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LETTER TO THE EDITOR

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Real-world use of dupilumab for 53 patients with atopic dermatitis in Japan

Dear Editor,

A single-center, retrospective chart review was conducted at Hyogo College of Medicine Hospital to assess the therapeutic effects and safety of dupilumab in patients with moderate-to-severe atopic dermatitis (AD) who visited the hospital from April 2018 to May 2019. Treatment began with a 600 mg loading dose of dupilumab, followed by a 300 mg dose, given every other week, combined with topical corticosteroids and/or tacrolimus, in accordance with Japanese National Health Insurance adaptation rules.[1] This study conformed to the Declaration of Helsinki and was approved by the Ethics Review Board of Hyogo College of Medicine (approval number: 3273).

Fifty-three Japanese patients (36 men and 17 women) were included. Disease activity was measured at the baseline visit and Weeks 4 and 16, with a window of assessment of approximately three days. The last observation carried forward method was used to impute missing values. The patients' baseline clinical characteristics were as follows:

- Age: 39.7 ± 10.9 (mean ± standard deviation)
- Investigator's Global Assessment (IGA): 3.5 ± 0.5
- Eczema Area and Severity Index (EASI): 37.5 ± 15.6
- Dermatology Life Quality Index (DLQI): 10.6 ± 6.2
- Patient-Oriented Eczema Measure (POEM): 17.2 ± 7.6
- Serum IgE: 13 269 ± 22 118 IU/mL
- Serum lactate dehydrogenase (LDH): 308.8 ± 90.8 U/L
- Serum level of thymus and activation-regulated chemokine (TARC): 5247 ± 7521 pg/mL.

The baseline disease characteristics were similar to those in the CHRONOS trials.[2] All the patients completed the 16-week treatment period, and their dermatitis improved. At the Week 16 follow-up, the following findings were obtained:

- EASI: 10.1 ± 8.1 (73.1% reduction) (Figure 1A, B)
- DLQI: 2.8 ± 2.9 (73.6% reduction) (Figure S1A)
- POEM: 4.8 ± 4.8 (72.1% reduction) (Figure S1B)
- Serum IgE: 7199 ± 17 730 IU/mL (45.7% reduction) (Figure S1C)
- Serum LDH: 193.2 ± 35.2 U/L (36.9% reduction) (Figure 1C)
- Serum TARC: 378.8 ± 219.9 pg/mL (92.8% reduction) (Figure 1D).

The effects of the drug in the real world were thus similar to those of the CHRONOS trials.[2]

Similarly to previous findings,[3] the TARC levels were closely related to the disease activity at baseline (Figure 1E). However, after administering dupilumab, the TARC levels in all the patients decreased independently of disease severity (Figure 1F). Another biomarker for AD should therefore be found when using dupilumab. The mean EASI reductions at the Week 16 follow-up and LDH at Weeks 4 and 16 were significantly correlated (Figure 1G). Accordingly, LDH at the Week 4 follow-up could be a predictive serum biomarker for dupilumab treatment.[4] Notwithstanding, a greater number of cases are needed to confirm this. Although well managed with anti-allergic or steroid eye drops,[5] conjunctivitis was the most common side effect (15/53 patients, 28%). Dupilumab-induced conjunctivitis was more frequent in patients with a previous history of conjunctivitis (6/15 patients, 40%) than in those with no history of conjunctivitis (4/38 patients, 10.5%), which is comparable to clinical trial findings.[5,6]

