Efficacy of Abrocitinib Versus Dupilumab in Adults With Moderate-to-Severe Atopic Dermatitis Who Had an Inadequate Response or Intolerance to Nonsteroidal Immunosuppressants: Results From JADE DARE

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INTRODUCTION

- Patients with moderate-to-severe atopic dermatitis (AD) who do not respond to topical therapy are frequently treated with systemic nonsteroidal immunosuppressants (NSISS); however, long-term use of NSISS may be limited due to a poor benefit-risk profile[1]
- Thus, there is an unmet need for new treatment options in patients who had an inadequate response or were intolerant to NSISS
- Abrocitinib, an oral once-daily Janus kinase 1–selective inhibitor, is approved as monotherapy and in combination with topical therapy for the treatment of moderate-to-severe AD[2-5]
- In the phase 3 JADE DARE trial (NCT04345367), abrocitinib demonstrated superior efficacy over dupilumab in itch relief at week 2 and skin clearance at week 4 (primary endpoints) in patients with moderate-to-severe AD who received background topical therapy[6]

OBJECTIVE

- To compare the efficacy of abrocitinib and dupilumab in patients with AD who had inadequate response or were intolerant to prior NSISS and were naïve to any systemic therapies, including systemic corticosteroids

METHODS

- This post hoc analysis includes data from the JADE DARE study, a randomised, multicentre, double-blind, double-dummy, phase 3b study of patients treated with abrocitinib and dupilumab
- Patients enrolled in the study were aged ≥18 years with a clinical diagnosis of chronic moderate-to-severe AD for at least 6 months and had a recent history of inadequate response to topical medication or required systemic therapy to control AD
- Eligible patients were randomly assigned 1:1 to receive oral abrocitinib 200 mg once daily or subcutaneous dupilumab 300 mg every 2 weeks for 26 weeks
- Subgroups of patients who a) had inadequate response or were intolerant to prior NSISS (excluding those who received systemic corticosteroids only) and b) were naïve to any prior systemic therapy (previously treated with topical therapies only) were assessed from baseline through week 26 for achievement of:
  - ≥75%, 90%, and 100% improvement in the Eczema Area and Severity Index (EASI-75, EASI-90, and EASI-100, respectively)
  - ≥4-point improvement in the Peak Pruritus Numerical Rating Scale (PP-NRS4; PP-NRS © Regeneron Pharmaceuticals Inc. and Sanofi [2017])
  - PP-NRS score of 0 (itch-free) or 1 (virtually itch-free)
- Comparisons were descriptive only without testing any type I error controlled hypotheses

RESULTS

Patient Demographics and Baseline Characteristics

- The analysis comprised 377 systemic therapy-naïve patients and 87 patients who had inadequate response or were intolerant to prior NSISS
- Overall, patients in the prior NSISS group had greater disease severity and worse symptoms of AD, with higher percentage of affected body surface area (%BSA), EASI, and PP-NRS scores than those in the systemic therapy-naïve group (**Table 1**)
- Baseline disease severity was generally similar across the treatment arms in both subgroups except for patients who received abrocitinib in the prior NSISS group, who had more severe AD (**Table 1**)
- Among patients who received prior NSISS, 89.7% had inadequate response, and 19.5% were intolerant to or experienced adverse events with prior NSISS treatments
- Cyclosporine was the most commonly used NSISS in both subgroups (**Table 2**)

Table 1. Patient Demographics and Baseline Characteristics in Patients Who Were Systemic Therapy-Naïve and Had Inadequate Response or Were Intolerant to Prior NSISS in JADE DARE

	Systemic Therapy-Naïve		Failure or Intolerance to Prior NSISS	
	Abrocitinib 200 mg n=188	Dupilumab 300 mg n=189	Abrocitinib 200 mg n=37	Dupilumab 300 mg n=50
Age, mean ± SD, y	36.9 ± 14.5	35.4 ± 13.7	34.4 ± 15.7	36.1 ± 12.6
Female, n (%)	100 (53.2)	80 (42.3)	15 (40.5)	20 (40.0)
Duration of disease, mean ± SD, y	24.0 ± 14.6	23.2 ± 14.2	23.0 ± 13.5	24.7 ± 13.0
%BSA, mean ± SD	42.4 ± 19.9	40.5 ± 20.4	48.6 ± 22.9	44.4 ± 21.7
IGA score of 4, n (%)	69 (36.7)	63 (33.3)	23 (62.2)	18 (36.0)
EASI, mean ± SD	27.8 ± 11.1	27.1 ± 11.6	33.4 ± 15.1	29.3 ± 12.8
PP-NRS, mean ± SD	7.4 ± 1.5	7.3 ± 1.7	8.1 ± 1.5	7.8 ± 1.4

%BSA, percentage of body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NSISS, nonsteroidal immunosuppressants; PP-NRS, Peak Pruritus Numerical Rating Scale.

