



HAL
open science

Effect of abrocitinib and dupilumab on eosinophil levels in patients with moderate-to-severe atopic dermatitis

Delphine Staumont-Sallé, Sébastien Barbarot, Jean David Bouaziz, Chan Chan, Claire Clibborn, Aurélie Du-Thanh, Claire Feeney, Alexandre Lejeune, Laurent Misery, Audrey Nosbaum, et al.

► To cite this version:

Delphine Staumont-Sallé, Sébastien Barbarot, Jean David Bouaziz, Chan Chan, Claire Clibborn, et al.. Effect of abrocitinib and dupilumab on eosinophil levels in patients with moderate-to-severe atopic dermatitis. *JEADV Clinical Practice*, 2023, 2 (3), pp.518-530. 10.1002/jvc2.192 . hal-04247793

HAL Id: hal-04247793

<https://hal.inrae.fr/hal-04247793>

Submitted on 21 Mar 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Effect of abrocitinib and dupilumab on eosinophil levels in patients with moderate-to-severe atopic dermatitis

Delphine Staumont-Sallé¹ | Sébastien Barbarot²  | Jean David Bouaziz³  | Chan Chan⁴ | Claire Clibborn⁵ | Aurélie Du-Thanh⁶ | Claire Feeney⁵ | Alexandre Lejeune⁷ | Laurent Misery⁸  | Audrey Nosbaum⁹ | Julien Seneschal¹⁰  | Angèle Soria¹¹  | Fan Zhang^{4,†}

¹Centre de Référence des Syndromes Hyperéosinophiliques, U1286 Inserm INFINITE, CHU Lille, Université de Lille, Lille, France

²CHU Nantes, UMR 1280 PhAN, INRA, Nantes Université, Nantes, France

³Saint-Louis Hospital, Paris University, Paris, France

⁴Pfizer Inc., Groton, CT, USA

⁵Pfizer Ltd., Surrey, UK

⁶Department of Dermatology, University of Montpellier, Montpellier, France

⁷Pfizer Inc., Paris, France

⁸University Hospital of Brest, Brest, France

⁹Department of Allergy and Clinical Immunology, Hospices Civils de Lyon, Centre Hospitalier Lyon-Sud, Pierre Bénite, France

¹⁰Department of Dermatology and Pediatric Dermatology, National Reference Center for Rare Skin Disorders, Hôpital Saint-André, Université de Bordeaux, CNRS, UMR5164, Immuno-Dermatology, Bordeaux, France

¹¹Department of Dermatology and Allergology, Tenon Hospital, AP-HP, Sorbonne Université, Paris, France

Correspondence

Delphine Staumont-Sallé, CEREO Centre de Référence des Syndromes Hyperéosinophiliques, U1286 Inserm INFINITE, CHU Lille, Université de Lille, Lille 59037, France.
 Email: delphine.salle@chru-lille.fr

Funding information

Pfizer Inc.

Abstract

Background: Eosinophilia is common in patients with atopic dermatitis (AD). Abrocitinib, an oral Janus kinase-1 inhibitor and dupilumab, an anti-interleukin-4 receptor- α antibody, are approved for moderate-to-severe AD. Dupilumab has been associated with transient eosinophilia.

Objectives: To assess the effect of abrocitinib and dupilumab on eosinophils in patients from the phase 3 JADE COMPARE (NCT03720470) and JADE EXTEND (NCT03422822) trials.

Methods: In JADE COMPARE, patients received once-daily oral abrocitinib (200/100 mg), placebo or subcutaneous dupilumab (300 mg, biweekly) with background topical therapy. In the ongoing long-term JADE EXTEND study (Data cutoff: April 22, 2020), dupilumab-treated patients from JADE COMPARE received once-daily abrocitinib (200/100 mg) with background topical therapy. The proportion of patients with

[†]Affiliation at the time of the study

eosinophilia and hypereosinophilia, and association of eosinophilia with clinical efficacy was assessed. Adverse events (AEs) were also assessed.

Results: Of the 837 patients in JADE COMPARE, 58 (25.7%), 47 (19.7%) and 51 (21.1%) had eosinophilia at baseline in the abrocitinib 200 mg, abrocitinib 100 mg and dupilumab groups, respectively. At Week 16, eosinophilia decreased with abrocitinib 200 mg (9.3%) and abrocitinib 100 mg (19.0%) but not dupilumab (21.5%); no cases of hypereosinophilia were observed with abrocitinib 200 mg compared with abrocitinib 100 mg (1.9%) and dupilumab (2.3%). Decreases in median eosinophil counts were greater with abrocitinib 200 mg (difference, $-100/\text{mm}^3$) and abrocitinib 100 mg ($-70/\text{mm}^3$) than dupilumab ($+25/\text{mm}^3$) or placebo ($+30/\text{mm}^3$) at Week 16. Similar trends were observed in patients with comorbid asthma and allergic rhinitis. Eosinophilia decreased from baseline to Week 12 in dupilumab-treated patients who switched to abrocitinib in JADE EXTEND. Decreased eosinophil counts with abrocitinib correlated positively with improvements in AD severity, itch and sleep loss. No eosinophilia-associated AEs occurred.

Conclusions: Abrocitinib decreased eosinophilia in patients with moderate-to-severe AD who had baseline eosinophilia. Resolution of eosinophilia was associated with abrocitinib clinical efficacy.

KEYWORDS

atopic dermatitis, clinical trials, eosinophil disorders

INTRODUCTION

Atopic dermatitis (AD) is a chronic, inflammatory skin disease associated with intense pruritus and impaired quality of life.^{1,2} Pro-inflammatory eosinophils play an important role in mediating the inflammatory response in AD.³ Under normal conditions, eosinophils localize to specific organs, excluding the skin and reside at low levels in the blood.⁴ In AD, T helper type 2 (Th2) responses in skin are characterized by interleukin (IL) -4, IL-5 and IL-13 release.^{5,6} IL-4 facilitates eotaxin-3 production, the main chemokine that mediates chemotaxis of eosinophils from the vasculature to sites of inflammation.⁷ IL-5 stimulates eosinophil proliferation, differentiation and maturation,⁸ whereas IL-13, a central mediator of inflammation in AD, promotes eosinophil survival and activation.^{9,10} The activity of these cytokines is mediated via the Janus kinase (JAK)-signal transducer and activator of transcription pathway, specifically JAK1/JAK2 (IL-5) and JAK1/tyrosine kinase 2 (IL-13).⁸⁻¹⁰

Approximately 30% of patients with moderate-to-severe AD have blood eosinophilia (eosinophil count $>500/\text{mm}^3$), with some categorized as having hypereosinophilia (eosinophil count $>1500/\text{mm}^3$).¹¹⁻¹⁴ In an observational study, the mean (SD) eosinophil count at

baseline in patients with moderate-to-severe AD was $290 \pm 205.7/\text{mm}^3$ compared with $153.3 \pm 113.7/\text{mm}^3$ in healthy individuals.¹⁵ A real-world study reported a mean eosinophil count of $460 \pm 400/\text{mm}^3$ at baseline in patients with AD.¹² Eosinophil levels can be associated with AD severity, with numerically higher counts observed in patients with severe disease.¹⁵⁻¹⁷

Dupilumab, a monoclonal anti-IL-4 receptor α antibody that blocks the effects of IL-4 and IL-13, is approved for treatment-resistant moderate-to-severe AD.¹⁸ Dupilumab was associated with a transient increase in eosinophil levels both in clinical trials and real-world studies.^{12-14,19-24} Patients with very high levels of circulating eosinophils tended to remain asymptomatic, with no increase in associated adverse events (AEs).^{13,20} However, the clinical consequence of this increase is not fully understood, and other studies have proposed that increased eosinophil levels after treatment with dupilumab are associated with the incidence of conjunctivitis in patients with AD.^{22,23,25} As such, eosinophilic conditions are a precaution for use of dupilumab^{18,26} and may prompt discontinuation in some patients with moderate-to-severe AD.¹³

