# Safety of Abrocitinib in 3582 Patients With Moderate-to-Severe Atopic Dermatitis With Over 900 Patients Exposed for Almost 2 Years

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## BACKGROUND

- Abrocitinib is an oral, once-daily, Janus kinase 1–selective inhibitor approved for the treatment of with moderate-to-severe AD[1-3]
- An integrated safety analysis was previously published for abrocitinib clinical trials that included 2856 patients with moderate-to-severe AD[4]
- Additional safety data have accrued from further randomized controlled trials and an ongoing long-term extension study
- The integrated safety analysis presented here includes data from the largest population and longest follow-up period reported to date

## OBJECTIVE

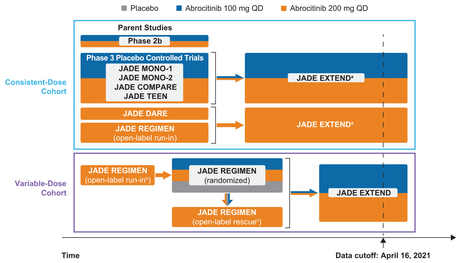
- To evaluate the long-term safety profile of abrocitinib and provide relevant information for practitioners

## METHODS

### Study Design

- Data from patients who received ≥1 dose of abrocitinib 200 mg or 100 mg in the JADE clinical trial program were pooled into 2 cohorts (**Figure 1**)
  - In the consistent-dose cohort, patients received the same abrocitinib dose during the entire exposure time in parent phase 3 studies and/or the long-term extension study JADE EXTEND (NCT03422822); data cutoff April 16, 2021
    - Parent studies were JADE MONO-1 (NCT03349060), JADE MONO-2 (NCT03575871), JADE TEEN (NCT03796676), JADE COMPARE (NCT03720470), JADE DARE (NCT04345367), and JADE REGIMEN (NCT03627767)
      - For JADE REGIMEN (200 mg only), only patients from the open-label run-in phase who did not subsequently enter the randomized phase were included
    - Patients may have received their first dose of abrocitinib in JADE EXTEND if they previously received placebo in the placebo-controlled parent studies and/or dupilumab in JADE COMPARE or JADE DARE
    - Patients from the phase 2b study (NCT02780167) who received abrocitinib 200 mg or 100 mg were also included
  - In the variable-dose cohort, patients received different doses of abrocitinib (200 mg and 100 mg) throughout exposure time in the parent study (JADE REGIMEN) and were enrolled in JADE EXTEND
    - Patients who completed the open-label period of JADE REGIMEN (abrocitinib 200 mg only) and entered the randomized phase (abrocitinib 200 mg, abrocitinib 100 mg, or placebo) were included
    - Some patients subsequently entered the JADE REGIMEN rescue phase (abrocitinib 200 mg) and/or JADE EXTEND (abrocitinib 200 mg or 100 mg)

**Figure 1.** Analysis Cohorts




EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; QD, once-daily.

JADE EXTEND is ongoing.

[a]Includes patients who received their first dose of abrocitinib (100 mg or 200 mg) in JADE EXTEND after receiving placebo in a phase 3 placebo-controlled trial or dupilumab in JADE COMPARE or JADE DARE.

[b]Patients in the open-label run-in period who achieved response (IGA score of 0 [clear] or 1 [almost clear] and ≥75% improvement from baseline on the EASI) after 12 weeks of treatment with abrocitinib 200 mg were randomly allocated to treatment with abrocitinib 200 mg, abrocitinib 100 mg, or placebo.

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

### Statistical Analysis

- Incidence rates (IRs; number of unique patients with events per 100 patient-years [PY]) of adverse events were calculated
  - For IR calculations, patient exposure was calculated up to the time of first event for patients with events
  - Time to event was censored at the end of the risk period for patients who did not experience an event
- A Cox proportional hazard regression analysis evaluated risk factors for specific events of interest

## RESULTS

### Patients

- Data from 3582 patients were analyzed, representing 4313.4 PY
  - The consistent-dose cohort (n=2784) included 1721.3 PY of exposure to abrocitinib 200 mg (n=1761) and 1284.4 PY of exposure to abrocitinib 100 mg (n=1023)
    - Duration of exposure was ≥48 weeks in 767 of 1761 patients (43.6%) and 684 of 1023 patients (66.9%) and ≥96 weeks in 317 of 1761 patients (18.0%) and 237 of 1023 patients (23.2%) in patients treated with abrocitinib 200 mg and 100 mg, respectively
  - In the variable-dose cohort (n=798), total abrocitinib exposure was 1307.7 PY; cumulative abrocitinib exposure was ≥48 weeks in 687 of 798 patients (86.1%) and ≥96 weeks in 362 of 798 patients (45.4%)
- In the consistent-dose and variable-dose cohorts, median age was 30.0 and 29.0 years, 490 patients (17.6%) and 145 patients (18.2%) were adolescents, and 143 patients (5.1%) and 30 patients (3.8%) were aged ≥65 years at screening, respectively (**Supplementary Table S1**, accessible via the QR code)

