Integrated Safety Analysis of Abrocitinib for the Treatment of Moderate-to-Severe Atopic Dermatitis (AD) From the Phase 2 and Phase 3 Clinical Trial Program

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Background: Janus kinase (JAK) inhibitor specificity and patient characteristics underlie JAK inhibitor safety. In a pooled analysis, we report the safety of abrocitinib, an oral once-daily JAK1 selective inhibitor under investigation for treatment of moderate-to-severe AD.

Objectives: To perform an integrated safety analysis of abrocitinib in patients with moderate-to-severe AD who received abrocitinib in the JADE clinical trial program, which included 1 phase 2 and 5 phase 3 clinical trials, and to identify potential risk factors for and dose-related differences in adverse reactions and laboratory values in abrocitinib-treated patients with moderate-to-severe AD in a pooled analysis from the JADE clinical development program.

Methods: An all-exposure pool, comprising all patients who received ≥1 dose of 200 mg or 100 mg abrocitinib from 1 phase 2b and 5 phase 3 trials, including a long-term extension study, was used to assess low-frequency/long-latency events, including infection, hematologic changes, cardiovascular events, and malignancy. Safety data were also analyzed in the primary pool, which included patients from shorter (12-16 weeks) placebo-controlled studies.

Results: Among 2856 patients, 1248 had ≥24 weeks and 606 had ≥48 weeks of abrocitinib exposure. In the primary pool, dose-related treatment-emergent adverse events (TEAEs; 200 mg, 100 mg, and placebo) were nausea (14.6%, 6.1%, and 2.0%), headache (7.8%, 5.9%, and 3.5%), acne (4.7%, 1.6%, and 0%), and herpes simplex virus infection (4.2%, 3.3%, and 1.8%). A transient dose-dependent decrease in platelet count was observed, with a deeper nadir at week 4 with 200 mg than with 100 mg; in 2 of 2718 patients (200-mg group) platelet number decreases were confirmed, necessitating discontinuation ($<50\times10^3/mm^3$). Incidence rates (IRs; 200 mg, 100 mg) were 2.33/100 patient-years (PYs) and 2.65/100 PYs for serious infections and 4.34/100 PYs and 2.04/100 PYs for herpes zoster infection. IRs for nonmelanoma skin cancer, other malignancy, and cardiovascular events (both doses) were <0.5/100 PYs.

Conclusion: Results of this integrated safety analysis were consistent with results in individual trials. Abrocitinib was well-tolerated in patients with AD; there were no unexpected safety findings.