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Treatment of atopic dermatitis with dupilumab in Taiwan: dynamic changes of IgE levels as a potential response biomarker

Atopic dermatitis (AD) is an inflammatory skin condition affecting a significant percentage of the population [1]. Dupilumab is a targeted biologic agent approved by the FDA and EMA for the treatment of moderate-to-severe AD. Dupilumab targets IL-4 receptor α and inhibits the IL-4 and IL-13-related cascades that are critically involved in the pathogenesis of AD, including inflammation, pruritus, and IgE production. Although dupilumab demonstrated efficacy in different clinical studies, a biomarker that correlates with its therapeutic response is currently unavailable.

In this study, we enrolled seven adult Taiwanese patients with AD for three months with dupilumab treatment. Our results confirm that dupilumab has a good therapeutic and safety profile for treating AD, and suggest that dynamic changes of total IgE levels may serve as a biomarker reflecting therapeutic response to dupilumab treatment. Patients older than 20 years of age with inadequately controlled moderate-to-severe AD for more than three years were recruited (KMUHIRB-F (I)-20180044). Patients received a dupilumab 600-mg loading dose and subsequent 300-mg dupilumab dose every two weeks for 12 weeks. Scores for Eczema Area and Severity Index (EASI) and Dermatology Life Quality Index (DLQI), as well as pruritus assessed by numerical rating scale (NRS) were documented at baseline and every two weeks during the study. Laboratory data, including haemogram, biochemistry, and IgE, were evaluated. Systemic antihistamine and topical steroid use were allowed if they were part of the regular regimen at baseline. No systemic immunosuppressant including corticosteroid was allowed. Overall, 6/7 achieved EASI-75 after 12 weeks of treatment (figure 1). This efficacy is better than previous reports [2, 3]. Allowing baseline regimen use likely contributed to this higher efficacy. Besides Patient 1 (who stopped taking antihistamines six weeks after dupilumab treatment initiation), no other patients modified their medication during the study. A disparity between EASI and NRS scores before the initiation of treatment was noted.

