Efficacy and Safety of Abrocitinib in Patients With Moderate-to-Severe Atopic Dermatitis: Results From the Open-Label Run-In Period of JADE REGIMEN

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BACKGROUND

- Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by intense pruritus and eczematous lesions[1]
- Abrocitinib, a Janus kinase 1 (JAK1) selective inhibitor, is being evaluated as a once-daily oral treatment for moderate-to-severe AD
- A phase 2b (NCT02780167) and 2 phase 3 monotherapy trials (JADE MONO-1 [NCT03349060] and JADE MONO-2 [NCT03575871]) previously showed that 12 weeks of abrocitinib monotherapy was safe and effective in reducing signs and symptoms of AD in patients with moderate-to-severe AD[2-4]
- AD manifests as a chronic or relapsing-remitting condition,[1] often necessitating long-term treatment
  - In everyday practice, continuous treatment may not always be feasible because of poor patient adherence, adverse drug reactions, and life events
  - It was of interest to systematically evaluate induction:maintenance treatment paradigms, including maintenance with lower doses of active drug or no drug
  - Accordingly, we conducted a multiperiod study with open-label induction, randomized withdrawal, and rescue periods (to evaluate response recapture in patients who had an AD flare) of patients with moderate-to-severe AD
- Herein, we report the results of the 12-week open-label induction period with once-daily abrocitinib 200 mg from the phase 3 JADE REGIMEN trial (NCT03627767)

OBJECTIVE

- To evaluate 12 weeks of once-daily, oral abrocitinib 200 mg for induction of response, defined as Investigator's Global Assessment (IGA) response (clear [0] or almost clear [1] with ≥2-grade improvement) and ≥75% improvement in Eczema Area and Severity Index (EASI-75) response in patients with moderate-to-severe AD

METHODS

Patient Inclusion Criteria

- Age ≥12 years, body weight ≥40 kg, and a confirmed diagnosis of chronic AD, per Hanifin and Rajka's diagnostic criteria, for ≥1 year before study entry[5]
- Moderate-to-severe AD (IGA ≥3, EASI[6] ≥16, percentage of affected body surface area [%BSA] ≥10, and Peak Pruritus Numerical Rating Scale [PP-NRS; the PP-NRS is used with permission of Regeneron Pharmaceuticals, Inc., and Sanofi][7] score ≥4) at baseline
- Documented recent history (within 6 months) of inadequate response to treatment with topical medications for AD for at least 4 weeks or use of systemic therapies (including dupilumab) for control of disease
- Oral antihistamines and topical nonmedicated emollient use permitted throughout the study
- Confirmed negative pregnancy test result for female patients of childbearing potential

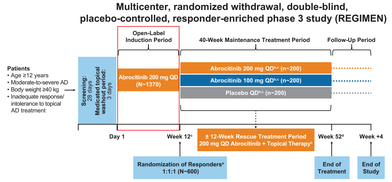
Patient Exclusion Criteria

- Preexisting conditions such as infection or history of infection, malignancy or history of malignancy, uncontrolled clinically significant laboratory abnormalities, or active or inadequately controlled tuberculosis
- Previous treatment with systemic JAK inhibitors
- Any major psychiatric conditions, recent or active suicidal ideation/behavior, clinically significant depression
- Medical history of or current conditions associated with thrombocytopenia, coagulopathy, or platelet dysfunction

Study Design

- 3-period study starting with an open-label induction period during which eligible patients with moderate-to-severe AD received once-daily oral abrocitinib monotherapy 200 mg (**Figure 1**)

Figure 1. JADE REGIMEN Study Design



This report is restricted to the open-label induction period (boxed in red).

AD, atopic dermatitis; EASI-75, ≥75% improvement in Eczema Area and Severity Index; IGA, Investigator's Global Assessment; QD, once daily.

