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

Dong Hun Lee, Hyun Chang Ko¹, Chan Ho Na², Joo Young Roh¹*, Kui Young Park⁴, Young Lip Park⁵, Young Min Park⁶, Chang Ook Park⁷, Chun Wook Park⁸, Youin Bae⁹, Young-Joon Seo¹⁰, Sang Wook Son¹¹, Jiyoung Ahn¹², Hye Jung Jung¹², Jun-Mo Yang¹³, Chong Hyun Won¹⁴, Kwang Ho Yoo⁹, Bark Lynn Lew¹⁵, Sang Eun Lee¹⁶, Sung Yul Lee¹⁷, Seung-Chul Lee¹⁸, Yang Won Lee¹⁹, Ji Hyun Lee⁶, Yong Hyun Jang²⁰, Jiehyun Jeon²¹, Tae-Young Han²², Sang Hyun Cho²³

Department of Dermatology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, ¹Department of Dermatology, Pusan National University School of Medicine, Busan, ²Department of Dermatology, College of Medicine, Chosun University, Gwangju, ³Department of Dermatology, Gil Medical Center, Gachon University School of Medicine, Incheon, ⁴Department of Dermatology, Chung-Ang University College of Medicine, Seoul, ⁵Department of Dermatology, Soonchunhyang University Bucheon Hospital, Bucheon, ⁶Department of Dermatology, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, ⁷Department of Dermatology, Severance Hospital, Cutaneous Biology Research Institute, Yonsei University College of Medicine, Seoul, ⁸Department of Dermatology, Hallym University Kangnam Sacred Heart Hospital, Hallym University College of Medicine, Seoul, ⁹Department of Dermatology, Hallym University Dongtan Sacred Heart Hospital, Hwaseong, ¹⁰Department of Dermatology, School of Medicine, Chungnam National University, Daejeon, ¹¹Department of Dermatology, Korea University Ansan Hospital, Korea University College of Medicine, Ansan, ¹²Department of Dermatology, National Medical Center, Seoul, ¹³Department of Dermatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, ¹⁴Department of Dermatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, ¹⁵Department of Dermatology, Kyung Hee University College of Medicine, Seoul, ¹⁶Department of Dermatology, Gangnam Severance Hospital, Cutaneous Biology Research Institute, Yonsei University College of Medicine, Seoul, ¹⁷Department of Dermatology, Soonchunhyang University Cheonan Hospital, Soonchunhyang University College of Medicine, Cheonan, ¹⁸Department of Dermatology, Chonnam National University Medical School, Gwangju, ¹⁹Department of Dermatology, Konkuk University School of Medicine, Seoul, ²⁰Department of Dermatology, Kyungpook National University Hospital, School of Medicine, Kyungpook National University, Daegu, ²¹Department of Dermatology, Korea University Guro Hospital, Korea University College of Medicine, Seoul, ²²Department of Dermatology, Nowon Eulji Medical Center, Eulji University, Seoul, ²³Department of Dermatology, The Catholic University of Korea, Incheon St. Mary’s Hospital, Incheon, Korea

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). Previous clinical trials and real-world evidence indicate that dupilumab is effective and well-tolerated in various populations. However, long-term real-world studies of dupilumab treatment for AD are still lacking, particularly in Asian populations.

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. 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. 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)
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 keratoconjunctivitis (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. 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), and from Japan (79.1% and 76.5% 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. 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. 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) and a pooled outcome (67.7% at 16 weeks) 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. Whereas the previous 16-week Korean study reported a relatively high frequency of facial erythema (9.9%), 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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**ORCID**

Dong Hun Lee, https://orcid.org/0000-0002-2925-3074
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