JAK selective inhibitors such as tofacitinib, ruxolitinib and upadacitinib have been shown to reduce

pathologically elevated eosinophil counts in patients with hypereosinophilic syndrome with cutaneous involvement, and in patients with AD.^{27,28} Abrocitinib is an oral, once-daily, JAK1-selective inhibitor approved for the treatment of adult^{29–32} and adolescent patients with moderate-to-severe AD.^{29,30} The efficacy and safety of abrocitinib was established in multiple randomized controlled clinical trials.^{33–37} In the phase 3 JADE COMPARE trial, abrocitinib 200 mg with background topical therapy rapidly improved itch, compared with dupilumab and placebo, in patients with moderate-to-severe AD.^{33,34} In addition, abrocitinib 200 and 100 mg significantly decreased the severity and extent of AD as assessed by Investigator's Global Assessment (IGA) and Eczema Area and Severity Index score (EASI) compared with placebo at Weeks 12 and 16.³³ The effect of abrocitinib treatment on circulating eosinophil levels in patients with AD is not known. This post hoc analysis investigated the effect of abrocitinib and dupilumab on eosinophil levels and the clinical consequences of eosinophilia in patients with moderate-to-severe AD from JADE COMPARE and the long-term extension study JADE EXTEND. The effect of abrocitinib and dupilumab treatment on eosinophil count in patients with comorbid inflammatory diseases (asthma and allergic rhinitis) was also examined.

METHODS

Study design and treatment

JADE COMPARE (NCT03720470) was a phase 3, multicenter, randomized, double-blind, double-dummy, placebo-controlled clinical trial designed to compare the efficacy and safety of abrocitinib, dupilumab and placebo in combination with background topical therapy in patients with moderate-to-severe AD.³³ Details of the study design have been previously described.³³ Briefly, eligible patients were ≥ 18 years of age and had an IGA score ≥ 3 , EASI score ≥ 16 , percentage of treatable body surface area (%BSA) ≥ 10 , and Peak Pruritus Numerical Rating Scale (PP-NRS; © Regeneron Pharmaceuticals, Inc., and Sanofi [2017]) score ≥ 4 for at least 1 year and an inadequate response to topical medicated therapy or requirement for systemic therapy to control AD ≤ 6 months before screening. Patients were randomly assigned 2:2:2:1 to receive once-daily (QD) oral abrocitinib (200 or 100 mg), dupilumab 300 mg subcutaneous injection once every 2 weeks (Q2W) (following a 600-mg loading dose) or placebo for 16 weeks. All patients used background medicated topical therapy once daily throughout the study.

Patients who completed the JADE COMPARE study or the phase 3 JADE MONO-1³⁵ and JADE MONO-2³⁶ studies could enroll in JADE EXTEND (NCT03422822), an ongoing, phase 3 long-term extension study.

Study population

This post hoc analysis included two separate patient populations:

1. Patients treated with abrocitinib, dupilumab and placebo in JADE COMPARE
2. Patients treated with dupilumab in JADE COMPARE who entered JADE EXTEND, where they were randomly assigned to receive double-blind treatment with either abrocitinib 200 or 100 mg in combination with topical medications for AD as needed. This was a planned, interim analysis of data from JADE EXTEND (data cutoff date: April 22, 2020).

Assessments

Circulating eosinophil levels in blood samples were measured at baseline and Weeks 2, 4, 8, 12 and 16 in JADE COMPARE and at baseline and Weeks 2, 4 and 12 in JADE EXTEND. Eosinophil counts of $\leq 500/\text{mm}^3$ were defined as normal, $>500/\text{mm}^3$ to $\leq 1500/\text{mm}^3$ as eosinophilia, and $>1500/\text{mm}^3$ as hypereosinophilia. To understand the relationship between comorbid conditions and eosinophilia, least-squares mean (LSM) change from baseline in eosinophil count was evaluated by comorbid condition in JADE COMPARE. The presence of comorbid conditions at baseline (i.e., asthma and allergic rhinitis) was based on medical history.³³

Assessments in JADE COMPARE included the proportion of patients with eosinophilia from baseline to Week 16; absolute eosinophil counts at baseline and Weeks 2, 4, 8, 12 and 16; and LSM change in eosinophil count from baseline to Week 16. Correlation analyses were performed to evaluate the relationship between baseline eosinophil levels and change from baseline to Week 16 in the efficacy endpoints of EASI, IGA, PP-NRS and SCORing Atopic Dermatitis-Visual Analog Scale (SCORAD-VAS) for sleep loss and pruritus. The relationship between change from baseline to Week 16 in eosinophil levels and change from baseline to Week 16 in the aforementioned efficacy endpoints was also assessed.

Assessments in JADE EXTEND included the proportions of patients with eosinophilia or hypereosinophilia

after switching from dupilumab in JADE COMPARE to abrocitinib in JADE EXTEND at baseline and Weeks 2, 4 and 12. Due to the small number of patients with hypereosinophilia entering JADE EXTEND from the dupilumab treatment arm of JADE COMPARE, patients with eosinophilia or hypereosinophilia were pooled for this analysis. Correlation analyses were performed to evaluate the relationships between baseline eosinophil levels in JADE COMPARE and change from baseline to Week 12 IGA, EASI and PP-NRS scores in JADE EXTEND. The relationship between change from baseline to Week 12 eosinophil levels and change from baseline to Week 12 IGA, EASI and PP-NRS scores in JADE EXTEND was also assessed.

Safety endpoints were assessed in JADE COMPARE via all-cause AEs and serious adverse events (SAEs).

Statistical analysis

The full analysis set and safety analysis set were identical and comprised all randomly assigned patients who received ≥ 1 dose of study drug. Baseline was defined as the last measurement before first dosing (Day 1), and the proportion of patients with eosinophilia was assessed by treatment group in the overall population, asthma status and allergic rhinitis status. Median eosinophil counts were assessed by treatment group (abrocitinib 200 mg, abrocitinib 100 mg, placebo and dupilumab) only. No formal statistical testing was conducted to compare the treatment groups; all comparisons were descriptive.

LSM change from baseline in eosinophil levels was evaluated by asthma status and allergic rhinitis status using a mixed model for repeated measures, with fixed factors of treatment, visit, treatment-by-visit interaction, baseline value and an unstructured covariance matrix.

In each treatment group, 95% CIs were reported. Correlation analyses were performed using Pearson's product-moment correlation coefficients. A correlation coefficient of equal to or less than -0.3 was considered a negative correlation, and equal to or greater than 0.3 was considered a positive correlation.

The LSM change from baseline analyses were conducted using SAS version 9.4 (SAS Institute Inc). For safety analyses, AEs and SAEs were coded using the Medical Dictionary for Regulatory Activities, version 22.1J.

Ethics and patient consent

The study was conducted in accordance with the principles of the Declaration of Helsinki and International Council for Harmonization Good Clinical Practice guidelines and was approved by the institutional review board or ethics committee at each trial site. Patients provided written informed consent before enrollment.

RESULTS

Baseline characteristics

A total of 837 patients were randomly assigned to treatment in JADE COMPARE (placebo: $n = 131$; abrocitinib 100 mg: $n = 238$; abrocitinib 200 mg: $n = 226$; dupilumab 300 mg: $n = 242$; Supporting Information: Figure S1). Of the patients in the JADE COMPARE dupilumab group, 203 were randomly assigned to receive abrocitinib in JADE EXTEND (abrocitinib 100 mg: $n = 130$; abrocitinib 200 mg: $n = 73$). Patient demographics and baseline disease characteristics were comparable across treatment groups in JADE COMPARE (Table 1). Common comorbid conditions at baseline were asthma ($n = 260$; 31.1%) and allergic rhinitis ($n = 139$; 16.6%); 210 patients (25.1%) had eosinophilia or hypereosinophilia.

Effect of abrocitinib treatment on eosinophilia in patients with moderate-to-severe AD from JADE COMPARE

At baseline, the proportion of patients with eosinophilia were comparable between the treatment arms (Figure 1). Abrocitinib rapidly decreased the proportion of patients with eosinophilia compared with placebo as early as Week 2 after treatment; abrocitinib treatment response occurred in a dose-dependent manner. Dupilumab had little effect on the proportion of patients with eosinophilia. The magnitude of decrease was greatest in the abrocitinib 200-mg group; there were no cases of hypereosinophilia at Weeks 12 and 16 following treatment with abrocitinib 200 mg.

