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COMMENTARY

Consistency of Response to Dupilumab in Adults with Moderate-to-Severe Atopic Dermatitis Over 1 Year

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Key Summary Points

Why carry out this study?

As the symptoms of atopic dermatitis (AD) can wax and wane over time, information about the consistency of response to treatment can assist physicians with their choice of therapy.

What did the study ask?

How consistent is the response to dupilumab treatment over 1 year of therapy?

What were the study outcomes/conclusions?

We analyzed the proportions of patients achieving the following endpoints by number of study visits (0–10) over 1 year: at least 50% improvement from baseline in Eczema Area and Severity Index (EASI-50), EASI-75, or EASI-90; at least a 4-point improvement from baseline in the Patient-Oriented Eczema Measure (POEM); at least a 3-point improvement from baseline in Peak Pruritus Numerical Rating Scale (NRS) score; and at least a 4-point improvement from baseline in the Dermatology Life Quality Index (DLQI).

We found that for all endpoints analyzed, dupilumab 300 mg q2w plus topical corticosteroids (TCS) (n = 106) demonstrated consistent improvement in AD signs and symptoms (in both clinician- and patient-reported measures) in a higher proportion of the 10 visits, when compared with placebo plus TCS.

What was learned from the study?

Overall, this study showed that most patients treated with dupilumab plus TCS achieved sustained and consistent improvement in signs, symptoms, and quality of life during 1 year of treatment.

DIGITAL FEATURES

This article is published with digital features, including a video, to facilitate understanding of the article. To view digital features for this article please also see video 1 in the online/HTML version of the manuscript or go to https://doi.org/10.6084/m9.figshare.17082293.

COMMENTARY

Atopic dermatitis (AD), a type 2 inflammatory disease, is characterized by skin lesions and pruritus that can significantly impair quality of life [1]. Dupilumab is a fully human monoclonal antibody that blocks the shared receptor component for interleukin (IL)-4 and IL-13, inhibiting signalling of both IL-4 and IL-13, key and central drivers of type 2-mediated inflammation in AD and multiple other diseases [2, 3]. In phase III randomized trials, dupilumab with or without topical corticosteroids (TCS) versus placebo showed significant improvement in AD signs, symptoms, and quality of life, with an acceptable safety profile in adults with moderate-to-severe AD [4–6].

As the symptoms of AD can wax and wane over time, information about the consistency of response to treatment can assist physicians with their choice of therapy. Unfortunately, this chronic, remitting-relapsing disease course limits the utility of single time point efficacy analyses of AD treatment. To better address long-term disease control of AD, we performed a post hoc analysis assessing the consistency of responses to dupilumab in the 52-week LIBERTY AD CHRONOS randomized controlled study [5], in 10 visits over the 52-week treatment period, using existing, validated clinician- and patient-reported outcome measures.

Detailed CHRONOS study methodology, primary efficacy, and safety results have been reported previously [5]. Briefly, the CHRONOS study evaluated dupilumab treatment [300 mg weekly or every 2 weeks(q2w)] or placebo, with concomitant TCS, in adults with moderate-to-severe AD for 52 weeks. The study was approved by the respective institutional review boards and conducted in accordance with the ethical

