Title: Clinical tailoring of baricitinib 2-mg in atopic dermatitis: baseline body surface area and rapid onset of action identifies response at Week 16

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Background: Baricitinib, an oral Janus kinase (JAK)1/JAK2 inhibitor, improved disease in moderate-to-severe atopic dermatitis (AD) in 5 randomized, placebo-controlled, Phase 3 trials. Understanding the patient population who will benefit most from treatment with baricitinib 2-mg based on clinical trial data would significantly improve patient experience with treatment. Here, we present results from a post-hoc analysis aiming to identify responders to baricitinib 2-mg, with a proposed clinical tailoring approach based on baseline body surface area affected (BSA) and early clinical improvement from the Phase 3 monotherapy trial BREEZE-AD5 (NCT03435081).

Methods: Classification and regression trees were applied to baseline patient demographics and disease characteristics to identify a patient population most likely to benefit from baricitinib 2-mg therapy. Two-by-two contingency tables evaluated the association between speed of onset on improvement in skin inflammation or itch (assessed at Week 4 or Week 8) and response at Week 16 for the proportion of patients achieving ≥75% improvement in Eczema Area and Severity Index (EASI75), validated Investigator Global Assessment for AD (vIGA-AD™) score of 0 or 1, or ≥4-point improvement in Itch (Itch≥4). Missing data due to rescue or treatment discontinuation were imputed as non-responder. Response rates were also summarized over time for identified subgroups.

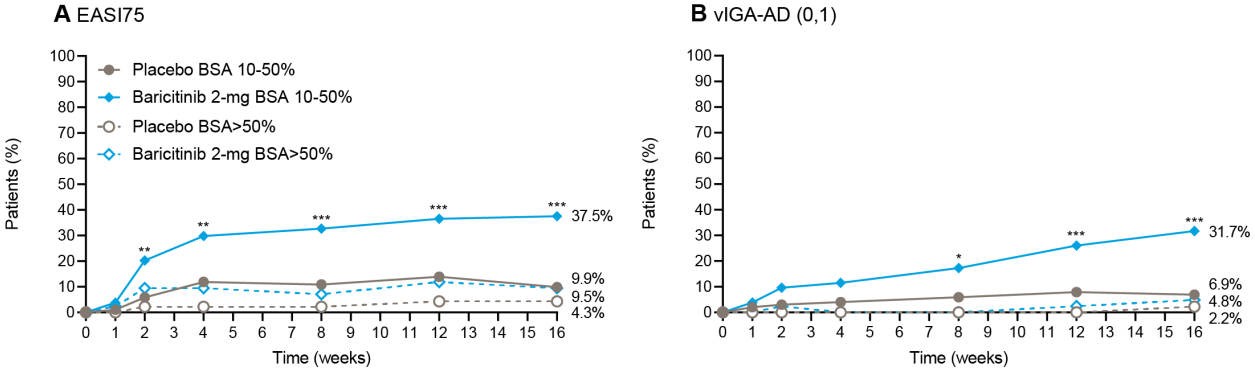
Results: Baseline BSA of 10-50% was associated with improved clinical response to baricitinib 2-mg (Figure A and B). At Week 16, EASI75 was achieved by 37.5% of baricitinib 2-mg-treated patients with baseline BSA 10-50% compared to 9.5% of patients with BSA>50% (Figure A). Similarly, at Week 16, vIGA-AD (0,1) was achieved by 31.7% of baricitinib 2-mg-treated patients with baseline BSA 10-50% compared to 4.8% of patients with BSA>50% (Figure B). Early meaningful response, defined as ≥50% improvement in BSA or ≥3-point improvement in itch from baseline at Week 4 or Week 8, was able to further refine which patients were most likely to benefit from baricitinib 2-mg therapy (Figure C-F). Early response in skin inflammation or itch at Week 4 was associated with corresponding EASI75, vIGA-AD (0,1), and Itch≥4 of 55.4%, 48.2%, and 39.3% at Week 16 (Figures C and D). Assessment of early

response at Week 8 was associated with EASI75, vIGA-AD (0,1), and Itch≥4 of 66.7%, 56.1%, and 42.1% at Week 16 (Figures E and F).