Absolute eosinophil counts were highly variable across all groups at Week 16 after treatment (Figure 2). There was a trend for lower eosinophil counts at Week 16 in patients who received active treatment. Decreases from baseline in median eosinophil counts were greater with abrocitinib 200mg (difference, $-100/\text{mm}^3$) and

TABLE 1 Patient demographics and baseline disease characteristics in JADE COMPARE (safety analysis set).

	Placebo <i>n</i> = 131	Abrocitinib 100 mg QD <i>n</i> = 238	Abrocitinib 200 mg QD <i>n</i> = 226	Dupilumab 300 mg Q2W <i>n</i> = 242	Total <i>N</i> = 837
Mean (SD) age, years	37.4 (15.2)	37.3 (14.8)	38.8 (14.5)	37.1 (14.6)	37.7 (14.7)
Female, <i>n</i> (%)	54 (41.2)	118 (49.6)	122 (54.0)	134 (55.4)	428 (51.1)
Duration of AD, mean (SD), years	21.4 (14.4)	22.7 (16.3)	23.4 (15.6)	22.8 (14.8)	22.7 (15.4)
%BSA, mean (SD)	48.9 (24.9)	48.1 (23.1)	50.8 (23.0)	46.5 (22.1)	48.5 (23.1)
IGA score, <i>n</i> (%)					
Moderate (3)	88 (67.2)	153 (64.3)	138 (61.1)	162 (66.9)	541 (64.6)
Severe (4)	43 (32.8)	85 (35.7)	88 (38.9)	80 (33.1)	296 (35.4)
EASI, mean (SD)	31.0 (12.6)	30.3 (13.5)	32.1 (13.1)	30.4 (12.0)	30.9 (12.8)
PP-NRS, mean (SD)	7.1 (1.8)	7.1 (1.7)	7.6 (1.5)	7.3 (1.7)	7.3 (1.7)
SCORAD, mean (SD)	67.9 (12.0)	66.8 (13.8)	69.3 (12.7)	67.9 (11.4)	67.9 (12.6)
Comorbid condition at baseline, <i>n</i> (%)					
Asthma	45 (34.4)	72 (30.3)	68 (30.1)	75 (31.0)	260 (31.1)
Allergic rhinitis	23 (17.6)	47 (19.7)	30 (13.3)	39 (16.1)	139 (16.6)
Eosinophilia status at baseline, <i>n</i> (%)					
Eosinophilia ^a	31 (23.7)	47 (19.7)	58 (25.7)	51 (21.1)	187 (22.3)
Hypereosinophilia ^b	4 (3.1)	10 (4.2)	3 (1.3)	6 (2.5)	23 (2.7)

Abbreviations: AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale (PP-NRS © Regeneron Pharmaceuticals, Inc., and Sanofi [2017]); QD, once daily; Q2W, once every 2 weeks; SCORAD, SCORing Atopic Dermatitis; %BSA, percentage of treatable body surface area.

^aEosinophilia was defined as eosinophil count $>0.5 \times 10^3/\text{mm}^3$ ($>500/\text{mm}^3$ and $\leq 1500/\text{mm}^3$).

^bHypereosinophilia was defined as eosinophil count $>1.5 \times 10^3/\text{mm}^3$ ($>1500/\text{mm}^3$).

abrocitinib 100 mg (difference, $-70/\text{mm}^3$) than dupilumab (difference, $+25/\text{mm}^3$) or placebo ($+30/\text{mm}^3$).

Effect of abrocitinib on eosinophil levels in patients with comorbid asthma and allergic rhinitis from JADE COMPARE

In JADE COMPARE, 92 patients (35.4%) with comorbid asthma and 45 patients (32.4%) with comorbid allergic rhinitis at baseline also had eosinophilia at baseline. At Week 2 through Week 16, the proportion of patients with eosinophilia in the subset with comorbid asthma was lower in the abrocitinib 200-mg group compared with the other treatment groups (Figure 3a), and a similar trend was observed in the subset with allergic rhinitis (Figure 3b). Reductions from baseline in eosinophil counts at Weeks 2 through 16 after abrocitinib 200 mg treatment were greater with abrocitinib compared with placebo, regardless of whether the patient had comorbid asthma or allergic rhinitis at baseline (Supporting Information: Figure S2a–d). Dupilumab treatment did

not decrease eosinophil counts relative to placebo; in patients with comorbid allergic rhinitis at baseline, eosinophil counts were increased from baseline by Week 2 and remained elevated through Week 16 of treatment with dupilumab.

Relationship between eosinophil levels and clinical efficacy at Week 16 of JADE COMPARE

To investigate the use of baseline eosinophil count as a potential predictor of response to treatment, correlation analyses were performed. Baseline eosinophil count was negatively associated with improvement in EASI score at Week 16 with abrocitinib 200 mg ($r = -0.35$; 95% CI -0.46 to -0.22) and dupilumab 300 mg ($r = -0.40$; 95% CI -0.50 to -0.28), but not with abrocitinib 100 mg or placebo (Table 2). No association was observed between baseline eosinophil count and change from baseline in IGA, PP-NRS or SCORAD-VAS at Week 16 with abrocitinib at either dose, placebo or dupilumab.

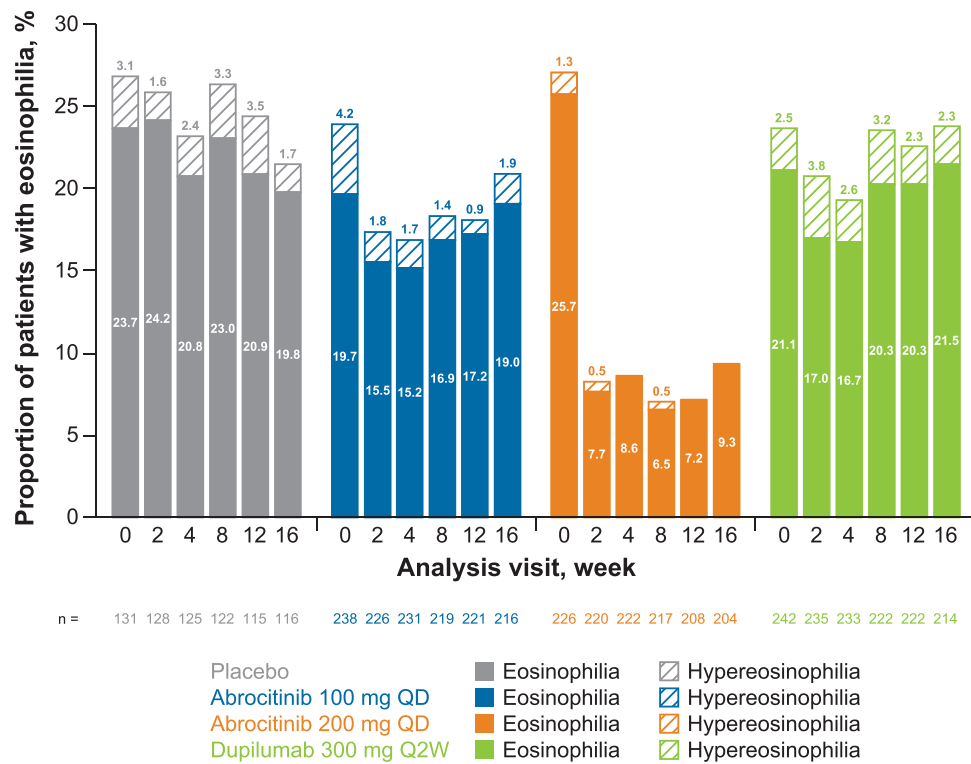


FIGURE 1 Proportion of patients with eosinophilia from baseline to Week 16 by treatment (safety analysis set). Eosinophilia was defined as eosinophil count $>0.5 \times 10^3/\text{mm}^3$ ($>500/\text{mm}^3$ and $\leq 1500/\text{mm}^3$). Hyper-eosinophilia was defined as eosinophil count $>1.5 \times 10^3/\text{mm}^3$ ($>1500/\text{mm}^3$). QD, once daily; Q2W, once every 2 weeks.

