Achieving Incrementally Greater Skin Improvement Thresholds with Upadacitinib in Moderate to Severe Atopic Dermatitis: A Pooled Analysis of Two Phase 3 Studies (Measure Up 1 and Measure Up 2)

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INTRODUCTION: Atopic dermatitis (AD) is a chronic, flaring, inflammatory disease associated with multiple skin manifestations and symptoms that can impact patients’ quality of life. Studies have shown that greater improvements on Eczema Area and Severity Index (EASI) are associated with to greater improvements in quality of life. Upadacitinib (UPA), an oral selective Janus kinase inhibitor, is being studied in phase 3 trials of adolescent and adult patients with moderate to severe AD (EASI ≥ 16; Body Surface Area ≥ 10%; validated Investigator Global Assessment of Atopic Dermatitis ≥ 3; age 12-75 years) randomized 1:1:1 to once-daily UPA 15mg, 30mg, or placebo (PBO). Reported here are the effects of UPA on skin improvement as assessed by EASI using pooled data from two phase 3 replicate trials (Measure Up 1 [NCT03569293; N=847]; Measure Up 2 [NCT03607422; N=836]).

METHODS: Degree of skin improvement was compared between UPA and PBO using the proportion of patients achieving ≥ 50%/75%/90%/100% improvement on EASI from baseline (EASI-50/EASI-75/EASI-90/EASI-100). Mutually exclusive categories of EASI improvement thresholds from baseline (EASI <50%; EASI 50–74%; EASI 75–89%; EASI 90–99%; EASI 100%) were used to characterize the distribution of skin improvement achieved. Distributions were descriptively compared to characterize the total proportion of patients achieving incrementally greater thresholds of skin improvement. This was computed by sequentially calculating the differences in EASI 100%, EASI 90–99%, EASI 75–89%, and EASI 50–74% proportions between two groups, then aggregating the differences to attain the total proportion of patients achieving an incrementally greater response threshold.

RESULTS: The proportion of patients achieving skin improvement was greater in both UPA 15mg and 30mg groups versus PBO at Week 16 for EASI-50 (75.9% and 83.9% versus 29.0%), EASI-75 (64.9% and 76.3% versus 14.8%), EASI-90 (47.8% and 62.2% versus 6.7%), and EASI-100 (15.4% and 22.9% versus 1.3%). The distribution of EASI improvement <50%/50-74%/75-89%/90-99%/100% at Week 16 was 24.1%/11.0%/17.1%/32.4%/15.4% for UPA 15mg, 16.1%/7.6%/14.1%/39.3%/22.9% for UPA 30mg, and 71.0%/14.2%/8.1%/5.4%/1.3%.
for PBO. Distribution comparisons showed that the total proportion of patients achieving incrementally greater skin improvement thresholds at Week 16 was 74.6% with UPA 15mg versus PBO, 82.6% with UPA 30mg versus PBO, and 40.9% with UPA 30mg versus UPA 15mg.  

**CONCLUSION:** Greater proportions of adolescent and adult patients with moderate to severe AD achieve higher thresholds of skin improvement with once-daily UPA 15mg and UPA 30mg versus PBO. The total proportion achieving incrementally greater thresholds of skin improvement was greatest with UPA 30mg followed by UPA 15mg compared to PBO.

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