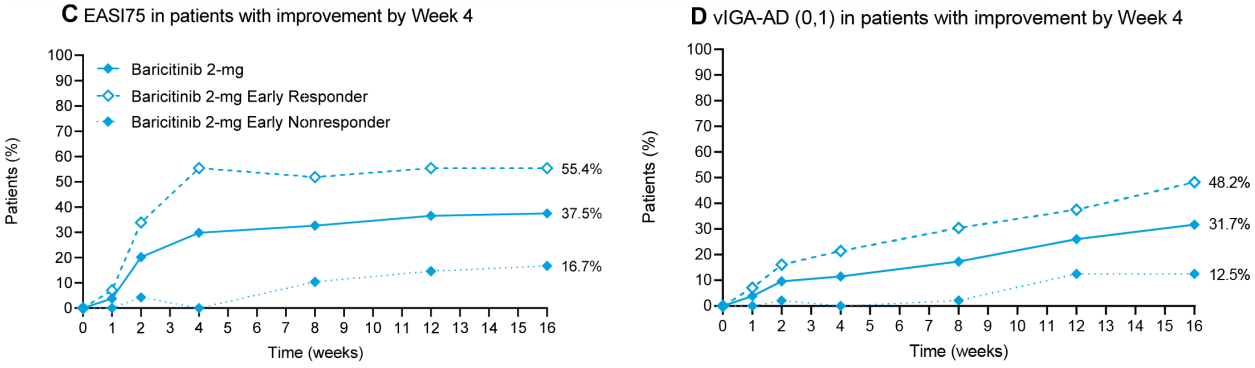
Conclusion: There are currently multiple therapies in development for AD. Understanding which patients are likely to benefit most from therapy, and which patients should not be considered for a given treatment can significantly improve patient experience with treatment, increase the cost-effectiveness of a therapy, and ensure that only patients who are likely to benefit from therapy are exposed to drug. This analysis suggests that patients with moderate-to-severe AD affecting between 10-50% of their BSA account for the majority of responders to baricitinib 2-mg. In addition, due to rapid onset of response, clinical assessment of patients after 4 or 8 weeks of initiation of baricitinib 2-mg treatment showed a meaningful clinical benefit to patients, providing positive feedback to patients who are likely to benefit from long-term therapy and allowing for rapid decision on discontinuation of treatment in those who are not likely to benefit from baricitinib 2-mg.

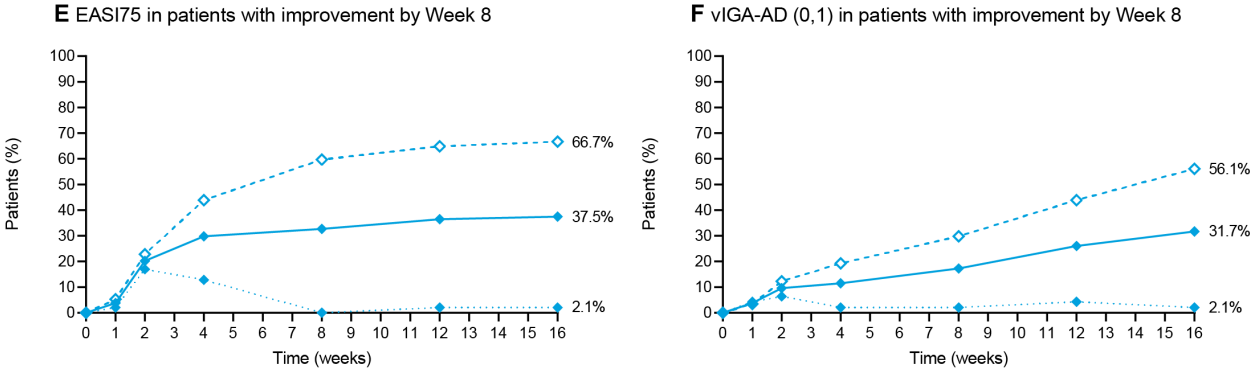
Figure. Efficacy responses over time

Efficacy responses by baseline BSA subgroups



Efficacy responses in baseline BSA 10-50% subgroup by early response at Weeks 4 or 8





* P≤0.05, ** P≤0.01, and *** P≤0.001 for baricitinib 2-mg compared with placebo.