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COMMENTARY

Dupilumab Maintains Long-Term Disease Control in Adults with Moderate-to-Severe Atopic Dermatitis as Measured by Well-Controlled Weeks: Results From the LIBERTY AD CHRONOS Clinical Trial

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Key Summary Points

In this analysis we aimed to assess disease control of moderate-to-severe atopic dermatitis (AD) in adults using the simple and pragmatic patient-reported outcome of well-controlled weeks

We found that AD patients receiving dupilumab plus topical corticosteroids (TCS) reported superior disease control during a 52-week treatment period, as assessed by patient-reported well-controlled weeks, compared to patients receiving placebo plus TCS

This simple patient-reported outcome measure offers additional confirmation that dupilumab treatment provides long-term disease control in AD patients, which has been previously established using other physician- and patient-reported efficacy assessments

We show that well-controlled weeks is a pragmatic and feasible measure of long-term disease control in patients with moderate-to-severe AD

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DIGITAL FEATURES

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Since its first availability in 2017, dupilumab has become an important treatment option for adult patients with moderate-to-severe atopic dermatitis (AD) that is not adequately controlled with topical therapy or when such therapies are not advisable. The rapid and sustained improvement in signs, symptoms, and quality of life and the long-term disease control achieved with dupilumab are demonstrated in a number of outcome measures evaluated during several randomized, phase 3 clinical trials [1]. Some of these outcome measures, however, are time consuming and involve calculations only used within a clinical trial setting. We aimed to assess disease control in adults with moderate-to-severe AD who had been enrolled in the phase 3 CHRONOS study [2] using a simple and pragmatic patient-reported outcome: the number of well-controlled weeks [3–5] (**Trial Registration:** ClinicalTrials.gov Identifier: NCT02260986).

CHRONOS (NCT02260986) was a randomized, double-blind, placebo-controlled, phase 3 clinical trial conducted in patients with moderate-to-severe AD [2]. Patients were treated over a 1-year period with dupilumab 300 mg weekly (qw) plus topical corticosteroids (TCS), dupilumab every 2 weeks (q2w) plus TCS, or placebo qw plus TCS. Patients had similar baseline disease characteristics across all treatment groups [2]. The median percentage of 'well-controlled' weeks over the 52-week treatment period was calculated from the percentage of patients in each treatment group responding positively to the question: 'In the last week was your AD well controlled?' Patients using rescue medication were considered non-responders, and missing values were handled using the last observation carried forward method.

As results for both dupilumab doses were similar, we present here only the results for the adult-approved dose (300 mg subcutaneous injectable q2w). A total of 110 patients were randomized to dupilumab plus TCS and 315 patients to subcutaneous injectable placebo plus TCS. Over the course of 52 weeks, the median (Q1:Q3 interquartile range) percentage of weeks reported as well controlled was 88% (39:98) in the dupilumab plus TCS group compared to 19% (4:65) for patients treated with placebo plus TCS ($P < 0.0001$, Fig. 1).

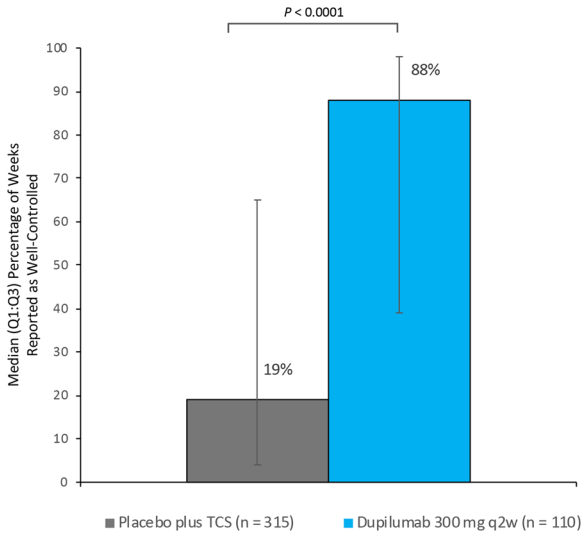

Fig. 1 Median percentage of well-controlled weeks (weeks 1–52) by treatment group. *q2w*, every 2 weeks; *TCS*, topical corticosteroids. Patients using rescue medication were considered non-responders, and missing values were handled using the last observation carried forward method. Imputed patients: placebo = 94/315; dupilumab 300 mg q2w = 49/110

Over the 52-week treatment period, patients receiving dupilumab plus TCS reported superior disease control as assessed by patient-reported well-controlled weeks. This simple outcome measure offers additional confirmation that treatment with dupilumab provides long-term disease control, which has been established using other physician- and patient-reported efficacy assessments.

While the burden of moderate-to-severe AD is not fully captured by clinical outcome measures, patient-reported assessments can provide a real-world assessment of disease status and treatment effectiveness from the patient's perspective. Given the chronic, relapsing nature of

AD, measuring long-term disease control is important. The Harmonizing Outcome Measures for Eczema (HOME) initiative includes long-term control as a key domain to be measured in all clinical trials of eczema [4, 5].

Although it is a simple and easy-to-understand concept, well-controlled weeks has not been fully validated as a patient-reported outcome in AD patients and needs further investigation. In contrast to other assessments, well-controlled weeks is a pragmatic and feasible measure of long-term disease control in patients with moderate-to-severe AD.

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Compliance with Ethics Guidelines. This study was conducted in accordance with the Declaration of Helsinki, International Conference on Harmonisation Good Clinical Practice guidelines (version R1), and applicable regulatory requirements. All patients provided signed written informed consent. The protocol and all relevant study forms were approved by all relevant institutional review boards and an independent ethics committee. An independent data monitoring committee monitored patient safety.

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