[a]Responder criteria are defined as (a) achieving an IGA of clear (0) or almost clear (1) (on a 5-point scale), (b) a reduction from IGA baseline of ≥2 points, and (c) reaching an EASI-75 response compared with baseline. [b]Patients who experience a flare will receive 12-week rescue treatment with open-label abrocitinib 200 mg QD + topical therapy. [c]Definition of flare: a loss of response associated with a decrease of at least 50% of the EASI response at week 12 and an IGA score ≥2. [d]Eligible patients will have the option to enter a long-term extension study (JADE EXTEND; NCT03422822).

Study Size Considerations and Statistical Analysis

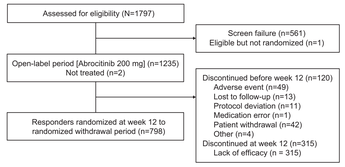
- Based on the assumption that 44% of patients would meet the protocol-defined criteria for response at week 12, approximately 1370 patients had to have enrolled in the open-label run-in period of the study to ensure that 600 responders would be available for randomization
- No formal hypothesis was tested in the open-label phase. Data were summarized using descriptive statistics

RESULTS

Demographics and Baseline Disease Characteristics

- Of 1707 patients screened in Asia, Europe, Latin America, and North America, 1233 patients were enrolled and treated with abrocitinib 200 mg once daily
- During the 12-week induction period, 120 patients (9.7%) discontinued, most as a result of adverse events (4.0%) or patient withdrawal (3.4%)
- After 12 weeks of induction treatment, 315 patients (25.5%) discontinued the study because they did not achieve the IGA 0/1 + EASI-75 response needed to enter the randomized maintenance period (**Figure 2**)

Figure 2. Patient Disposition



- Demographics and baseline disease characteristics of the treated patients are shown in **Table 1**. Most enrolled patients were male (55.5%) and White (75.5%); median duration of disease was 17.6 years

Table 1. Baseline Demographic and Disease Characteristics of Patients in the Open-Label Induction Period

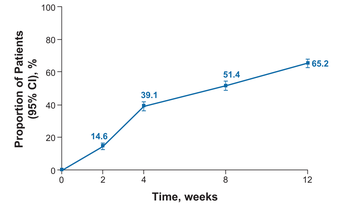
	Induction N=1233
Age, y <18 Median (Q1, Q3)	 246 (20) 28.0 (20.0, 41.0)
Sex, male, n (%)	684 (55.5)
Race, n (%) White Black or African American Asian Other[a]	 931 (75.5) 75 (6.1) 196 (15.9) 31 (2.5)
Duration of disease, median (Q1, Q3), y	17.6 (9.4, 28.3)
IGA, n (%) Moderate Severe	 729 (59.1) 504 (40.9)
EASI, median (Q1, Q3)	27.9 (21.0, 37.8)
%BSA with AD, median (Q1, Q3)	45.5 (31.0, 63.0)
PP-NRS, median (Q1, Q3)	8.0 (6.0, 9.0)
SCORAD, median (Q1, Q3)	67.1 (57.7, 77.1)
DLQI, median (Q1, Q3)	16.0 (12.0, 21.0)
POEM, median (Q1, Q3)	21.0 (16.0, 25.0)

%BSA, percentage of affected body surface area; AD, atopic dermatitis; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; POEM, Patient-Oriented Eczema Measure; PP-NRS, Peak Pruritus Numerical Rating Scale; SCORAD, Scoring Atopic Dermatitis.
[a]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, Multiracial, and not reported.

Improvement in AD Signs and Symptoms

- After 12 weeks of treatment, 65.2% of patients had a protocol-defined response of IGA 0/1 and EASI-75 (**Figure 3**)

Figure 3. Approximately Two-Thirds of Study Patients Achieve IGA 0/1 and EASI-75 Response by Week 12

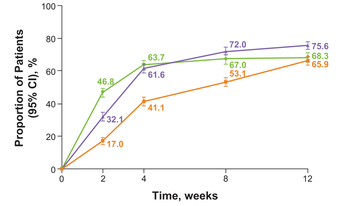


Evaluable patients, n				
	1208	1223	1227	1227

EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment.

