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Real-World Experience of Long-Term Dupilumab Treatment for Atopic Dermatitis in Korea

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Dear Editor:

Dupilumab, a human monoclonal antibody against interleukin (IL)-4 receptor α, is the first biologic therapy approved for the treatment of patients with moderate to severe atopic dermatitis (AD)[1,2]. Previous clinical trials and real-world evidence indicate that dupilumab is effective and well-tolerated in various populations[3-5]. However, long-term real-world studies of dupilumab treatment for AD are still lacking, particularly in Asian populations[3].

This retrospective study investigated the long-term efficacy and safety of dupilumab for the treatment of moderate to severe AD. A total of 27 adult patients from 26 hospitals in Korea were enrolled via the early access program approved by the Ministry of Food and Drug Safety, Republic of Korea, and

received subcutaneous dupilumab injections (600 mg loading dose followed by 300 mg maintenance dose every other week). Concomitant treatments were allowed but not required. At baseline and biannual follow-up visits, patients' Eczema Area and Severity Index (EASI) and Dermatology Life Quality Index (DLQI) scores were evaluated. Harmonising Outcome Measures for Atopic Dermatitis (HOME) Initiative recommends EASI and DLQI to assess clinical signs and health-related quality of life in AD, respectively. Besides, the latest consensus Korean diagnostic guidelines classify the severity of AD and treatment refractoriness by using EASI and subjective assessments, including DLQI and itch numerical rating scale[6]. Adverse events (AEs), as well as comorbidities and concurrent medications, were recorded. This study was approved by the Institutional Review Board of each hospital. The informed consent was waived.

The mean duration of dupilumab treatment was 13.0±3.3 months (5.9 to 20.5 months). A total of 26 patients was subject to efficacy and safety analysis because one patient withdrew from treatment due to a personal reason after 1 month. At baseline, the mean EASI score of the patient cohort (73.1% male, 26.9% female; mean age 33.3±10.9 years) was 25.68±11.72, and their mean DLQI score was 19.71±5.60, indicating that they had suffered from uncontrolled disease and substantial impairment in quality of life[6]. We also identified multiple baseline atopic comorbidities (57.7%), which included allergic rhinitis (34.6%), food allergy (34.6%), allergic conjunctivitis (23.1%), asthma (11.5%), seasonal allergy (7.7%), and urticaria (3.8%). Before dupilumab treatment, all subjects used both topical and systemic treatments, with limited efficacy. Prior topical treatments included topical corticosteroids (88.5%), antihistamines/antibiotics (84.6%), and topical calcineurin inhibitors (76.9%). For systemic treatment, both corticosteroid and cyclosporine were the most commonly used (each 84.6%), followed by phototherapy (42.3%), allergen-specific immunotherapy (23.1%), methotrexate (19.2%), and other immunosuppressants (11.5%).

Dupilumab treatment was associated with significant improvement after approximately 6 months (visit 2: EASI, 6.37±5.40; DLQI, 6.96±4.57; Fig. 1A, B). Additionally, EASI50, EASI75, EASI90, and a change of at least four points in the DLQI score (minimal clinically important difference, MCID)

