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Title: Efficacy and Safety of Abrocitinib Versus Dupilumab in Adults With Moderate-to-Severe Atopic Dermatitis Who Received Background Topical Therapy in a 26-Week, Randomized, Head-to-Head Trial

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Introduction

Abrocitinib, an orally administered, preferential inhibitor of Janus kinase 1, has been efficacious vs placebo and has an acceptable safety profile in patients with moderate-to-severe atopic dermatitis (AD). Direct comparisons with treatments for moderate-to-severe AD, such as dupilumab (interleukin 4 and interleukin 13 inhibitor), are limited. In this head-to-head trial, we compared the efficacy and safety of abrocitinib and dupilumab treatment in adults with moderate-to-severe AD.

Material and Methods

JADE DARE (NCT04345367) was a 26-week, multicenter, randomized (1:1), double-blind, double-dummy, active-controlled, phase 3b trial designed to assess the efficacy and safety of oral abrocitinib (200 mg once daily) and of subcutaneous dupilumab (300 mg every 2 weeks, following a loading dose of 600 mg) in adults with moderate-to-severe AD (affected body surface area [BSA] ≥10%, Investigator's Global Assessment [IGA] score ≥3, Eczema Area Severity Index [EASI] score ≥16, and Peak Pruritus Numerical Rating Scale [PP-NRS] score ≥4) who received background medicated topical therapy. The off-treatment follow-up period was 4 weeks. Primary outcomes were PP-NRS4 response (≥4-point improvement in PP-NRS score) at week 2 and response based on ≥90% improvement in EASI score (EASI-90) at week 4. The key secondary outcome was an EASI-90 response at week 16, which was first assessed for noninferiority of abrocitinib versus dupilumab with a 10% margin and, if achieved, for superiority. The overall familywise type 1 error rate for testing of the primary and key secondary endpoints was controlled at the 2-sided 5% level, using a sequential multiple-testing procedure. *P*-values were obtained from a Cochran-Mantel-Haenszel analysis adjusted for baseline AD severity (moderate or severe). Safety and tolerability assessments included adverse events (AEs) and laboratory evaluations.

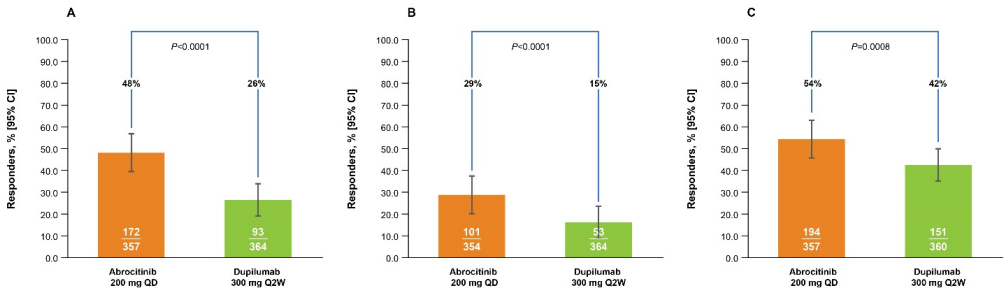
Results

Altogether, 727 individuals were enrolled (abrocitinib, 362; dupilumab, 365). Overall, 397 (55%) were men and 517 (71%) were White. A mean ± SD EASI score of 28.1 ± 11.7, affected BSA of 42.5% ± 20.6%, and PP-NRS score of 7.4 ± 1.6 were observed at baseline. Compared with dupilumab-treated patients, significantly more abrocitinib-treated patients achieved PP-NRS4 response at week 2 (172/357 [48%] vs 93/364 [26%]; *P*<0.0001; **Fig 1A**), EASI-90 response at week 4 (101/354 [29%] vs 53/364 [15%]; *P*<0.0001; **Fig 1B**), and EASI-90 response at week 16 (194/357 [54%] vs 151/360 [42%], *P*=0.0008; **Fig 1C**). Over 26 weeks of treatment, 268/362 abrocitinib-treated (74%) and 239/365 dupilumab-treated (65%) patients experienced ≥1 treatment-emergent AE. The occurrence of serious AEs was similar between the 2 groups (abrocitinib, 6/362 [2%]; dupilumab, 6/365 [2%]). Two deaths occurred, both in the abrocitinib group, and both were considered unrelated to study drug. No unexpected laboratory value abnormalities were observed in either treatment group.

Discussion

The JADE DARE study met the coprimary endpoints of PP-NRS4 at week 2 and number of EASI-90 responders at week 4 and the key secondary endpoint at week 16, showing superiority of abrocitinib vs dupilumab in adults with moderate-to-severe AD. The safety and tolerability profile of abrocitinib was consistent with that from previous studies.

Figure 1. PP-NRS4 response at week 2 (A), EASI-90 response at week 4 (B), and EASI-90 response at week 16 (C)



EASI-90, proportion of patients achieving ≥90% improvement on Eczema Area Severity Index; PP-NRS4, proportion of patients achieving ≥4-point improvement in Peak Pruritus Numerical Rating Scale score; QD, daily; Q2W, once every 2 weeks