### Safety Events

- IRs for SAEs, AEs leading to treatment discontinuation, deaths, and other specific adverse events of interest are reported in **Figure 2** for the consistent-dose cohort and in **Supplementary Figure S1** for the variable-dose cohort
  - IRs for SAEs were higher in patients aged ≥65 years versus younger patients in the consistent-dose cohort
  - Serious infections were the most frequent SAEs reported in both the consistent-dose cohort and the variable-dose cohort
  - IRs for TEAEs leading to discontinuation were higher with abrocitinib 200 mg than with abrocitinib 100 mg
- 7 deaths were reported in the consistent-dose cohort, including 5 in the abrocitinib 200 mg group (coronavirus disease 2019 [COVID-19], n=2; septic shock, n=1; cardiac failure, n=1; cardiorespiratory arrest, n=1) and 2 in the abrocitinib 100 mg group(sudden death, n=1; COVID-19, n=1); 2 of the deaths described here were previously reported. There was also an additional death (>200 days after last dose of abrocitinib) that was previously reported which involved gastric adenocarcinoma[4]
  - No deaths were reported in the variable-dose cohort

### Infections

- IRs for infections are reported in **Figure 2** for the continuous-dose cohort and in **Supplementary Figure S1** for the variable-dose cohort
- Herpes zoster, herpes simplex, and pneumonia were the most frequent serious infections
  - Most (95%) adjudicated opportunistic herpes zoster infections were cutaneous; 2 (5%) were extracutaneous (1 serious disseminated varicella zoster virus infection, 1 serious herpes zoster meningitis)
  - A trend towards a dose-dependent relationship was observed with herpes zoster infections
- No risk factors were identified for serious infections in a Cox regression analysis
- Potential risk factors for treatment-emergent herpes zoster included abrocitinib dose, age ≥65 years, medical history of herpes zoster, absolute lymphocyte count <1000/mm$^3$ prior to infection, and region (**Supplemental Table S2**)

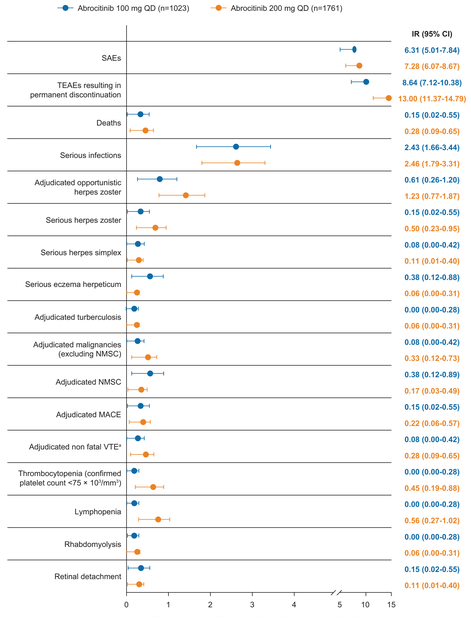
### Malignancies and Cardiovascular Events

- IRs for malignancies and cardiovascular events are reported in **Figure 2** for the continuous-dose cohort, and in **Supplementary Figure S1** for the variable-dose cohort
  - IRs were higher in patients aged ≥65 years compared with younger patients

### Hematological Events

- IRs for thrombocytopenia and lymphopenia are reported in **Figure 2** for the continuous-dose cohort and in **Supplementary Figure S1** for the variable-dose cohort
  - IRs for thrombocytopenia and lymphopenia events were higher in patients aged ≥65 years compared with younger patients

**Figure 2.** IRs (95% CI) for Adverse Events of Special Interest in the Consistent-Dose Cohort




IR, incidence rate; MACE, major adverse cardiac events; NMSC, non-melanoma skin cancer; PY, person-years; QD, once-daily; SAE, serious adverse events; TEAE, treatment-emergent adverse event; VTE, venous thromboembolism.

[a]1 pulmonary embolism embolism event (not adjudicated) was included.

## CONCLUSIONS

- For patients requiring Janus kinase inhibitors to control moderate-to-severe AD, these data further clarify the overall long-term safety profile of abrocitinib
  - In this largest and longest analysis of abrocitinib in patients with moderate-to-severe AD to date, the AEs identified were generally consistent with previous safety analyses[4,5]
- Patient selection and dose selection are important considerations for prescribers
  - Risk of SAEs, herpes zoster infection, malignancies, cardiovascular events, lymphopenia, and thrombocytopenia increased in patients aged ≥65 years
  - Increased risk of herpes zoster also appeared to be related to higher abrocitinib dose, medical history of herpes zoster, geographic region, and absolute lymphocyte count <1000/mm$^3$ prior to infection
- These data support the acceptable safety profile of abrocitinib in the treatment of moderate-to-severe AD in eligible patients

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## DISCLOSURES

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