Effectiveness and safety of upadacitinib in adolescent and adult patients with atopic dermatitis: an analysis of long-term (week 52) data from a real-world multicenter retrospective review

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Introduction:
While clinical trial data demonstrates the efficacy and safety of upadacitinib (UPA), an oral Janus kinase inhibitor (JAKi) for atopic dermatitis (AD), long-term real-world evidence remains limited.

Objectives:
Our study evaluated the real-world effectiveness and safety of UPA for AD at week 52±6.

Methods:
We conducted a multicenter retrospective review of 3 practices in Canada. Effectiveness endpoints were evaluated at weeks 52±6 and including the following: Investigator Global Assessment (IGA) score of clear or almost clear (IGA 0/1) as well as improvements in Eczema Area and Severity Index (EASI), body surface area (BSA), IGAxBSA, and Dermatology Life Quality Index (DLQI)/Children’s DLQI (CDLQI). Safety was determined via incidence of treatment-related adverse events (AEs).

Results:
A total of 102 patients with AD were included in the analysis; mean age was 44.2 (range: 12-79) years and 52.9% (54/102) were female. Initial UPA doses were 15 mg (UPA15: 41.2%, 42/102) or 30 mg (UPA30: 58.8%, 60/102) once daily. Previous systemic therapies included conventional non-biologics (72.5%), biologics (30.4%), and JAKi (2.9%).
At week 52±6: 78.4% (80/102) of patients achieved Investigator Global Assessment (IGA) 0/1; 87.5% (49/56), 78.6% (44/56), and 50.0% (28/56) achieved Eczema Area and Severity Index (EASI) improvements of 75% (EASI75), 90% (EASI90), and 100% (EASI100), respectively; 75.0% (42/56) achieved EASI90 + IGA 0/1; mean EASI was reduced from 12.9 to 0.8 (mean EASI improvement = 91.4%); 91.9% (52/56), 92.9% (52/56), 82.1% (46/56), and 75.0% (42/56) achieved absolute EASI scores ≤7, ≤5, ≤3, and ≤1, respectively; mean body surface area (BSA) was reduced from 17.0% to 0.6% (mean BSA improvement=87.8%); mean IGAxBSA was reduced from 52.1 to 0.8 (mean IGAxBSA improvement=90.7%); and mean Dermatology Life Quality Index (DLQI)/Children’s DLQI was reduced from 13 to 1.8 (mean DLQI/CDLQI improvement=86%), with 66.0% (33/50) of patients achieving DLQI/CDLQI 0/1. For patients not achieving IGA 0/1, EASI75, EASI90, and EASI100 at weeks 8-20, these responses were subsequently achieved in 60.0% (6/10), 88.9% (8/9), 84.6% (11/13), and 38.1% (8/21) of patients at week 52±6. Dose alterations occurred in 13 patients (12.7%) (escalation: 6.9%, 7/102; reduction: 5.9%, 6/102).

Concomitant systemic therapies were used in 1.0% (1/102) of patients. We noted higher statistically significant achievement of endpoints for systemic biologic/JAKi-naïve vs -experienced patients (EASI75; EASI≤7; EASI≤5; DLQI/CDLQI ≥4-point improvement). No significant differences in outcomes were identified between dosing regimens.

Frequent AEs included: acne (19.6%, 20/102), hypertriglyceridemia (17.6%, 18/102), elevated creatine phosphokinase (13.7%, 14/102), neutropenia (7.8%, 8/102), and transaminitis (7.8%, 8/102). Seven patients (6.8%) discontinued UPA owing to treatment-related AEs, including one case of venous thromboembolism; four patients (3.9%) discontinued UPA due to patient preference, and one patient (1%) discontinued UPA due to lack of efficacy. No serious infections, tuberculosis, major adverse cardiovascular events, gastrointestinal perforation, malignancy, or deaths were observed in 102.5 patient-years of follow-up.

Conclusions:
In contrast to 52-week data from the Measure Up 1/2 and AD Up clinical trials, our results were superior for several outcome parameters (IGA 0/1, EASI90, EASI100, and DLQI 0/1), possibly owing to a patient population with less extensive baseline disease severity. Additionally, we noted similar achievement of these endpoints versus comparable long-term real-world studies. Safety was consistent with existing data, highlighting acne as a common AE (5.3%-20.3% versus 19.6%). Study limitations include its sample size and retrospective nature.

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