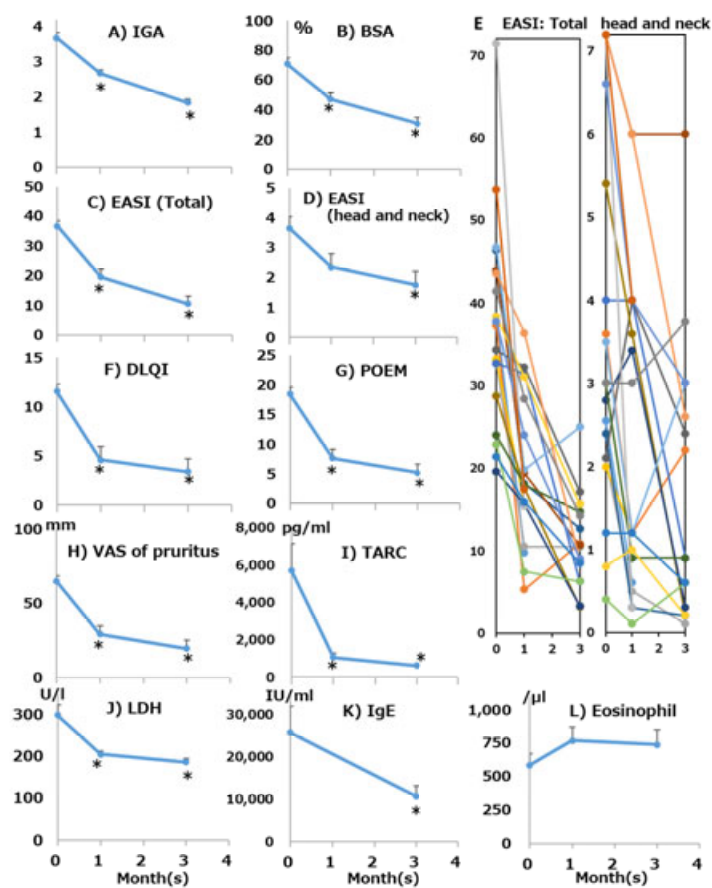


Figure 1. Uchida et al.