Table 2. Previous NSISS Treatments Received by Patients Who Had Inadequate Response or Were Intolerant to Prior NSISS in JADE DARE

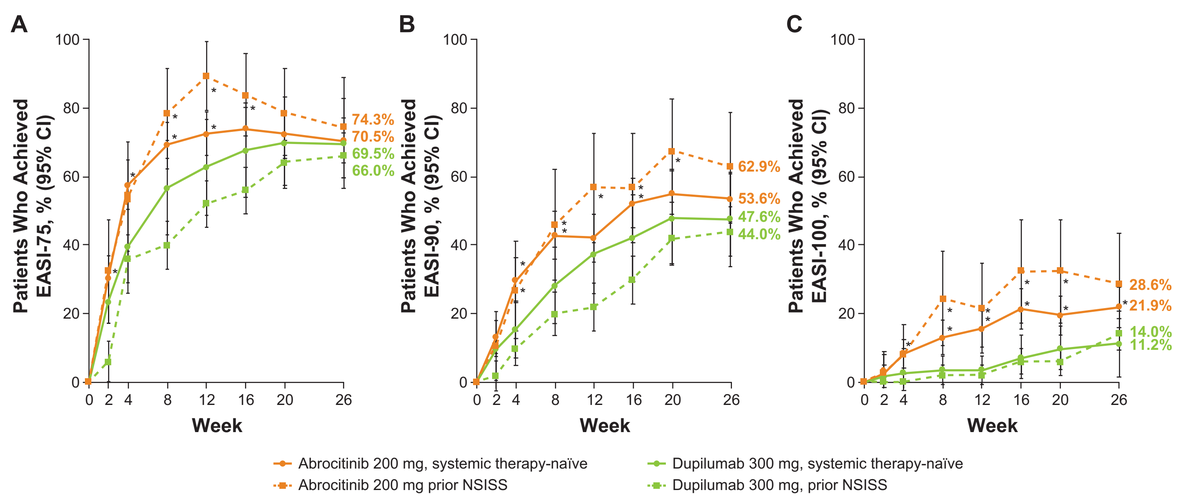
Prior treatment, n (%)	Patients With Inadequate Response to Prior NSISS n=87	Patients With Intolerance to or Who Experienced AEs With Prior NSISS n=87
Azathioprine	5 (5.7)	0 (0.0)
Cyclosporine	51 (58.6)	11 (12.6)
Methotrexate	22 (25.3)	5 (5.7)
Methotrexate sodium	12 (13.8)	1 (1.1)
Mycophenolate mofetil	2 (2.3)	0 (0.0)
Mycophenolate sodium	1 (1.1)	0 (0.0)

AE, adverse event; NSISS, nonsteroidal immunosuppressants.

EASI Response up to Week 26

- EASI-75 response with abrocitinib was rapid and sustained through 26 weeks in both the prior NSISS and the systemic therapy-naïve subgroups (**Figure 1A**)
  - The proportion of patients achieving EASI-75 response was significantly greater with abrocitinib than dupilumab ($P<0.05$) at various (not all) timepoints in both subgroups
- Similar trends were observed for abrocitinib response at the stringent thresholds of EASI-90 and EASI-100 in both subgroups (**Figure 1B, C**)
  - Treatment with abrocitinib resulted in significantly greater responses at various (not all) timepoints compared with dupilumab ($P<0.05$) in both subgroups

Figure 1. (A) EASI-75, (B) EASI-90, and (C) EASI-100 Responses up to Week 26



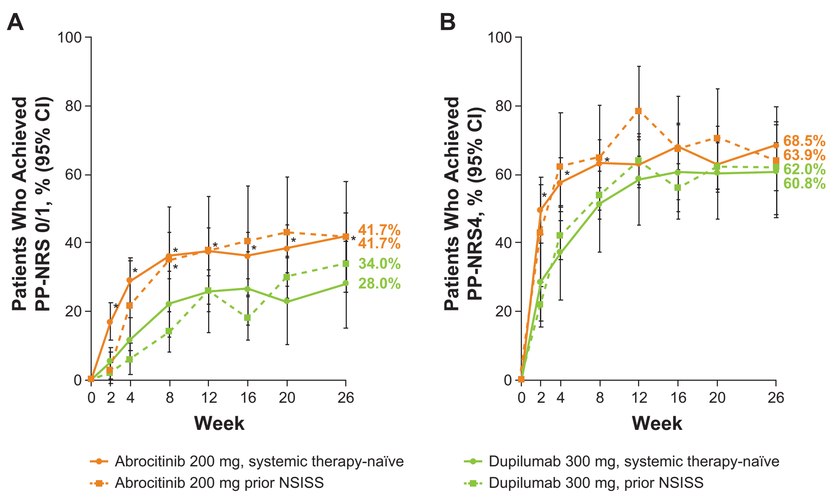
EASI, Eczema Area and Severity Index; EASI-75, ≥75% improvement in EASI; EASI-90, ≥90% improvement in EASI; EASI-100, ≥100% improvement in EASI; NSISS, nonsteroidal immunosuppressants.