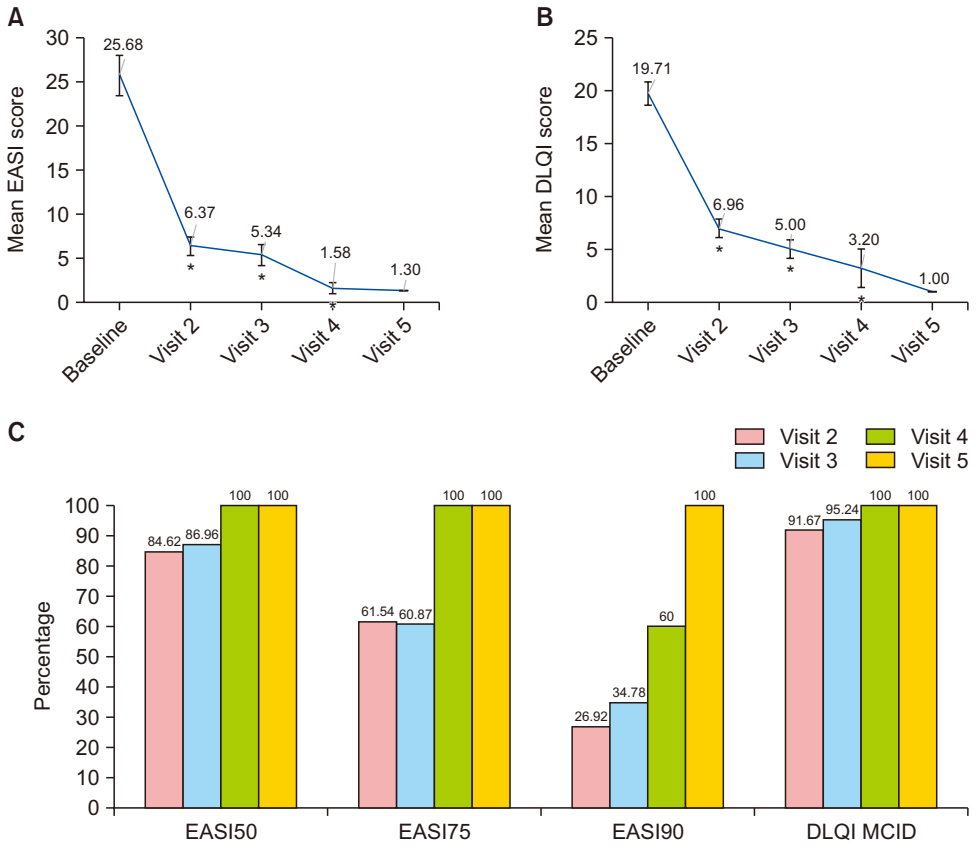

Fig. 1. (A) Mean Eczema Area and Severity Index (EASI) and (B) mean Dermatology Life Quality Index (DLQI) scores after dupilumab treatment in atopic dermatitis patients. Values are presented as mean±standard error (baseline, n=26; visit 2, n=26; visit 3, n=23; visit 4, n=5; visit 5, n=1). (C) Percentage of patients achieving EASI50, EASI75, EASI90, and DLQI minimal clinically important difference (MCID) after dupilumab treatment in atopic dermatitis patients. Mean values are indicated. *$p<0.05$ (vs. baseline) by paired t-test or Wilcoxon signed-rank test.

Table 1. Mean change of EASI and DLQI score in the efficacy populations

Score	Baseline	Visit 2	Visit 3	Visit 4	Visit 5
EASI	25.68±2.30	6.37±1.06	5.34±1.21	1.58±0.62	1.30±0.00
% Improvement from baseline		75.2	79.2	93.8	94.9
DLQI	19.71±1.10	6.96±0.90	5.00±0.89	3.20±1.82	1.00±0.00
% Improvement from baseline		64.7	74.6	83.8	94.9

Values are presented as mean±standard error. The number of patients are 26 at baseline, 26 at visit 2, 23 at visit 3, 5 at visit 4, and 1 at visit 5. EASI: Eczema and Area Severity Index, DLQI: Dermatology Life Quality Index.

were achieved after 6 months in 84.6%, 61.5%, 26.9%, and 91.7% of treated patients, respectively (Fig. 1C). The EASI and DLQI scores continued to improve until visit 5 (Table 1). Notably, after visit 4, the proportion of patients achieving EASI50, EASI75, and DLQI MCID reached 100%. A subgroup analysis revealed no significant difference in treatment efficacy, as determined by EASI50, EASI75, EASI90, and DLQI MCID, between sexes or prior and concomitant treatments. Twelve AEs occurred in 6 patients (23.1%), but no patient discontinued dupilumab due to these AEs. Hair loss was reported for two patients. AEs of herpes zoster, joint stiffness, neurasthenia, nasopharyngitis, myalgia, pain, keratitis, cataract exacerbation, retinal detachment, and retinal tear were reported for one patient each. Persistent keratoconjuctivitis (3.8%) was considered related. No new safety concerns were identified, and most AEs resolved and were considered not related to dupilumab.

In three phase 3 pivotal trials (LIBERTY AD SOLO 1 [NCT02277743], SOLO 2 [NCT02277769], and CHRONOS [NCT02260986]), the Asian subgroup (n=501) showed that the mean EASI and DLQI scores were improved by 73.8% and 55.6%, respectively, after 16 weeks of dupilumab treatment[5]. In our long-term real-world study, the mean EASI improvement at visit 2 (6 months) and visit 3 (12 months) were 75.1% and 79.4%, respectively; this is consistent with the previous real-world studies from Korea (77.4% at 16 weeks)[7], and from Japan (79.1%[8] and 76.5%[9] at 12 months). A recent meta-analysis showed a slightly lower pooled efficacy of 69.6% at 16 weeks from 22 real-world studies, but only one study from Asia was included[3]. On the other hand, a more remarkable EASI improvement of 82.4% at 16 weeks and 84.64% at 52 weeks was observed in Spain[10]. Similarly, the mean DLQI improvement at visits 2 and 3 were 64.5% and 74.6%, respectively, comparable to the Korean study (65.0% at 16 weeks)[7] and a pooled outcome (67.7% at 16 weeks)[3] but less than the improvement observed in Spain (71.46% at 16 weeks, 83.14% at 52 weeks). In terms of safety associated with dupilumab use, the rate of keratoconjunctivitis was 3.8%, similar to that of conjunctivitis in a previous Korean real-world study (5.0%). In contrast, higher rates of conjunctivitis (26.1%), blepharitis (9.6%), keratitis (6.2%), and overall ocular surface disorders (45.2%) were reported from the real-world studies[3]. Whereas the previous 16-week Korean study reported a relatively high frequency of facial erythema (9.9%)[7], there were no instances of facial erythema in the present study. The limitation of this study was that the numbers of patients at visit 4 and visit 5 were only 5 and 1, respectively. Due to the small sample size, a further large-scale investigation is needed to reinforce the long-term efficacy and safety of dupilumab for treating AD in the Korean population.

In conclusion, our findings show that dupilumab treatment is effective in reducing disease severity and improving quality of life, and is well-tolerated for more than 1 year, in Korean patients with moderate to severe AD.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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