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IRB approval statement: The protocol was reviewed and approved by institutional review boards/ethics committees at all centers.
Abbreviations used

AD, atopic dermatitis
CI, confidence interval
qw, weekly
q2w, every 2 weeks
TCS, topical corticosteroids
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.\textsuperscript{1–3} Patients experiencing flares often visit emergency rooms, a costly and burdensome course of action, and are treated with systemic steroids, which are not recommended by treatment guidelines.\textsuperscript{1,4} Flare prevention is a primary goal of long-term AD disease control.\textsuperscript{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).\textsuperscript{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 (\textbf{Fig 1}). The estimated cumulative flare-free rate was greater for patients treated with dupilumab plus TCS compared with patients on TCS alone at all time points, with increasing differences between the treatment arms over time (\textbf{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 number of flares (standard deviation) per patient was 6.2 (15.8) and 4.5 (7.5), respectively. Of patients who experienced \( \geq 1 \) flare before treatment, 84% (75/89) of patients receiving dupilumab plus TCS were flare-free during the treatment period vs 57% (138/243) receiving TCS alone (\( P < 0.0001 \)).
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.\textsuperscript{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 prior to treatment and that these results cannot be directly compared with other reports of flare prevention due to 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.
REFERENCES


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, 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.
Relative risk = 0.22, 95% CI: 0.13, 0.39
Nominal P-value < 0.0001

Patients receiving TCS alone were 4.5 times more likely to experience a flare vs. patients treated with dupilumab plus TCS.

78% relative reduction