Rapid and Concurrent Improvements in Signs and Symptoms of Atopic Dermatitis with Baricitinib in Phase 3 Studies

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Background: The efficacy and safety of baricitinib (BARI), an oral selective inhibitor of Janus kinases (JAK)1 and JAK2, were evaluated in adult patients with moderate-to-severe atopic dermatitis (AD) and a history of inadequate response or intolerance to existing topical therapies in two double-blind, placebo (PBO)-controlled Phase 3 studies, BREEZE-AD1 (NCT03334396) and BREEZE-AD2 (NCT03334422).

Objective: The objective of this analysis was to assess the onset and magnitude of changes across different severity scales and patient-reported outcomes (PROs) for the first 4 weeks of treatment in these two monotherapy trials.

Methods: In BREEZE-AD1 (N=624) and BREEZE-AD2 (N=615), adult patients were randomized 2:1:1:1 to once daily PBO, BARI 1-mg, 2-mg, or 4-mg for 16-weeks. The use of topical and systemic AD therapies were not allowed during the double-blind period and could be used only as rescue therapy. In this intent-to-treat analysis, the weekly least squares mean change from baseline up to Week 4 in Eczema Area and Severity Index (EASI), Itch Numeric Rating Scale (NRS), Skin Pain NRS, AD Sleep Scale (ADSS) Item 2 (measuring the frequency of nighttime awakenings), Dermatology Life Quality Index (DLQI), and Patient-Oriented Eczema Measure (POEM) were compared between treatments using mixed model repeated measure analysis. Data after any rescue therapy or discontinuation was considered missing from the analysis

Results: In BREEZE-AD1/BREEZE-AD2, respectively, significantly more patients achieved an EASI75 on BARI than PBO at Week 4 (BARI 4-mg 23.2%/25.2% [p<0.001]; 2-mg 13.0%/20.3% [p<0.001]; 1-mg 7.9%/9.6% [p<0.05] and PBO 2.4%/3.7%). Speed of onset of improvement in the 6 outcomes were compared using a spider-web diagram and the animated video is available at: https://lillyscience.lilly.com/download/53AeGmQteuv6mjm9DY16T5. Statistically significant improvements in physician assessments (EASI), PROs (Itch NRS, Skin Pain NRS, ADSS Item 2, POEM) and

quality of life (DLQI) were observed as early as Week 1 in BARI-treated patients (all doses) in both studies compared to PBO. Improvements in itch and skin pain severity as well as the number of nighttime awakenings were evident within 2-4 days after treatment initiation at Day 1. All BARI doses continued to show statistically significant improvements compared to PBO in itch and skin pain severity, POEM and DLQI from Week 1 through Week 4 while improvements in EASI and sleep (ADSS Item 2) were observed with BARI 2-mg and 4-mg doses in both studies (Table 1). BARI significantly improved the signs and symptoms of moderate-to-severe AD compared to PBO at Week 16.

Conclusion: Treatment with BARI showed rapid and concurrent improvements not only in skin measures (EASI), but also in key symptoms and outcomes like sleep, itch and skin pain severity, POEM and DLQI, with statistically significant improvements seen as early as Week 1 for all assessments.

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