Dupilumab prevents flares in adults with moderate to severe atopic dermatitis in a 52-week randomized controlled phase 3 trial

To the Editor: Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by flares, defined as worsening of the disease requiring escalation/intensification of AD treatment.[1-3] Patients experiencing flares often visit emergency departments, a costly and burdensome course of action, and are treated with systemic steroids, which are not recommended by treatment guidelines.[1,4] Flare prevention is a primary goal of long-term AD disease control.[2] Dupilumab, a fully human monoclonal antibody, blocks the shared receptor subunit for interleukin 4 and interleukin 13; dupilumab clinical trials have shown that these cytokines are key and central drivers of multiple type 2 inflammatory diseases. We assessed the impact of 52 weeks of dupilumab treatment on flare prevention in adults with moderate to severe AD.

LIBERTY AD CHRONOS was a randomized, double-blind, placebo-controlled, phase 3 trial in adults with moderate to severe AD (NCT02260986).[5] This analysis included patients receiving placebo or dupilumab 300 mg every 2 weeks for 52 weeks. All patients received concomitant medium-potency topical corticosteroids (TCS).

During the treatment period, the annualized flare rate was significantly higher in patients treated with TCS alone (0.77; 95% confidence interval [CI], 0.63-0.93) compared with dupilumab plus TCS (0.17; 95% CI, 0.10-0.29), a 78% relative reduction in annual flares for patients treated with dupilumab plus TCS (Fig 1). The estimated cumulative flare-free rate was greater for patients treated with dupilumab plus TCS compared with patients receiving TCS alone at all time points, with increasing differences between the treatment arms over time (Fig 2).

Based on patient self-reporting, during the 12 months before enrollment, 84% (89/106) of patients receiving dupilumab plus TCS and 77% (243/315) of patients receiving TCS alone experienced flares, and the mean numbers of flares (standard deviation) per patient were 6.2 (15.8) and 4.5 (7.5), respectively. Of patients who experienced at least 1 flare before treatment, 84% (75/89) of patients receiving dupilumab plus TCS were flare-free during the treatment period versus 57% (138/243) receiving TCS alone ($P < .0001$).

Dupilumab prevented flares in adults with moderate to severe AD, despite high initial disease burden. Even with optimal TCS use, patients receiving TCS alone were 4.5 times more likely to experience a flare compared with patients treated with dupilumab plus TCS (annualized rate ratio: 0.77 vs 0.17). Reducing the likelihood of disruptive and costly flares with long-term AD disease control is an important treatment goal that reduces patient burden and risk of inappropriate short-term AD management with systemic corticosteroids.[1,4]

Strengths of this analysis include the 52-week treatment duration in a large international population with moderate to severe AD and the randomized, double-blind, placebo-controlled study design. Limitations include potential recall bias in patient-reported number of flares before treatment and the fact that these results cannot be directly compared with other reports of flare prevention because of differing definitions of flare, duration of treatment, and patient baseline disease severity.

Dupilumab prevents flares in adults with moderate to severe AD by providing continuous, long-term disease control. Flare prevention is an important and tangible goal of AD treatment that can inform discussions between health care providers and patients to ensure compliance and continuity in treatment.

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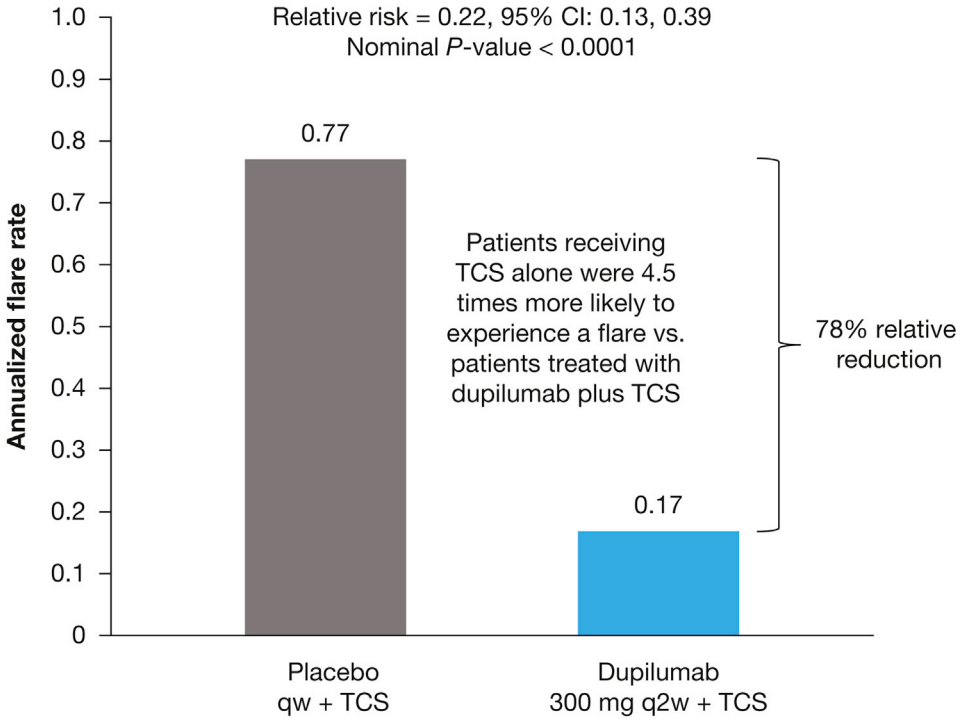

Fig 1. Annualized flare rate during the 52-week treatment period. All inferential results were developed from a parametric Poisson model, with an offset of time to first event/censor in log-scale. *CI*, Confidence interval, *q2w*, every 2 weeks; *qw*, weekly; *TCS*, topical corticosteroids.