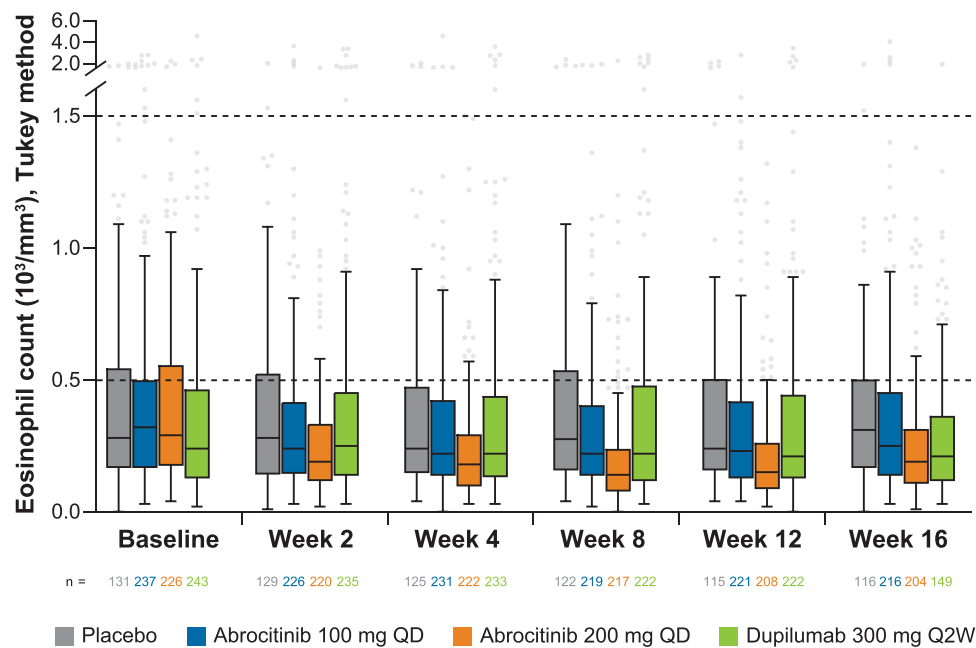


FIGURE 2 Median circulating eosinophil levels from baseline to Week 16 by treatment in the overall patient population (safety analysis set). Eosinophilia was defined as eosinophil count $>0.5 \times 10^3/\text{mm}^3$ ($>500/\text{mm}^3$ and $\leq 1500/\text{mm}^3$). Hyper-eosinophilia was defined as eosinophil count $>1.5 \times 10^3/\text{mm}^3$ ($>1500/\text{mm}^3$). Box plot indicates median and 25th/75th percentiles; outliers and whiskers were calculated using the Tukey method. QD, once daily; Q2W, once every 2 weeks.

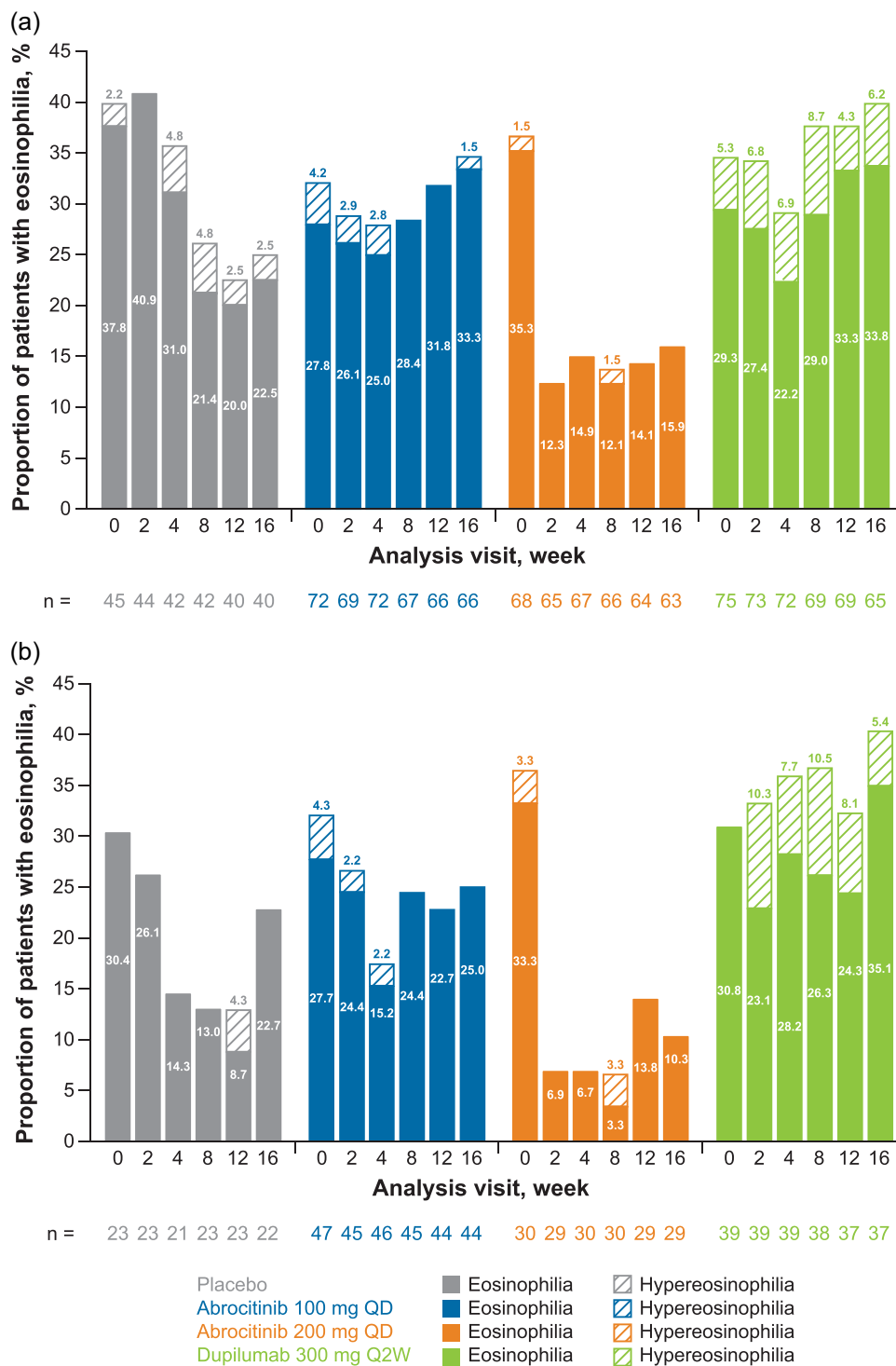


FIGURE 3 Proportion of patients from JADE COMPARE with (a) asthma and (b) allergic rhinitis at baseline who had eosinophilia or hyper-eosinophilia (safety analysis set). Eosinophilia was defined as eosinophil count $>0.5 \times 10^3/\text{mm}^3$ ($>500/\text{mm}^3$ and $\leq 1500/\text{mm}^3$). Hyper-eosinophilia was defined as eosinophil count $>1.5 \times 10^3/\text{mm}^3$ ($>1500/\text{mm}^3$). QD, once daily; Q2W, once every 2 weeks.

There was no correlation observed between the change from baseline in eosinophil counts at Week 16 and change from baseline in most of the efficacy endpoints at Week 16; a modest correlation was observed

with EASI improvement score in the abrocitinib 200-mg group ($r = 0.32$; 95% CI 0.20–0.44) and SCORAD-VAS sleep loss score in the abrocitinib 100-mg group ($r = 0.30$; 95% CI 0.17–0.42) (Table 2).

TABLE 2 Correlation between eosinophil count and change from baseline in Week 16 efficacy endpoints^a in JADE COMPARE (safety analysis set).

