Integrated Safety Analysis of Abrocitinib in 635 Adolescent Patients With Moderate-To-Severe Atopic Dermatitis With Over 1000 Patient-Years of Exposure

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BACKGROUND

- Abrocitinib is an oral, once-daily, Janus kinase 1–selective inhibitor approved for the treatment of moderate-to-severe atopic dermatitis (AD)[1]
- Recently, the US Food and Drug Administration expanded the indication of abrocitinib to include adolescent patients with moderate-to-severe AD aged 12 to <18 years[1]
- In a previous post hoc analysis, abrocitinib was efficacious and well tolerated in adolescent patients with approximately 1 year of exposure in the JADE clinical program[2]

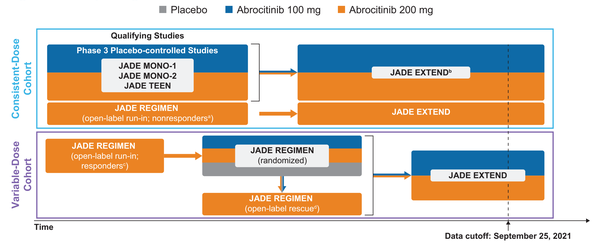
OBJECTIVE

- To describe the updated long-term integrated safety profile of abrocitinib in adolescent patients treated in the JADE clinical program

METHODS

- This interim integrated safety analysis assessed data from patients aged 12 to <18 years who participated in the phase 3 JADE clinical trials MONO-1 (NCT03349060), MONO-2 (NCT03575871), TEEN (NCT03796676), and REGIMEN (NCT03627767) and subsequently enrolled in the ongoing phase 3 extension trial, JADE EXTEND (NCT03422822; data cutoff: September 25, 2021)
- Data were pooled into 2 cohorts (**Figure 1**)
  - The consistent-dose cohort comprised patients who received the same abrocitinib dose (200 mg or 100 mg) during the entire exposure time in the qualifying JADE trials, MONO-1, MONO-2, or TEEN and in JADE EXTEND
    - This cohort also included patients who did not meet the inclusion criteria for the maintenance period of JADE REGIMEN after abrocitinib 200 mg induction in the open-label period and subsequently received abrocitinib 200 mg in JADE EXTEND
  - The variable-dose cohort included patients who were randomly assigned to the maintenance period of JADE REGIMEN after induction and, therefore, could have received different abrocitinib doses throughout exposure time in JADE REGIMEN and who subsequently entered JADE EXTEND
- Incidence rates (IRs) and 95% CIs are presented as numbers of patients with events per 100 patient-years (PY)

Figure 1. Study Design



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

JADE EXTEND is an ongoing, long-term extension phase 3 trial.

[a]Patients who did not achieve an IGA score of 0 (clear) or 1 (almost clear) with a ≥2-grade improvement from baseline and ≥75% improvement from baseline in EASI after 12 weeks of treatment with abrocitinib 200 mg.

[b]The cohort includes patients who received their first dose of abrocitinib (200 mg or 100 mg) in JADE EXTEND after receiving placebo in a phase 3 placebo-controlled trial.

[c]Patients in the open-label run-in period who were considered responders (IGA score of 0 [clear] or 1 [almost clear] with a ≥2-grade improvement from baseline and ≥75% improvement from baseline in EASI) after 12 weeks of treatment with abrocitinib 200 mg were randomly assigned to treatment with abrocitinib 200 mg, abrocitinib 100 mg, or placebo.

[d]Patients who experienced a flare (≥50% loss of week 12 EASI response and new IGA score ≥2) during the maintenance period of JADE REGIMEN entered a 12-week open-label rescue period (abrocitinib 200 mg + topical medicated treatment).

RESULTS

Patients and Baseline Characteristics

- The analysis included 635 adolescent patients
  - The consistent-dose cohort comprised 490 adolescents, and the variable-dose cohort comprised 145 adolescents
- Baseline patient characteristics are shown in **Table 1**

Table 1. Baseline Patient Characteristics for the Adolescent Consistent-Dose and Variable-Dose Cohorts

	Consistent-Dose Cohort n=490	Variable-Dose Cohort n=145
Age, mean (SD), y	14.9 (1.8)	15.1 (1.8)
Male, %	52	55
Race, %		
White	64	75
Black or African American	8	5
Asian	23	19
Other[a]	5	1
Disease duration, median (Q1, Q3), y	12.7 (7.9, 14.9)	12.1 (6.4, 15.0)
EASI score, median (Q1, Q3)	26.9 (20.1, 40.5)	29.2 (21.4, 38.4)
IGA score, %		
3 (moderate)	55	63
4 (severe)	45	37
Prior therapy, %		
Systemic	34	51
Topical only	65	49

EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; Q1, first quartile; Q3, third quartile; y, years.

[a]Other categories included American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, multiracial, or not reported.

