LETTER TO THE EDITOR

Successful dupilumab dose spacing in controlled severe atopic dermatitis and predictive factors

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Key words

Atopic dermatitis; dupilumab; dose reduction.

To the Editor,

Dupilumab, targeting the IL-4 receptor α, greatly improves severe atopic dermatitis (AD) outcomes, with a recommended loading dose of 600mg, followed by 300mg every 2 weeks (Q2W) (1). While effective (2), long-term use increases the risk of adverse events (e.g., conjunctivitis, injection site reactions, arthralgia, oral herpes, eosinophilia) and imposes a financial strain. Real-world data on dose/interval adjustments is limited. We aim to evaluate the effectiveness and safety of spacing dupilumab doses in severe AD and identify factors predicting dose reduction.

We performed a retrospective analysis of AD patients taking dupilumab between January 2020 and June 2023. Twenty-seven patients were included (mean age 27.3±16.7 years; 33% women). Atopic comorbidities were as follows: 74% rhinitis; 67% conjunctivitis; 56% asthma; 22% food

allergy; and 15% allergic contact dermatitis. Baseline IgE was 6890.4±8303.8 kIU/L, and eosinophil count was 715.3±634.9 cells/µL.

At baseline (T0), all patients were prescribed the standard regimen, showing significant improvement at 1 month (T1): EASI reduced by 78.9% (p<0.001; T0 32.55; T1 6.87), SCORAD by 57.8% (p<0.001; T0 63,53; T1 26,83), and DLQI by 53.5% (p<0.001; T0 16.13; T1 7.50). We defined controlled disease as EASI ≤7 and SCORAD ≤20 maintained for 3 consecutive administrations, indicating sustained mild disease activity. The administration interval of controlled AD patients was gradually extended by one additional week (Q2W→Q3W→Q4W→…).

Dose spacing was accomplished in 16 patients (59.3%): six achieved Q3W, three Q4W, five Q5W, and two Q6W. Tapering started after an average of 63.3±36.9 weeks (range 14-135). Disease severity was monitored after each administration. Only one patient, a 25-year-old male who tapered after 135 weeks, worsened AD at Q3W and reverted to Q2W. All remaining patients (93.8%) maintained criteria for disease control and reported DLQI scores of ≤5. Although this one patient appeared to be a delayed responder, the treatment response pattern varied significantly among patients and could not be linked to dose spacing.

We explored predictive factors for dose spacing using a generalized linear model weighted by treatment duration. Dupilumab doses were analysed in relation to the age of eczema onset, atopic comorbidities, clinical scores, serum IgE, and serum eosinophil count. Two significant predictors of the average weekly dose of dupilumab emerged: baseline eosinophil count (r=0.476; p<0.001), with 62.4% predictor importance, showing a moderate positive relationship; and age of eczema onset (r=-0.311; p<0.001), with 37.6% predictor importance, indicating a weaker but significant negative relationship. Lower eosinophil counts may indicate a lower Th2 inflammation, requiring smaller doses of inhibitory Th2 mediators and allowing longer dosing intervals. Older AD onset may also predict longer intervals, though further studies are needed to confirm this and explore underlying mechanisms.

The SOLO-continue trial advocated that longer administration intervals (Q4W or Q8W) reduced efficacy based on lower EASI scores (1). However, real-world studies show mixed results with different dosing regimens (3-7). A recent large study with 595 patients reported successful tapering in 83.3% of cases for those with low disease activity, based on EASI ≤7 for ≥6 months, with the majority achieving Q3W/Q4W (3). These findings suggest that lower doses may be effective once the disease is controlled.

We provide data on successful and safe dupilumab dose spacing. Using a patient-orientated approach, we were able to identify good responders who seem to require lower dupilumab doses to maintain AD control. Longer administration intervals benefit patients by reducing injection frequency, which may lead to a lower adverse event risk, while decreasing financial burdens on healthcare systems. Cost reductions amounted to 29.5%, approximately €115,864 annually, enhancing cost-effectiveness and treatment accessibility. Despite the small sample size, this study highlights the need for a randomized clinical trial on dupilumab tapering in controlled AD. Further investigation may uncover response patterns that can predict dose spacing while maintaining long-term disease control.

Keywords: atopic dermatitis; dupilumab; dose reduction

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JV - Writing – original draft, Investigation, Formal Analysis

JM - Writing – review & editing, Conceptualization, Supervision

MP - Writing – review & editing

JG - Investigation, Formal Analysis

CD - Investigation, Formal Analysis

ET - Project administration, Supervision

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