	Change from baseline at Week 16	Correlation (95% CI)			
		Placebo	Abrocitinib 100 mg QD	Abrocitinib 200 mg QD	Dupilumab 300 mg Q2W
Baseline eosinophil count ^a	IGA	0.09 (−0.09 to 0.27)	0.01 (−0.13 to 0.14)	−0.14 (−0.27 to −0.01)	−0.10 (−0.23 to 0.03)
	EASI	−0.07 (−0.25 to 0.12)	−0.26 (−0.38 to −0.13)	−0.35 (−0.46 to −0.22)	−0.40 (−0.50 to −0.28)
	PP-NRS	−0.08 (−0.29 to 0.14)	−0.01 (−0.17 to 0.15)	−0.03 (−0.19 to 0.13)	−0.20 (−0.34 to −0.05)
	SCORAD-VAS sleep loss	−0.08 (−0.26 to 0.11)	−0.07 (−0.20 to 0.07)	−0.20 (−0.32 to −0.06)	−0.23 (−0.35 to −0.10)
Change from baseline in eosinophil count at Week 16 ^b	IGA	0.14 (−0.05 to 0.32)	0.17 (0.04 to 0.30)	0.23 (0.10 to 0.36)	0.18 (0.05 to 0.31)
	EASI	0.20 (0.01 to 0.37)	0.26 (0.13 to 0.38)	0.32 (0.20 to 0.44)	0.28 (0.15 to 0.40)
	PP-NRS	0.18 (−0.04 to 0.38)	0.25 (0.10 to 0.39)	0.17 (0.01 to 0.32)	0.08 (−0.07 to 0.23)
	SCORAD-VAS sleep loss	0.22 (0.03 to 0.38)	0.30 (0.17 to 0.42)	0.21 (0.07 to 0.34)	0.14 (0.01 to 0.27)

Note: Values ≥ 0.3 were considered a positive correlation and values ≤ 0.3 were considered a negative correlation and are shown in bold.

Abbreviations: EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; PP-NRS, Peak Pruritus-Numerical Rating Scale; QD, once daily; Q2W, once every 2 weeks; SCORAD-VAS, SCORing Atopic Dermatitis-Visual Analog Scale.

^aSafety analysis set.

^bFull analysis set.

Effect of abrocitinib on eosinophilia in dupilumab-treated patients from JADE COMPARE who enrolled in JADE EXTEND

A total of 203 patients treated with dupilumab in JADE COMPARE entered the JADE EXTEND study and were randomly assigned to receive abrocitinib 100 mg ($n = 130$) or abrocitinib 200 mg ($n = 73$); 30 of 130 patients (23.1%) in the abrocitinib 100-mg group and 18 of 73 patients (24.7%) in the abrocitinib 200-mg group had eosinophilia or hypereosinophilia at baseline in EXTEND. After switching from dupilumab in JADE COMPARE to abrocitinib treatment in JADE EXTEND, reductions from baseline in eosinophil counts were observed from Week 2 through Week 24 in a dose-dependent manner (Supporting Information: Figure S3). The proportion of patients with eosinophilia or hypereosinophilia decreased rapidly at Week 2 and continued to decrease through Week 12 in both abrocitinib treatment groups (Figure 4).

Relationship between eosinophil levels and clinical efficacy at Week 12 in JADE EXTEND

The relationship between eosinophil count and improvements in EASI, IGA and PP-NRS at Week 12 of JADE EXTEND were assessed using correlation analyses. Baseline eosinophil counts were negatively associated with Week 12 EASI scores in JADE EXTEND in the abrocitinib 200 mg ($r = -0.37$; 95% CI -0.55 to -0.14) and abrocitinib 100 mg ($r = -0.46$; 95% CI -0.59 to -0.30) treatment groups (Supporting Information: Table S1). No associations were observed between baseline eosinophil counts and change from baseline in IGA or PP-NRS score at Week 12 with abrocitinib at either dose.

In the abrocitinib 200 mg group, change from baseline to Week 12 of JADE EXTEND in eosinophil count was positively associated with Week 12 IGA ($r = 0.39$; 95% CI 0.16 to 0.58) and EASI scores ($r = 0.44$; 95% CI 0.21 to 0.61; Supporting Information: Table S1). A modest but positive

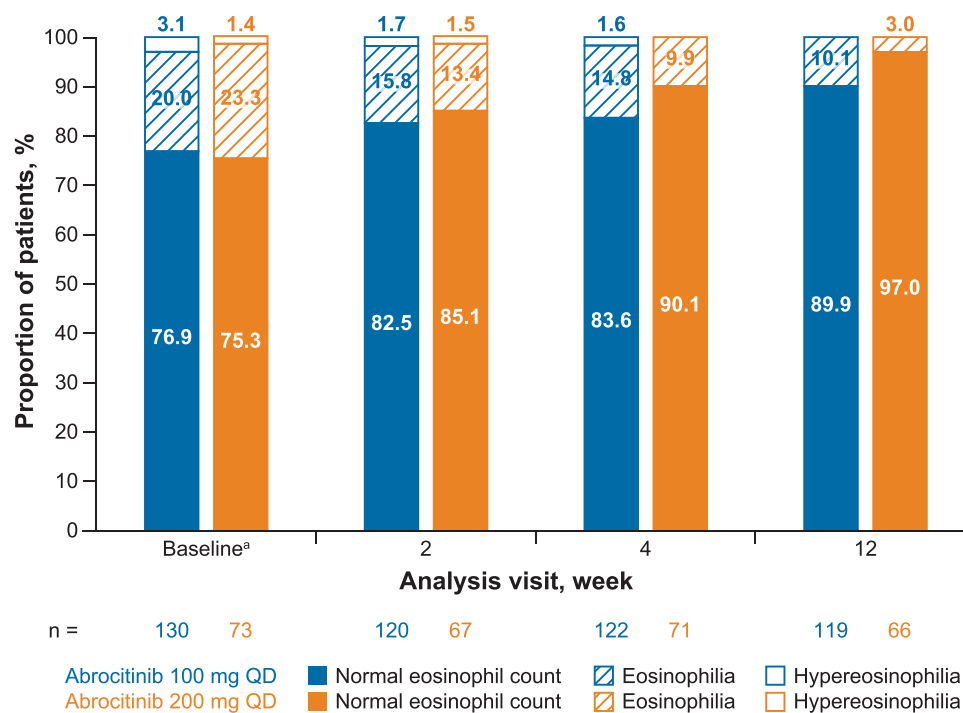


FIGURE 4 Eosinophilia status in patients treated with dupilumab from JADE COMPARE after switching to abrocitinib treatment in the long-term JADE EXTEND study (safety analysis set). Normal eosinophil count was defined as $\leq 0.5 \times 10^3/\text{mm}^3$ ($\leq 500/\text{mm}^3$). Eosinophilia was defined as eosinophil count $> 0.5 \times 10^3/\text{mm}^3$ ($> 500/\text{mm}^3$ and $\leq 1500/\text{mm}^3$). Hypereosinophilia was defined as eosinophil count $> 1.5 \times 10^3/\text{mm}^3$ ($> 1500/\text{mm}^3$). ^aBaseline in JADE EXTEND. QD, once daily.

correlation was also observed with the PP-NRS score at Week 12 ($r = 0.30$; 95% CI 0.06 to 0.50; Supporting Information: Table S1). In the abrocitinib 100 mg group, change from baseline in eosinophil count was positively associated with EASI score at Week 12 ($r = 0.48$; 95% CI 0.32–0.61); no correlations were observed between change from baseline in eosinophil count and IGA or PP-NRS (Supporting Information: Table S1).

Safety

To assess for any possible eosinophilia-associated clinical consequences, we investigated whether safety events in JADE COMPARE were associated with elevated circulating eosinophil counts. AEs were mainly mild or moderate, and no AEs or SAEs were attributed to eosinophilia. A detailed summary of the abrocitinib safety profile has been published previously.³³

DISCUSSION

In this post hoc analysis of JADE COMPARE, abrocitinib 200 mg was associated with rapid resolution of eosinophilia in patients with moderate-to-severe AD. In contrast,

eosinophil levels did not decrease in patients treated with dupilumab for the duration of this analysis (16 weeks after treatment). A similar trend was observed in the subset with comorbid asthma and allergic rhinitis; rapid resolution of hypereosinophilia was observed as early as Week 2 after treatment with abrocitinib 200 mg but not dupilumab.