Exposure

- The analyzed data from 635 adolescents represent 1011.4 PY of exposure
- Exposure to abrocitinib in the 2 cohorts is shown in **Table 2**

Table 2. Exposure to Abrocitinib

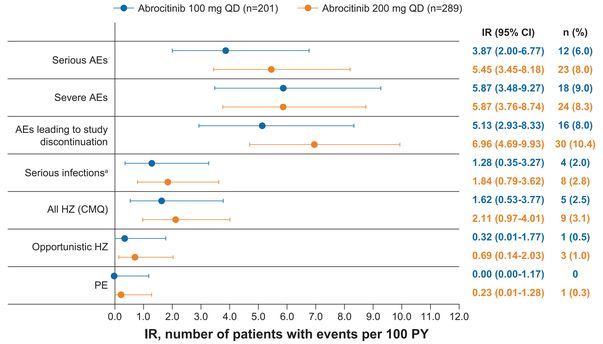
	Consistent-Dose Cohort		Variable-Dose Cohort
	Abrocitinib 100 mg n=201	Abrocitinib 200 mg n=289	All Abrocitinib n=145
PY	306.1	424.5	280.8
Exposure ≥48 weeks, %	74	68	89
Exposure ≥96 weeks, %	37	38	68
Exposure ≥144 weeks, %	4	8	3

PY, patient-years.

Adverse Events in the Consistent-Dose Cohort

- Adverse events (AEs) occurred in 243 (84%) and 153 (76%) adolescent patients in the abrocitinib 200-mg and 100-mg groups, respectively
  - IRs (95% CI) for AEs were 273.01 (239.76-309.58) for abrocitinib 200 mg and 155.76 (132.06-182.49) for abrocitinib 100 mg
- IRs for serious AEs, severe AEs, AEs leading to study discontinuation, and AEs of special interest in the consistent-dose cohort are shown in **Figure 2**
  - No meaningful dose-response relationship was observed for serious AEs, severe AEs, AEs leading to study discontinuation, or AEs of special interest, including serious infections, all herpes zoster infections, and opportunistic herpes zoster infections
  - Excluding herpes zoster, there were no other opportunistic infections observed and no tuberculosis cases
  - 1 patient (aged 16 years) in the 200-mg arm had a nonfatal venous thromboembolism event (pulmonary embolism; IR, 0.23 [95% CI, 0.01-1.28]); this patient had a notable family history of pulmonary embolism[2]
  - There was 1 event of retinal detachment with a concurrent diagnosis of cataracts and a concurrent diagnosis of left eyebrow folliculitis in an adolescent (aged 17 years) in the abrocitinib 100-mg group

Figure 2. IRs (95% CIs) for Serious AEs, Severe AEs, AEs Leading to Study Discontinuation, and AEs of Special Interest in the Consistent-Dose Cohort



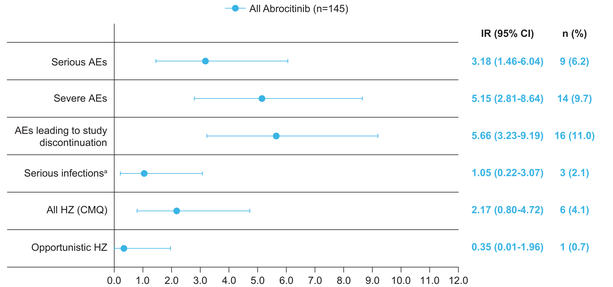
AE, adverse event; CMQ, customized MedDRA query; HZ, herpes zoster; IR, incidence rate; MedDRA, Medical Dictionary for Regulatory Activities; PE, pulmonary embolism; PY, patient-years; QD, once daily.

[a]Serious infections in the consistent-dose cohort were peritonsillitis, eczema herpeticum, skin infection,arthritis bacterial, muscle abscess, osteomyelitis, staphylococcal sepsis, pharyngitis, COVID-19, infectious mononucleosis, pneumonia, Clostridium difficile infection, and COVID-19 pneumonia.

Adverse Events in the Variable-Dose Cohort

- AEs occurred in 139 adolescents (96%) exposed to either dose of abrocitinib
- IRs for serious AEs, severe AEs, AEs leading to study discontinuation, and AEs of special interest in the variable-dose cohort are shown in **Figure 3**
  - The IRs in the variable-dose cohort were consistent with those in the consistent-dose cohort
  - Similar to the consistent-dose cohort, there were no tuberculosis events or other opportunistic infections (excluding herpes zoster)
  - There were no venous thromboembolism events observed in the variable-dose cohort

Figure 3. IRs (95% CIs) for Serious AEs, Severe AEs, AEs Leading to Study Discontinuation, and AEs of Special Interest in the Variable-Dose Cohort



AE, adverse event; CMQ, customized MedDRA query; HZ, herpes zoster; IR, incidence rate; MedDRA, Medical Dictionary for Regulatory Activities; PY, patient-years.

[a]Serious infections in the variable-dose cohort were skin bacterial infection, pneumonia, and appendicitis.

Malignancies, Cardiovascular Events, and Deaths

- In both the consistent-dose and variable-dose cohorts, there were no events of nonmelanoma skin cancer or other malignancies, major adverse cardiovascular events, or deaths

CONCLUSIONS

- In this integrated safety analysis using the September 2021 data cut from the ongoing JADE EXTEND trial, abrocitinib had an acceptable long-term safety profile in adolescents with moderate-to-severe AD
- There were no unique safety concerns related to adolescents compared to the findings observed previously in the integrated safety analysis using the same data cut in which most patients were adults[3]

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