**Title:**

Efficacy and safety of baricitinib in moderate-to-severe atopic dermatitis: Results from a randomized, double-blinded, placebo-controlled phase 3 clinical trial (BREEZE-AD5)

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**Abstract Body:**

**Background**

Baricitinib is an oral, selective Janus kinase (JAK)1/JAK2 inhibitor in development for moderate-to-severe atopic dermatitis (AD).

**Objectives**

To report the efficacy and safety of baricitinib monotherapy in a multicenter, randomized, parallel-group, double-blinded, placebo-controlled, Phase 3 trial (BREEZE-AD5, NCT03435081) in the United States and Canada of adult patients with moderate-to-severe AD who were intolerant or who responded inadequately to topical therapy.

**Methodology**

Patients (N=440) were randomized 1:1:1 to once daily placebo, baricitinib 1 mg, or baricitinib 2 mg. The primary endpoint was the proportion of patients achieving ≥75% reduction in Eczema Area and Severity Index (EASI75) at Week 16. Secondary endpoints included the proportion of patients achieving a validated Investigator Global Assessment for AD (vIGA-AD™) of 0/1 with a ≥2-point improvement, the proportion of patients achieving at least a 4-point improvement on the Itch Numeric Rating Scale (NRS), the mean change from baseline in the Skin Pain NRS and in the AD Sleep Scale (ADSS) Item 2 (nighttime awakening due to itch), and the mean change in Dermatology Life Quality Index (DLQI) score. Multiplicity-adjusted analyses were performed on the primary and key secondary endpoints. Data from patients who discontinued treatment or received any rescue therapy were imputed with non-responder imputation for categorical variables. For continuous variables, mixed models for repeated measures were performed.

**Results**

Patient demographics included approximately 50% women, 57% white, 18% African American, 19% Asian, and 6% other, and a mean patient age of 40 years. Approximately one-third of patients had

adult-onset AD. 42% of patients had an IGA of 4 (severe disease), and the mean EASI score was 27. At Week 16, the proportion of patients achieving EASI75 for placebo, baricitinib 1 mg, and baricitinib 2 mg, respectively, were 8%, 13%, and 30% ($P$<0.001 for baricitinib 2 mg vs. placebo) and the proportion of patients achieving a vIGA-AD of 0/1 was 5%, 13% ($P$<0.05 vs. placebo), and 24% ($P$<0.001 vs. placebo). At Week 16, the proportion of patients achieving at least a 4-point improvement on Itch NRS was 6% for placebo, 16% for baricitinib 1 mg ($P$<0.05 vs. placebo) and 25% for baricitinib 2 mg ($P$<0.001 vs. placebo). Statistically significant improvement in the proportion of patients who achieved at least a 4-point improvement on the Itch NRS was observed as early as Week 2 for both baricitinib 1 mg and 2 mg. Statistically significant reduction in skin pain severity and number of nighttime awakenings due to itch were observed as early as Week 1 and were maintained to Week 16 for baricitinib 2 mg compared with placebo. At Week 16, the mean change in DLQI was -4.0 for placebo, -5.5 for baricitinib 1 mg, and -7.5 for baricitinib 2 mg ($P$<0.01 for baricitinib 2 mg vs. placebo). During the first 16-week treatment period, for placebo, baricitinib 1 mg, and baricitinib 2 mg, respectively, adverse events (AEs) were reported in 49%, 54%, and 51%, with 2%, 1%, and 1% experiencing serious AEs (SAEs); the most common AEs were nasopharyngitis (8%, 2%, 5%), upper respiratory tract infection (6%, 6%, 8%), and diarrhea (1%, 2%, 4%). No cases of malignancy, gastrointestinal perforation, deep vein thrombosis, pulmonary embolism, major adverse cardiovascular events, or deaths occurred. There were no cases of Grade 3 or 4 anemia, 1 case of Grade 3 neutropenia reported with baricitinib 1 mg, and 2 cases (1 with placebo and 1 with baricitinib 2 mg) of Grade 3 lymphopenia.

**Conclusions**

This is the fifth positive Phase 3 trial for baricitinib in AD. Baricitinib significantly improved skin inflammation, pain, itch, sleep, and quality of life outcomes in patients with moderate-to-severe AD compared with placebo. There was no increase in the frequencies of SAEs in patients treated with baricitinib compared with placebo, and no new safety findings.