The mechanism by which abrocitinib and dupilumab exert their clinical effect on eosinophilia has not been fully elucidated. It is likely that JAK inhibition with abrocitinib disrupts IL-5 signaling, leading to subsequent inhibition of eosinophil development and activation, which suggests a direct or indirect role of JAK1 in eosinophil biology.⁸ Consistent with our findings, other JAK inhibitors have also been shown to resolve hypereosinophilia, including dramatic decreases in blood eosinophil counts in patients with hypereosinophilic syndrome with cutaneous involvement after treatment with tofacitinib, a JAK 1/3 inhibitor, and ruxolitinib, a JAK1/2 inhibitor.²⁷

Increases in circulating eosinophils induced by dupilumab may be due to inhibition of IL-4 and IL-13, which in turn increases IL-5, promoting eosinophil proliferation and activation^{8,38} and suppressing the production of eotaxin-3 and/or reduces IL-13-positive Langerhans cell-mediated CCL5 production, which precludes chemotaxis

of eosinophils from the vasculature to the inflamed tissue.^{7,39,40}

Consistent with this hypothesis, clinical and real-world studies have reported elevated eosinophil counts in patients with moderate-to-severe AD after treatment with dupilumab.^{12–14,19–24} In a retrospective real-world cohort of patients from France with moderate-to-severe AD, 9.0% developed hypereosinophilia ($\geq 1500/\text{mm}^3$) soon after initiating treatment with dupilumab, followed by a subsequent decrease of circulating eosinophils.⁴¹ Similarly, in a recent prospective study of a Dutch cohort, the proportion of patients with eosinophilia increased at Week 16 after dupilumab treatment before decreasing to baseline levels at Week 52.¹⁴

The clinical implications of elevated eosinophils in patients with moderate-to-severe AD remain to be fully elucidated. Some studies of dupilumab-treated patients found that increased eosinophil levels had no clinically meaningful impact on adverse events,^{13,20} whereas in other studies, they were associated with a history of allergic conjunctivitis and food allergies²² and an increased risk of dupilumab-associated conjunctivitis,^{42,43} supporting the interplay between AD, conjunctivitis and circulating eosinophil counts.^{22,23,25} Furthermore, a recent analysis of dupilumab efficacy by eosinophilic endotypes in patients with moderate-to-severe AD from the TREATgermany clinical registry demonstrated a more robust treatment effect in the subset with low-eosinophilic endotype compared with high-eosinophilic endotype.⁴⁴ This suggests a potential impact of eosinophil levels on the magnitude of treatment benefit, although further study is warranted to help guide disease management in these patients.

There were no eosinophilia-associated AEs observed in our analysis. Reduced levels of circulating eosinophils at Week 16 of JADE COMPARE had a modest correlation with improvements in EASI and SCORAD-VAS sleep loss score with both abrocitinib doses but not with dupilumab or placebo. This is consistent with a retrospective study of patients with AD treated with dupilumab, in which patients who achieved an EASI-75 response at Week 16 had a numerically greater percentage change from baseline in eosinophil count.⁴⁵ Interestingly, in patients who were treated with dupilumab in JADE COMPARE and subsequently received abrocitinib in the long-term JADE EXTEND study, lower eosinophil levels were associated with improvements in EASI, IGA and PP-NRS, suggesting that abrocitinib-mediated decreases in eosinophils could contribute, at least in part, to improvement in signs and symptoms of AD. Our findings are in line with previous evidence that suggests a contributing role for eosinophils in the pathophysiology of AD⁴⁶ mediated by secretion of IL-31, a cytokine

associated with pruritus in AD,^{47–49} and expression of receptors for substance P, which has been associated with scratching behavior in mice.⁵⁰ Thus, eosinophils could potentially modulate pruritus via interactions with the peripheral nervous system.

This analysis was limited by its post hoc nature and small sample sizes. The comparisons between abrocitinib and dupilumab were descriptive and not subjected to formal statistical testing. Finally, the data presented here are from a 16-week study (i.e., JADE COMPARE) and an interim analysis (data cutoff April 22, 2020) of the ongoing long-term JADE EXTEND study. Final analysis of the EXTEND study will further inform the impact of abrocitinib on circulating eosinophil counts.

CONCLUSIONS

In summary, abrocitinib decreased the proportion of patients with eosinophilia in JADE COMPARE and JADE EXTEND. Decreases in eosinophil levels occurred early after treatment with abrocitinib and were sustained through Week 16 in a dose-dependent manner, irrespective of the status of comorbid asthma and allergic rhinitis at baseline. Abrocitinib at the 200-mg dose resolved all cases of hypereosinophilia by Week 12 and may thus provide a therapeutic alternative for patients who discontinue dupilumab treatment due to hypereosinophilia. Resolution of eosinophilia with abrocitinib appeared to be associated with clinical efficacy, as was evident by improvements in AD severity, itch and sleep loss, although further studies are needed to better understand the link between decreased circulating eosinophils and abrocitinib efficacy.

AUTHOR CONTRIBUTIONS

All authors contributed to the study design, and data analysis and interpretation. Fan Zhang performed the statistical analyses. All authors participated in drafting and revising the manuscript and approved the final version for submission.

ACKNOWLEDGMENTS

Editorial/medical writing support under the guidance of authors was provided by Megan K. Elder, PhD, and Stephanie Agbu, PhD, at ApotheCom, San Francisco, CA, USA, and was funded by Pfizer Inc., New York, NY, USA, in accordance with Good Publication Practice (GPP3) guidelines (*Ann Intern Med.* 2015;163:461-464).

CONFLICTS OF INTEREST STATEMENT

D. Staumont-Sallé is a scientific adviser, consultant and/or clinical study investigator for Pfizer Inc., AbbVie,

Almirall, Amgen, AstraZeneca, Boehringer, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Novartis, Sanofi Genzyme and UCB. S. Barbarot is a scientific advisor, consultant and/or clinical study investigator for Pfizer Inc., AbbVie, Almirall, Eli Lilly and Company, Janssen, LEO Pharma, Novartis, Sanofi Genzyme and UCB Pharma. J. D. Bouaziz is a scientific advisor, consultant and/or clinical study investigator for Pfizer Inc., AbbVie, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Novartis and Sanofi Genzyme. A Du-Thanh is a consultant and/or clinical study investigator for Pfizer Inc., AbbVie, LEO Pharma, Novartis and Sanofi Genzyme. L. Misery is an investigator for Pfizer Inc., AbbVie, Amgen, Eli Lilly and Company, Galderma, Kiniksa, Menlo Therapeutics, Novartis, Sanofi Genzyme, and Trevi Therapeutics, and a consultant for AbbVie, Amgen, Bayer, Beiersdorf, Clexio, Galderma, Eli Lilly and Company, Menlo Therapeutics, Novartis, Sanofi Genzyme, Sienna Biopharmaceuticals and Trevi Therapeutics. A. Nosbaum is an investigator for AbbVie, Eli Lilly and Company, Incyte, LEO Pharma, Novartis, and Sanofi Genzyme; consultant for Pfizer Inc., AbbVie, Eli Lilly and Company, Galderma, LEO Pharma, Novartis and Sanofi Genzyme; a speaker for AbbVie, Regeneron, and Sanofi Genzyme; and on advisory boards for Pfizer Inc., AbbVie, LEO Pharma and Sanofi Genzyme. J. Seneschal is a scientific adviser, consultant and/or clinical study investigator for Pfizer Inc., AbbVie, Eli Lilly and Company, Janssen, Le Laboratoire La Roche-Posay, LEO Pharma, Les Laboratoires Pierre Fabre, Novartis and Sanofi Genzyme. A. Soria is a scientific adviser, consultant and/or clinical investigator for AbbVie, Eli Lilly and Company, LEO Pharma, Novartis and Sanofi Genzyme. G. Chan, C. Clibborn, C. Feeney and A. Lejeune are employees and shareholders of Pfizer Inc. F. Zhang was an employee of Pfizer Inc. at the time this analysis was conducted.

