Dupilumab demonstrates higher likelihood of achieving improvements in signs, symptoms, and quality of life vs lebrikizumab: results from a placebo-adjusted indirect comparison analysis

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Introduction/Background: Dupilumab and lebrikizumab are both monoclonal antibodies that have demonstrated efficacy and safety in clinical trials of patients with moderate-to-severe atopic dermatitis (AD). Dupilumab targets both interleukin (IL)-4 and IL-13, and is fully human, whereas lebrikizumab selectively targets IL-13 and is humanized. However, no direct head-to-head clinical trials have been performed to compare efficacy of dupilumab vs lebrikizumab in combination with topical corticosteroids (TCS). Bucher indirect treatment comparisons (ITCs), in which treatment effects are anchored to a common comparator (e.g. placebo), provide a robust and widely accepted method of evaluating the relative efficacy of drugs in the absence of direct comparisons.

Objective: To report the results of a placebo-adjusted Bucher ITC of 16-week therapy for moderate-to-severe AD, comparing the efficacy of dupilumab every 2 weeks (q2w) (LIBERTY AD CHRONOS) vs lebrikizumab q2w (ADhere), in combination with TCS.

Methods: Placebo-adjusted Bucher ITC was conducted using published phase 3 trial data from LIBERTY AD CHRONOS (NCT02260986) and ADhere (NCT04250337). For both studies, data
from the 16-week period were used, employing non-responder imputation, with the following doses: 300mg dupilumab + TCS q2w, or placebo + TCS, and 250mg lebrikizumab q2w + TCS, or placebo + TCS. No adjustments were made for baseline characteristics. Outcomes included proportion of patients achieving ≥75% improvement from baseline in Eczema Area and Severity Index (EASI-75), Investigator’s Global Assessment score 0/1 (IGA-0/1; clear/almost clear), 4-point improvement from baseline in peak pruritus Numerical Rating Scale score (PP-NRS ≥4), and ≥4-point improvement from baseline in Dermatology Life Quality Index (DLQI ≥4). Odds ratio (OR) with 95% confidence interval (CI) are reported.

**Results:** Examination of baseline disease characteristics indicated that the patient populations enrolled in ADhere presented with lower disease severity compared with LIBERTY AD CHRONOS, based on IGA; however, PP-NRS, EASI, and DLQI scores were similar between both trials. This placebo-adjusted Bucher ITC favored dupilumab vs lebrikizumab with TCS combination treatment for all outcomes evaluated. Patients treated with dupilumab + TCS had a significantly higher likelihood of achieving EASI-75 (OR=2.39, 95%CI 1.10–5.19) and PP-NRS ≥4 (OR=2.63, 95%CI 1.17–5.95) at Week 16 vs those treated with lebrikizumab + TCS. OR for the endpoints IGA 0/1 and DLQI ≥4 favored dupilumab, but did not reach statistical significance: IGA 0/1 (OR=1.90, 95%CI 0.81–4.42), DLQI ≥4 (OR=2.35, 95%CI 0.94–5.87).

**Conclusion:** A placebo-anchored Bucher ITC approach showed that the likelihood of achieving improvements in signs, symptoms, and quality of life is higher for patients treated with dupilumab + TCS vs lebrikizumab + TCS.

**Keywords:** atopic dermatitis, dupilumab, lebrikizumab, indirect treatment comparison, topical corticosteroids
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