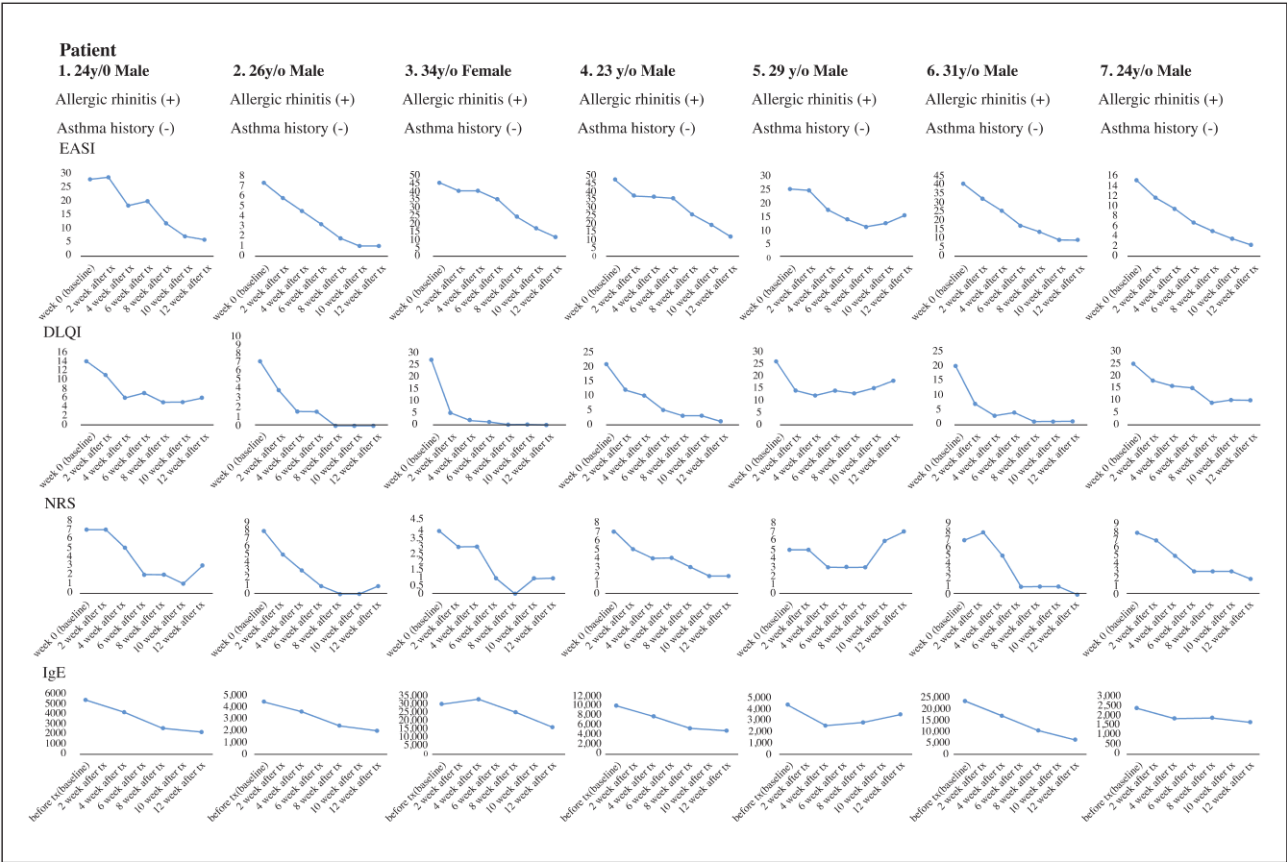


Figure 1. The clinical and laboratory profiles of the patients in this study. Each column represents the profiles of each individual patient.

Various factors are known to contribute to itch in AD; in addition to inflammation, barrier abnormalities, neurogenic mediators, and psychological and environmental factors may contribute to the development of itch [4]. In fact, a previous study showed that EASI scores do not significantly correlate with itch scores. [5] These results are supported by our findings. For responding patients, both DLQI and pruritus (NRS) showed remarkable reduction. At three months of follow-up, after treatment cessation, 4/6 responding patients reported a flare of itch, and none was able to maintain EASI-75. Disease recurrence after cessation of dupilumab is an important issue that should be carefully addressed in the near future. For Patient 6 and 7, in particular, although clinical severity returned to more than 50% of the baseline, their NRS and DLQI scores remained significantly improved (<50% of baseline). Therefore, while treatment cessation is associated with recurrence, alleviation of itch may be longer-lasting compared to improvement of clinical signs (skin inflammation) in a subset of patients.

During this study, one patient reported conjunctivitis and had uneventful recovery. Dupilumab treatment is associated with a decrease in IgE levels [2, 6]. This phenomenon is expected as IL-4 and IL-13 cascades increase IgE production, and dupilumab blocks IL-4 and IL-13 signalling. In another study, no correlation was found between EASI scores and IgE levels, or between EASI reduction and IgE reduction [3]. Therefore, IgE levels before and after dupilumab treatment seem to provide limited information. In our study, reduction of IgE levels was observed in all patients after dupilumab treatment. However, while a persistent decreasing trend was observed in 6/7 patients during treatment, Patient 5 showed increasing IgE levels during treatment, although the absolute IgE levels were still significantly lower than the baseline value (*figure 1*). Of note, Patient 5 was the only patient with suboptimal response. This observation could not have been made if IgE levels were determined only at the beginning and the end of the treatment. We propose that increasing IgE levels under dupilumab treatment may reflect suboptimal blocking of IL-4 and IL-13 signalling. Therefore, dynamic changes in IgE levels may serve as a tool to monitor the therapeutic efficacy of dupilumab for AD. Further large-scaled studies are warranted to validate this hypothesis.

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High-dosage ustekinumab for the treatment of severe hidradenitis suppurativa

Hidradenitis suppurativa (HS) is a severe, debilitating, and painful chronic inflammatory follicular disease, which is challenging to manage. The need for new medical treatment options is obvious, as only adalimumab has been approved for moderate to severe HS. In daily clinical practice, moderate to severe HS frequently requires a combination of medical and surgical treatment [1]. Surgery is indicated in cases of irreversible tissue destruction, such as the presence of fistulas/sinus tracts, accordion-like and/or contracted scars, and suspected malignancy [2]. The altered cytokine network in HS suggests that the IL-12/Th1 and the IL-23/Th17 pathways are expressed in lesional skin, resulting in potential treatment targets [3]. Ustekinumab, a human IgG1K monoclonal antibody targeting the p40 subunit of IL-12 and IL-23, recently showed clinical efficacy in preliminary clinical studies, using the standard dosage for psoriasis [4, 5]. As patients with HS have shown to respond significantly better to high-dosage adalimumab, due to the high inflammatory load of the disease, we report on three patients with severe HS treated with ustekinumab on high-dose regimen, as recently approved for Crohn's disease [6]. All patients had severe HS (Hurley IIC-III), with long disease duration, significant inflammatory load (CRP values >7.2 mg/L), and a progressive disease course, resistant to at least one biological agent (adalimumab) and first- or second-line antibiotic regimens.

All patients were treated with ustekinumab on a high-dosing schedule, consisting of an initial intravenous loading dose adapted to the body weight (≤ 55 kg, 260 mg; > 55 - ≤ 85 kg, 390 mg; > 85 kg, 520 mg), followed by the application of ustekinumab (90 mg subcutaneously) after eight weeks, and afterwards every 8 to 12 weeks depending on disease course and tolerability. Adjunctive antibiotics and surgical interventions were added based on our pro-