DATA AVAILABILITY STATEMENT

Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions and exceptions, Pfizer may also provide access to the related individual deidentified participant data. See <https://www.pfizer.com/science/clinical-trials/trial-data-and-results> for more information.

ETHICS STATEMENT

This study was conducted in accordance with the principles of the Declaration of Helsinki and International Council for Harmonization Good Clinical Practice guidelines and was approved by the institutional review board or ethics committee at each trial site. All patients


in this manuscript have given written informed consent for participation in the study and the use of their deidentified, anonymized, aggregated data and their case details (including photographs) for publication.

ORCID

Sébastien Barbarot  <https://orcid.org/0000-0002-6629-9100>

Jean David Bouaziz  <https://orcid.org/0000-0002-4993-2461>

Laurent Misery  <https://orcid.org/0000-0001-8088-7059>

Julien Seneschal  <https://orcid.org/0000-0003-1139-0908>

Angèle Soria  <https://orcid.org/0000-0002-8726-6658>

REFERENCES

- Boguniewicz M, Fonacier L, Guttman-Yassky E, Ong PY, Silverberg J, Farrar JR. Atopic dermatitis yardstick: practical recommendations for an evolving therapeutic landscape. *Ann Allergy Asthma Immunol*. 2018;120(1):10–22. <https://doi.org/10.1016/j.anai.2017.10.039>
- Chrostowska-Plak D, Reich A, Szepietowski JC. Relationship between itch and psychological status of patients with atopic dermatitis. *J Eur Acad Dermatol Venerol*. 2013;27(2):e239–42. <https://doi.org/10.1111/j.1468-3083.2012.04578.x>
- Kita H. Eosinophils: multifunctional and distinctive properties. *Int Arch Allergy Immunol*. 2013;161(Suppl 2):3–9. <https://doi.org/10.1159/000350662>
- Ramirez GA, Yacoub MR, Ripa M, Mannina D, Cariddi A, Saporiti N, et al. Eosinophils from physiology to disease: a comprehensive review. *BioMed Res Int*. 2018;2018:1–28. <https://doi.org/10.1155/2018/9095275>
- Hamid Q, Boguniewicz M, Leung DY. Differential in situ cytokine gene expression in acute versus chronic atopic dermatitis. *J Clin Invest*. 1994;94(2):870–6. <https://doi.org/10.1172/jci117408>
- Hamid Q, Naseer T, Minshall E, Song Y, Boguniewicz M, Leung D. In vivo expression of IL-12 and IL-13 in atopic dermatitis. *J Allergy Clin Immunol*. 1996;98(1):225–31. [https://doi.org/10.1016/s0091-6749\(96\)70246-4](https://doi.org/10.1016/s0091-6749(96)70246-4)
- Wu AY, Sur S, Grant JA, Tripple JW. Interleukin-4/interleukin-13 versus interleukin-5: a comparison of molecular targets in biologic therapy for the treatment of severe asthma. *Curr Opin Allergy Clin Immunol*. 2019;19(1):30–7. <https://doi.org/10.1097/ACI.0000000000000490>
- Ogata N, Kouro T, Yamada A, Koike M, Hanai N, Ishikawa T, et al. JAK2 and JAK1 constitutively associate with an interleukin-5 (IL-5) receptor α and β subunit, respectively, and are activated upon IL-5 stimulation. *Blood*. 1998;91(7):2264–71.
- Bieber T. Interleukin-13: targeting an underestimated cytokine in atopic dermatitis. *Allergy*. 2020;75(1):54–62. <https://doi.org/10.1111/all.13954>
- Doran E, Cai F, Holweg CTJ, Wong K, Brumm J, Arron JR. Interleukin-13 in asthma and other eosinophilic disorders. *Front Med*. 2017;4:139. <https://doi.org/10.3389/fmed.2017.00139>

11. Kuang FL. Approach to patients with eosinophilia. *Med Clin North Am.* 2020;104(1):1–14. <https://doi.org/10.1016/j.mcna.2019.08.005>
12. Ribero S, Giura MT, Viola R, Ramondetta A, Siliquini N, Cardone P, et al. Effectiveness and safety of dupilumab for the treatment of atopic dermatitis in adult cohort: a real-life Italian tertiary centre experience. *J Eur Acad Dermatol Venereol.* 2020;34(8):e380–3. <https://doi.org/10.1111/jdv.16219>
13. Faiz S, Giovannelli J, Podevin C, Jachiet M, Bouaziz JD, Reguiai Z, et al. Effectiveness and safety of dupilumab for the treatment of atopic dermatitis in a real-life French multicenter adult cohort. *J Am Acad Dermatol.* 2019;81(1):143–51. <https://doi.org/10.1016/j.jaad.2019.02.053>
14. Ariëns LFM, van der Schaft J, Spekhorst LS, Bakker DS, Romeijn GLE, Kouwenhoven TA, et al. Dupilumab shows long-term effectiveness in a large cohort of treatment-refractory atopic dermatitis patients in daily practice: 52-Week results from the Dutch BioDay registry. *J Am Acad Dermatol.* 2021;84(4):1000–9. <https://doi.org/10.1016/j.jaad.2020.08.127>
15. Jenerowicz D, Czarnecka-Operacz M, Silny W. Peripheral blood eosinophilia in atopic dermatitis. *Acta Dermatoven APA.* 2007;16(2):47–52.
16. Uehara M, Izukura R, Sawai T. Blood eosinophilia in atopic dermatitis. *Clin Exp Dermatol.* 1990;15(4):264–6. <https://doi.org/10.1111/j.1365-2230.1990.tb02086.x>
17. Holm JG, Agner T, Clausen ML, Thomsen SF. Determinants of disease severity among patients with atopic dermatitis: association with components of the atopic march. *Arch Dermatol Res.* 2019;311(3):173–82. <https://doi.org/10.1007/s00403-019-01895-z>
18. DUPIXENT® (dupilumab) injection, for subcutaneous use. 03/2019. Tarrytown, NY: Regeneron Pharmaceuticals Inc.; 2019. p. 48.
19. Simpson EL, Bieber T, Guttman-Yassky E, Beck LA, Blauvelt A, Cork MJ, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med.* 2016;375(24):2335–48. <https://doi.org/10.1056/NEJMoa1610020>
20. Siegfried EC, Bieber T, Simpson EL, Paller AS, Beck LA, Boguniewicz M, et al. Effect of dupilumab on laboratory parameters in adolescents with atopic dermatitis: results from a randomized, placebo-controlled, phase 3 clinical trial. *Am J Clin Dermatol.* 2021;22(2):243–55. <https://doi.org/10.1007/s40257-020-00583-3>
21. Jang DH, Heo SJ, Jung HJ, Park MY, Seo SJ, Ahn J. Retrospective study of dupilumab treatment for moderate to severe atopic dermatitis in Korea: efficacy and safety of dupilumab in real-world practice. *J Clin Med.* 2020;9(6):1982. <https://doi.org/10.3390/jcm9061982>
22. Ferrucci S, Angileri L, Tavecchio S, Fumagalli S, Iurlo A, Cattaneo D, et al. Elevation of peripheral blood eosinophils during dupilumab treatment for atopic dermatitis is associated with baseline comorbidities and development of facial redness dermatitis and ocular surface disease. *J Dermatolog Treat.* 2022;33(5):2587–92. <https://doi.org/10.1080/09546634.2022.2049588>
23. Katsuta M, Ishiuiji Y, Matsuzaki H, Yasuda K, Kharma B, Nobeyama Y, et al. Transient increase in circulating basophils and eosinophils in dupilumab-associated conjunctivitis in patients with atopic dermatitis. *Acta Dermato Venereologica.* 2021;101(6):adv00483. <https://doi.org/10.2340/00015555-3842>
24. Zhou B, Peng C, Li L, Liu R, Zhu L, Chen X, et al. Efficacy and safety of dupilumab in Chinese patients with atopic dermatitis: a real-world study. *Front Med.* 2022;9:838030. <https://doi.org/10.3389/fmed.2022.838030>
25. Neagu N, Dianzani C, Avallone G, Dell'Aquila C, Morariu S-H, Zalaudek I, et al. Dupilumab ocular side effects in patients with atopic dermatitis: a systematic review. *J Eur Acad Dermatol Venereol.* 2022;36(6):820–35. <https://doi.org/10.1111/jdv.1798126>
26. Dupixent 300 mg solution for injection in pre-filled syringe. 09/26/2017. Paris, France: Sanofi-Aventis Groupe; 2017.
27. King B, Lee AI, Choi J. Treatment of hypereosinophilic syndrome with cutaneous involvement with the JAK inhibitors tofacitinib and ruxolitinib. *J Invest Dermatol.* 2017;137(4):951–4. <https://doi.org/10.1016/j.jid.2016.10.044>
28. Beck LA, Silverberg JI, Grebe K, Hong F, Parmentier J, Teixeira H, et al. Eosinophil count and serum immunoglobulin E levels in atopic dermatitis: analysis of upadacitinib phase 2 study findings. *J Allergy Clin Immunol.* 2019;143(2):AB125.
29. Pfizer L. Cibinqo 100 mg film-coated tablets (summary of product characteristics). 09/10/2021. Kent, UK: Pfizer, Limited; 2021.
30. Pfizer, Inc. Japan's MHLW approves Pfizer's Cibinqo® (abrocitinib) for adults and adolescents with moderate to severe atopic dermatitis. [updated 2021 Sep 30; cited 2022 June, 29]. Available from: <https://www.pfizer.com/news/press-release/press-release-detail/japans-mhlw-approves-pfizers-cibinqor-abrocitinib-adults>
31. CIBINQO® (abrocitinib). Summary of Product Characteristics (SmPC). Belgium: Pfizer Europe MA EEIG; 2021.
32. CIBINQO (abrocitinib) tablets, for oral use. Prescribing information. New York, NY: Pfizer Inc.; 2022.
33. Bieber T, Simpson EL, Silverberg JI, Thaçi D, Paul C, Pink AE, et al. Abrocitinib versus placebo or dupilumab for atopic dermatitis. *N Engl J Med.* 2021;384(12):1101–12. <https://doi.org/10.1056/NEJMoa2019380>
34. Ständer S, Kwatra SG, Silverberg JI, Simpson EL, Thyssen JP, Yosipovitch G, et al. Early itch response with abrocitinib is associated with later efficacy outcomes in patients with moderate-to-severe atopic dermatitis: subgroup analysis of the randomized phase III JADE COMPARE trial. *Am J Clin Dermatol.* 2023;24(1):97–107. <https://doi.org/10.1007/s40257-022-00738-4>
35. Simpson EL, Sinclair R, Forman S, Wollenberg A, Aschoff R, Cork M, et al. Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet.* 2020;396(10246):255–66. [https://doi.org/10.1016/s0140-6736\(20\)30732-7](https://doi.org/10.1016/s0140-6736(20)30732-7)
36. Silverberg JI, Simpson EL, Thyssen JP, Gooderham M, Chan G, Feeney C, et al. Efficacy and safety of abrocitinib in patients with moderate-to-severe atopic dermatitis: a randomized clinical trial. *JAMA Dermatol.* 2020;156(8):863–73. <https://doi.org/10.1001/jamadermatol.2020.1406>