Despite the short follow-up period and small sample, this study indicates that dupilumab is effective in treating patients with moderate-to-severe AD in daily practice. TARC reduction, however, did not necessarily reflect improved AD.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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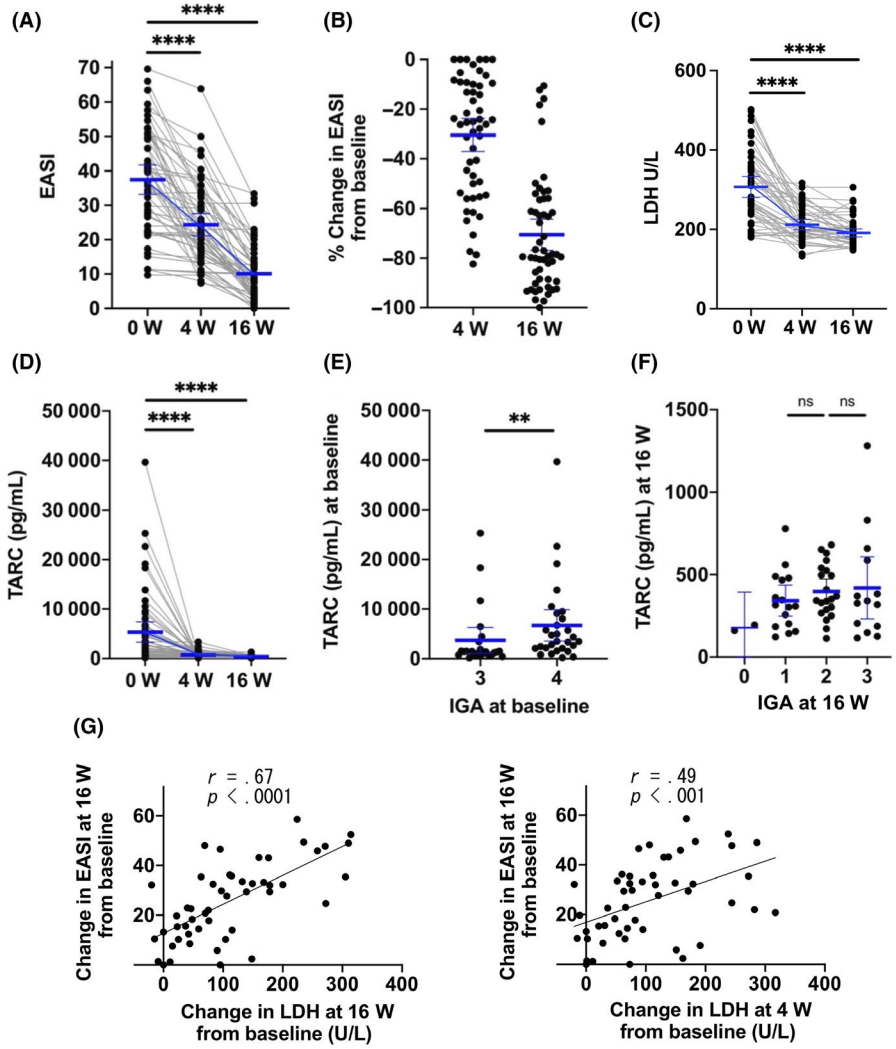

FIGURE 1 A–D, Changes in clinical data before, and 4 and 16 weeks after, initial dupilumab treatment. A, EASI score. B, % change from baseline of EASI at Weeks 4 and 16. C, Serum LDH. D, Serum TARC. E, Serum TARC levels among moderate (IGA 3, n = 24) and severe (IGA 4, n = 29) disease at baseline. F. Serum TARC levels among clear (IGA 0, n = 2), almost clear (IGA 1, n = 16), mild (IGA 2, n = 21), and moderate (IGA 3, n = 14) disease at Week 16. G, Comparison of the change in EASI from baseline at Week 16 and LDH from baseline at Week 4 or 16. *r* = Spearman's correlation coefficient. A–G, Each dot represents a value for each patient. The bold lines represent the estimated mean, and the thin lines stand for the 95% confidence interval. The data were analyzed using GraphPad Prism version 8 (GraphPad Software Inc, San Diego, CA). The Mann-Whitney *U* test (E), Dunn's multiple comparisons test (A, C, D, F), or the Spearman rank correlation test (G) were used to assess statistical significance. **** $P < .0001$; ** $P < .01$; ns = not significant

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.