*$P<0.05$ for abrocitinib versus dupilumab.

PP-NRS Response up to Week 26

- PP-NRS 0/1 response with abrocitinib was rapid and sustained through 26 weeks in both subgroups (**Figure 2A**)
  - The proportion of patients achieving the stringent threshold of PP-NRS 0/1 response was significantly greater with abrocitinib than dupilumab ($P<0.05$) at weeks 8 and 16 in the prior NSISS group and at all timepoints in the systemic therapy-naïve group
- The proportion of patients achieving PP-NRS4 response was numerically greater (not statistically significant) with abrocitinib than dupilumab from week 2 through week 26 in the prior NSISS group and significantly greater ($P<0.05$) from week 2 through week 8 in the systemic therapy-naïve group (**Figure 2B**)

Figure 2. (A) PP-NRS 0/1 and (B) PP-NRS4 Responses up to Week 26



NSISS, nonsteroidal immunosuppressants; PP-NRS, Peak Pruritus Numerical Rating Scale; PP-NRS 0/1, PP-NRS score of 0 or 1; PP-NRS4, ≥4-point improvement from baseline in PP-NRS.

*$P<0.05$ for abrocitinib versus dupilumab.

CONCLUSIONS

- Abrocitinib 200 mg provided generally greater improvements in itch and skin clearance compared with dupilumab in both patients who had inadequate response or were intolerant to prior NSISS and those who were naïve to systemic therapies
  - Improvements with abrocitinib occurred as early as week 2 and were sustained through week 26
- Additionally, a greater proportion of patients achieved a more stringent threshold of improvement in skin clearance and itch after treatment with abrocitinib than dupilumab, regardless of prior use of NSISS
- These results support the use of abrocitinib 200 mg in patients with moderate-to-severe AD in those who were systemic therapy-naïve and in those who had inadequate response or were intolerant to prior NSISS

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Abrocitinib improves atopic dermatitis in people who did not get symptom relief or could not tolerate the side effects from previous medications by mouth or injection

Date of summary: 5−7 July 2022

What is atopic dermatitis (AD)?

- AD, also known as atopic eczema, is a skin disease that can affect a person for a long time
- People with AD often use skin creams to lessen the red or flaky skin patches that may itch and become infected
- Some people with AD who do not benefit from skin creams often get treated with medications by mouth or injection that suppress the immune system called nonsteroidal immunosuppressants (NSISS)

Do NSISS medications work for AD, and can they be used for a long time?

- NSISS medications work well in some people with AD but not all
- Using NSISS medications for a long time may have side effects
- Some people may stop taking these medications because they do not get relief from AD symptoms or cannot tolerate the side effects

What is abrocitinib?

- Abrocitinib is a drug that has been shown to improve symptoms of AD in clinical studies
- Abrocitinib is approved for the treatment of moderate or severe AD in adults
- Abrocitinib is a tablet that is taken by mouth once a day

Who participated in this study?

- Adults who were 18 years of age or older and had moderate or severe AD

What did this analysis look at?

- This analysis compared the effect of abrocitinib and dupilumab, another medication for AD, in two groups of people with AD
  - People who did not get symptom relief with NSISS medications or could not tolerate the side effects
  - People who had never been treated with any medications (by mouth or injection) for AD

What did this analysis find?

- People who received abrocitinib were more likely to report fast relief from itch, redness, and dry skin than those who received dupilumab
- People who received abrocitinib were more likely to have complete/almost complete relief from itch and clear/almost clear skin than those receiving dupilumab
- This benefit with abrocitinib was maintained throughout the study period

What are the main conclusions of this analysis?

- This analysis supports the use of abrocitinib in people with AD who did not get symptom relief or tolerate the side effects from previous medications and in those who had never been treated with any medications (by mouth or injection) for AD

Who sponsored this study?

- This study was sponsored by Pfizer
- This summary reports the results of a single study. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, not on the results of a single study

Where can I find more information?

- The clinical number of the study included in this analysis is NCT04345367
- More information on this study can be found by entering the study number into the search field at www.clinicaltrials.gov
- For more information on clinical studies in general, please visit www.clinicaltrials.gov/ct2/about-studies/learn
- More information on immune system suppressing drugs including NSISS can be found at https://www.healthline.com/health/immunosuppressant-drugs

The full title of this presentation is:

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