- After 12 weeks of treatment, 65.9%, 75.6%, and 68.3% of patients had an IGA 0/1, EASI-75, or improvement of ≥4 points in PP-NRS (PP-NRS4), respectively (**Figure 4**)

Figure 4. Most Patients Achieve IGA 0/1, EASI-75, or PP-NRS4 Response Within the First 8 Weeks of Initiating Induction Treatment



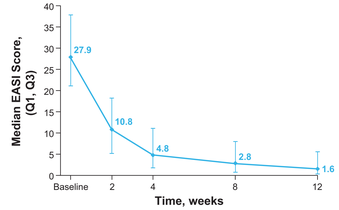
Evaluable patients, n				
IGA 0/1	1208	1223	1227	1227
EASI-75	1208	1223	1227	1227
PP-NRS-4	1223	1064	1095	940

EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; PP-NRS4, improvement of ≥4 points in Peak Pruritus Numerical Rating Scale score.

- Consistent with the results observed with the early induction of response by EASI and PP-NRS category, the median EASI and PP-NRS scores decreased to 61.3% and 50.0% from baseline, respectively, by week 2 after initiation of treatment and to 82.8% and 75%, respectively by week 4 (**Figures 5A, 5B**)

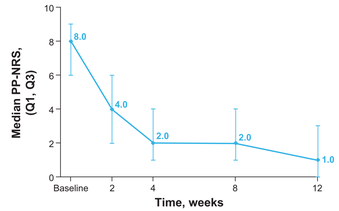
Figure 5. By Week 12 of Induction Treatment, (A) Median EASI Scores Decreased to 1.6 and (B) Median PP-NRS Scores Decreased to 1.0

A



Evaluable patients, n					
	1233	1198	1201	1185	1147

B



Evaluable patients, n					
	1232	1228	1036	1032	847

EASI, Eczema Area and Severity Index; PP-NRS, Peak Pruritus Numerical Rating Scale; PP-NRS4, improvement of ≥4 points in Peak Pruritus Numerical Rating Scale score; Q, quartile.

Exposure and Safety

- Mean (±SD) duration of exposure to abrocitinib 200 mg during the open-label induction was 82.1 (±14) days, and the proportion of patients with <80% adherence to planned medication was low (2.3%)
- Overall, 555 patients (45.0%) experienced a treatment-emergent adverse event
  - Most patients (63.4%) reported mild-to-moderate events
- The most commonly reported adverse events (by preferred term) in the open-label period were nausea (16.1%), headache (9.7%), nasopharyngitis (6.2%), acne (5.5%), and upper respiratory tract infection (5.1%; **Table 2**)
- In the open-label period, 49 patients (4.0%) discontinued treatment

Table 2. Incidence of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (any causality) Reported in ≥5% of Patients

System Organ Class Preferred term	N=1233
Gastrointestinal disorders, n (%) Nausea	261 (21.2) 199 (16.1)
Infection and infestation, n (%) Nasopharyngitis Upper respiratory tract infection	198 (16.1) 77 (6.2) 63 (5.1)
Nervous system disorders, n (%) Headache	143 (11.6) 119 (9.7)
Skin and subcutaneous tissue disorders, n (%) Acne	113 (9.2) 68 (5.5)

CONCLUSIONS

- Abrocitinib monotherapy 200 mg was effective and well-tolerated in adolescents and adults with moderate-to-severe AD during the 12-week open-label induction period of JADE REGIMEN
- Onset of response was rapid, with more than two-thirds of eventual responders meeting the respective response criteria within 4 weeks of initiating abrocitinib monotherapy 200 mg
- These results are consistent with the efficacy and safety observed in the phase 3 JADE MONO-1 and JADE MONO-2 abrocitinib monotherapy clinical trials

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