37. Gooderham MJ, Forman SB, Bissonnette R, Beebe JS, Zhang W, Banfield C, et al. Efficacy and safety of oral janus kinase 1 inhibitor abrocitinib for patients with atopic dermatitis: a phase 2 randomized clinical trial. *JAMA Dermatol.* 2019;155(12):1371–9. <https://doi.org/10.1001/jamadermatol.2019.2855>
38. Barranco P, Phillips-Angles E, Dominguez-Ortega J, Quirce S. Dupilumab in the management of moderate-to-severe asthma: the data so far. *Ther Clin Risk Manag.* 2017;13:1139–49. <https://doi.org/10.2147/tcrm.S125964>
39. Matsui K, Shibata R, Mogi K. Influence of the Th1 cytokine environment on CCL5 production from langerhans cells. *Biol Pharm Bull.* 2022;45(4):491–6. <https://doi.org/10.1248/bpb.b21-00985>
40. Miranda E, Roberts J, Novick S, Lapointe JM, Buijnzeel-Koomen C, Thijs J, et al. Immunohistochemical characterization of the IL-13:IL-4 receptor α axis in the skin of adult patients with moderate to severe atopic dermatitis and healthy controls. *J Invest Dermatol.* 2021;141(2):440–3. <https://doi.org/10.1016/j.jid.2020.05.108>
41. Marcant P, Balayé P, Merhi R, Jendoubi F, Nosbaum A, Raison-Peyron N, et al. Dupilumab-associated hypereosinophilia in patients treated for moderate-to-severe atopic dermatitis. *J Eur Acad Dermatol Venereol.* 2021;35(6):e394–6. <https://doi.org/10.1111/jdv.17177>
42. Akinlade B, Guttman-Yassky E, Bruin-Weller M, Simpson EL, Blauvelt A, Cork MJ, et al. Conjunctivitis in dupilumab clinical trials. *Br J Dermatol.* 2019;181(3):459–73. <https://doi.org/10.1111/bjd.17869>
43. Nettis E, Ferrucci SM, Ortoncelli M, Pellacani G, Foti C, Di Leo E, et al. Use of dupilumab for 543 adult patients with moderate-to-severe atopic dermatitis: a multicenter, retrospective study. *J Invest Allergol Clin Immunol.* 2022;32(2):124–32. <https://doi.org/10.18176/jiaci.0641>
44. Möbus L, Rodriguez E, Harder I, Boraczynski N, Szymczak S, Hübenthal M, et al. Blood transcriptome profiling identifies 2 candidate endotypes of atopic dermatitis. *J Allergy Clin Immunol.* 2022;150(2):385–95. <https://doi.org/10.1016/j.jaci.2022.02.001>
45. Lee Y, Kim ME, Nahm DH. Real clinical practice data of monthly dupilumab therapy in adult patients with moderate-to-severe atopic dermatitis: clinical efficacy and predictive markers for a favorable clinical response. *Allergy, Asthma Immunol Res.* 2021;13(5):733–45. <https://doi.org/10.4168/aaair.2021.13.5.733>
46. Folci M, Ramponi G, Arcari I, Zumbo A, Brunetta E. Eosinophils as major player in type 2 inflammation: autoimmunity and beyond. *Adv Exp Med Biol.* 2021;1347:197–219. https://doi.org/10.1007/5584_2021_640
47. Ruppenstein A, Limberg MM, Loser K, Kremer AE, Homey B, Raap U. Involvement of neuro-immune interactions in pruritus with special focus on receptor expressions. *Front Med.* 2021;8:627985. <https://doi.org/10.3389/fmed.2021.627985>
48. Kunsleben N, Rüdrieh U, Gehring M, Novak N, Kapp A, Raap U. IL-31 induces chemotaxis, calcium mobilization, release of reactive oxygen species, and CCL26 in eosinophils, which are capable to release IL-31. *J Invest Dermatol.* 2015;135(7):1908–11. <https://doi.org/10.1038/jid.2015.106>
49. Raap U, Wichmann K, Bruder M, Ständer S, Wedi B, Kapp A, et al. Correlation of IL-31 serum levels with severity of atopic dermatitis. *J Allergy Clin Immunol.* 2008;122(2):421–3. <https://doi.org/10.1016/j.jaci.2008.05.047>
50. Lee JJ, Protheroe CA, Luo H, Ochkur SI, Scott GD, Zellner KR, et al. Eosinophil-dependent skin innervation and itching following contact toxicant exposure in mice. *J Allergy Clin Immunol.* 2015;135:477–87.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Staumont-Sallé D, Barbarot S, Bouaziz JD, Chan C, Clibborn C, Du-Thanh A, et al. Effect of abrocitinib and dupilumab on eosinophil levels in patients with moderate-to-severe atopic dermatitis. *JEADV Clin Pract.* 2023;2:518–530. <https://doi.org/10.1002/jvc2.192>