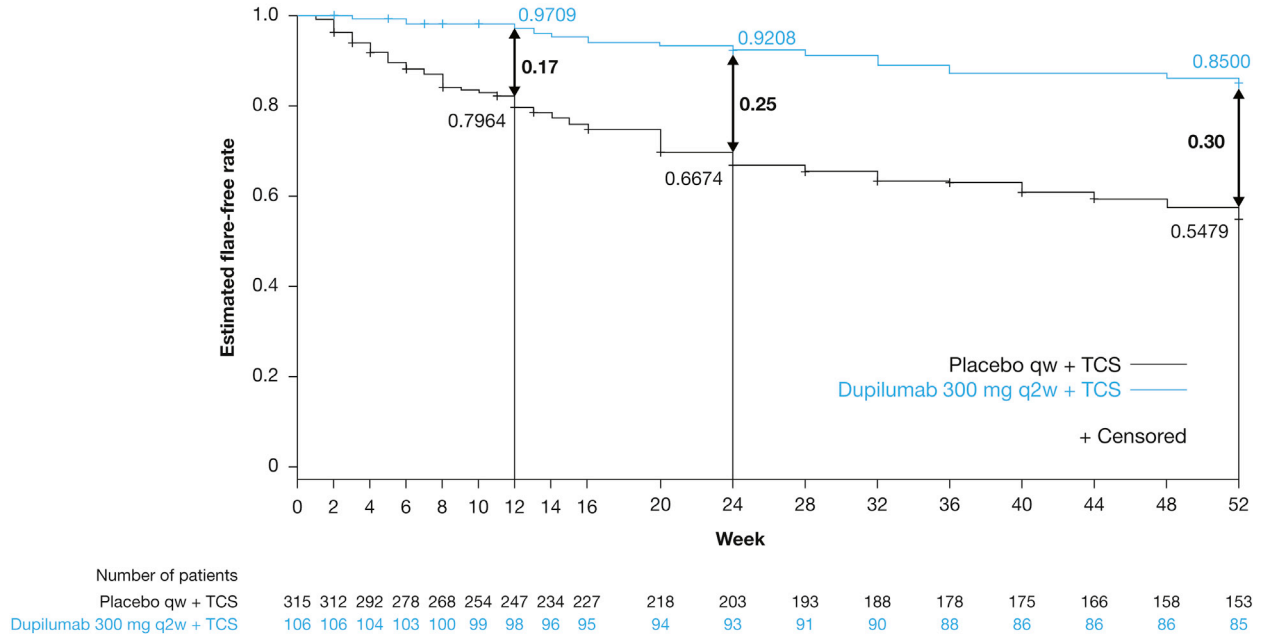

Fig 2. Kaplan-Meier curve of time to first flare during the 52-week treatment period. If a patient did not report a flare in the study, then the patient was censored at the last available date during which they remained in the study. *q2w*, Every 2 weeks; *qw*, weekly; *TCS*, topical corticosteroids.

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Retrospective analysis of laboratory abnormalities in patients prescribed terbinafine for onychomycosis

To the Editor: Onychomycosis is a common nail condition with worldwide prevalence of 3% to 10%.[1,2] Oral terbinafine is frequently prescribed because of its efficacy and infrequent adverse events.[1] Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) baseline and interval testing are recommended, without supporting evidence.[1] Our objectives were to retrospectively analyze the frequency and severity of abnormal laboratory test results in adults without pre-existing hepatic and hematologic conditions prescribed terbinafine for onychomycosis.

Data from patients ages 19 years and older diagnosed with onychomycosis and prescribed oral terbinafine for 12 weeks, January 1, 2000, through February 1, 2019, were extracted after institutional review board approval. Patients with pre-existing liver or hematologic diseases and those taking taking oral ketoconazole, amphotericin, or itraconazole were excluded. Demographics, baseline and interval complete blood count (CBC), AST, and ALT measurements were recorded and analyzed.

Inclusion criteria were met by 944 patients; overall demographics are shown in the supplemental material (Supplemental Table 1; available via Mendeley at https://doi.org/10.17632/zd7gknwmdr.1). In total, 27 of 944 (2.9%) and 32 of 944 (3.4%) patients had abnormal results on baseline liver function tests (LFTs) and CBCs, respectively. In sum, 23 of 944 (2.4%) and 26 of 944 (2.8%) had abnormal monitoring LFT and CBC results, respectively. In all, 3 of 944 (0.3%) and 5 of 944 (0.5%) had abnormal baseline and monitoring LFT, and CBC results, respectively (Table I). Baseline LFT elevations resolved in 24 of 27 patients, and 3 of 27 completed treatment despite mildly elevated LFTs. Elevated monitoring LFTs resolved in 17 of 23 patients after therapy or after stopping terbinafine (4/23), and 2 of 23 discontinued medication and were lost to follow-up (Table II).

In this study, abnormal LFT and CBC results in adults without pre-existing hepatic or hematologic conditions who were prescribed 3 months of