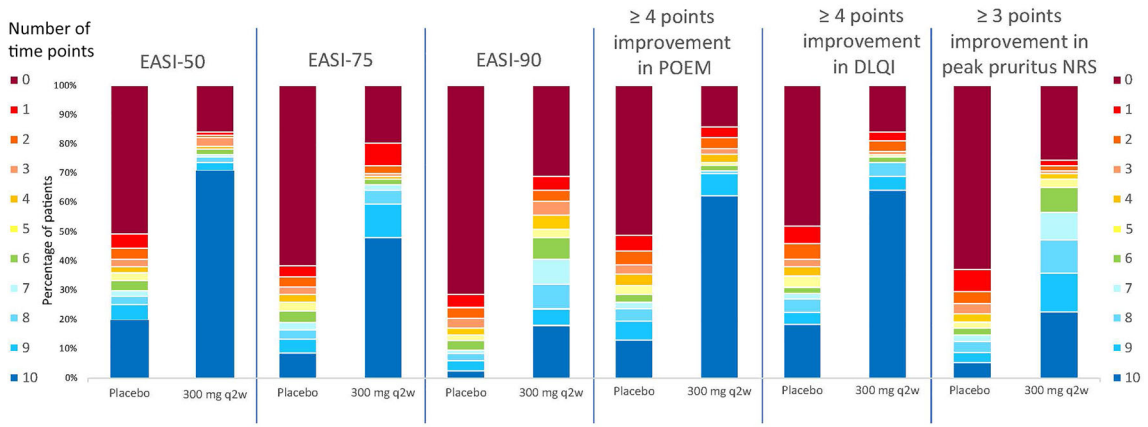

Fig. 1 Percentage of patients with maintained response at 10 time points (week 16, 20, 24, 28, 32, 36, 40, 44, 48, 52) with dupilumab 300 mg every 2 weeks (q2w) plus topical corticosteroids (TCS) vs placebo plus TCS. Placebo plus TCS: $n = 315$; dupilumab 300 mg q2w plus TCS: $n = 106$. For the analysis of Patient-Oriented Eczema Measure (POEM), Dermatology Life Quality Index (DLQI), and Peak Pruritus Numerical Rating Scale (NRS), only patients who had baseline values of POEM ≥ 4, DLQI ≥ 4, and NRS ≥ 3 were included. 300 mg q2w, dupilumab 300 mg q2w plus TCS; EASI, Eczema Area and Severity Index; EASI-50/-75/-90, at least a 50, 75 or 90% improvement in EASI

principles outlined in the Declaration of Helsinki, the International Conference on Harmonisation Good Clinical Practice guideline, and applicable regulatory requirements. All patients provided written informed consent before participating in the trial.

This analysis assessed the proportions of patients receiving either placebo plus TCS or the approved 300 mg q2w adult dose of dupilumab plus TCS that achieved a significant improvement in six clinician- or patient-reported endpoints over the 1-year treatment period. Analyses assessed the proportions of patients achieving the following endpoints by number of study visits (0–10): at least 50% improvement from baseline in Eczema Area and Severity Index (EASI-50), EASI-75, or EASI-90; at least a 4-point improvement from baseline in the Patient-Oriented Eczema Measure (POEM); at least a 3-point improvement from baseline in Peak Pruritus Numerical Rating Scale (NRS) score; and at least a 4-point improvement from baseline in the Dermatology Life Quality Index (DLQI) [7]. Patients missing an assessment or who received rescue treatment were censored and set to missing. Means were calculated using the least-squares method. All analyses were performed using SAS v9.4 or higher.

For all endpoints analyzed, patients with AD treated with dupilumab 300 mg q2w plus TCS ($n = 106$) demonstrated consistent improvement in AD signs and symptoms (in both clinician- and patient-reported measures) in a higher proportion of the 10 visits, during the 52-week treatment period, when compared with patients receiving placebo plus TCS ($n = 315$, Fig. 1). For the clinician-assessed measurements of EASI-50, EASI-75, and EASI-90, 70.8% vs 19.7%, 48.1% vs 8.6%, and 17.9% vs 2.5%, respectively, of the dupilumab plus TCS group vs the placebo plus TCS group achieved the endpoints at all 10 visits. For the patient-assessed DLQI, at least a 4-point improvement was achieved at all 10 visits in 64.2% of patients receiving dupilumab plus TCS vs 18.4% receiving placebo plus TCS. Similarly, for POEM, at least a 4-point improvement was observed at all 10 visits in 62.3% of dupilumab plus TCS-treated patients vs 13.0% of placebo plus TCS-treated patients. Lastly, for the patient-reported weekly Peak Pruritus NRS score, at least a 3-point reduction was observed in 65.1% of dupilumab plus TCS-treated patients in at least six visits vs 17.1% of placebo plus TCS-treated patients. Figure 1 shows that for all assessments, a greater percentage of patients receiving

dupilumab plus TCS achieved the respective endpoint at consistently more visits compared with patients receiving placebo plus TCS.

The Harmonising Outcome Measures for Eczema (HOME) group has identified long-term control as one of four important domains to measure in AD clinical trials [8]. In other words, it is essential for prescribers to consider if patients achieved a meaningful response consistently over time, rather than just at a single time point (e.g., at the end of treatment). This analysis demonstrates that most patients treated with dupilumab plus TCS achieved sustained and consistent improvement in signs, symptoms, and quality of life during 1 year of treatment. Limitations of this analysis include its post hoc nature and a relatively small sample size in the dupilumab q2w plus TCS treatment group that was not powered for statistical significance.

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Compliance with Ethics Guidelines. The study was approved by the respective institutional review boards and conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, the International Conference on Harmonisation Good Clinical

Practice guideline, and applicable regulatory requirements. All patients provided written informed consent before participating in the trial.

Data Availability. Qualified researchers may request access to patient level data and related study documents including the clinical study report, study protocol with any amendments, blank case report form, statistical analysis plan, and dataset specifications. Patient level data will be anonymized, and study documents will be redacted to protect the privacy of our trial participants. Further details on Sanofi's data sharing criteria, eligible studies, and process for requesting access can be found at http://www.clinicalstudydatarequest.com/.

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