Effectiveness and safety of upadacitinib in adolescent and adult patients with atopic dermatitis: an analysis of short-term (week 8-20) data from a real-world multicenter retrospective review

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Introduction:
Upadacitinib (UPA), an oral, selective Janus kinase inhibitor (JAKi), is approved for moderate-to-severe atopic dermatitis (AD). While its efficacy and safety are supported by clinical trial data\textsuperscript{1-3}, real-world evidence is limited.

Objectives:
Our study evaluated the real-world effectiveness and safety of UPA for AD between weeks 8-20.

Methods:
We conducted a multicenter retrospective review at three practices in Canada. Effectiveness endpoints measured between weeks 8-20 included: Investigator Global Assessment (IGA) score of clear or almost clear (IGA 0/1) and improvements in Eczema Area and Severity Index (EASI), body surface area (BSA), IGAxBSA, and Dermatology Life Quality Index (DLQI)/Children’s DLQI (CDLQI) improvements. Safety was assessed via treatment-related adverse events (AEs).

Results:
A total of 179 patients were included in the analysis. The mean age was 44.6 ± 17.5 (range: 12-79) years; 53.6% (96/179) were female. Previous treatments included: topicals (100%, 179/179), light (29.1%, 52/179), systemic non-biologics (74.9%, 134/179), and systemic biologics/JAKi (37.4%, 67/179). Initial UPA doses were 15 mg (44.7%, 80/179) or 30 mg (55.3%, 99/179) once daily.
At weeks 8-20: 87.2% (156/179) of patients achieved IGA 0/1; 83.3% (85/102), 74.5% (76/102), and 57.8% (59/102) of patients achieved EASI improvements from baseline of 75% (EASI75), 90% (EASI90), and 100% (EASI100), respectively; mean EASI was reduced from 13.4 to 1.0 (p=0.0001; mean EASI improvement = 88.5%); 98% (100/102), 96.1% (98/102), 88.2% (90/102), and 70.6% (72/102) of patients achieved absolute EASI scores ≤7, ≤5, ≤3, and ≤1, respectively; mean BSA was reduced from 18.2% to 1.1% (p=0.0001; mean BSA improvement=92.2%); mean IGAXBSA was reduced from 60.9 to 2.1 (p=0.0001; mean IGAXBSA improvement=94.7%); and mean DLQI/CDLQI was reduced from 13.6 to 1.4 (p=0.0001; mean DLQI/CDLQI improvement=87.1%), with 75.9% (63/83) of patients achieving DLQI/CDLQI 0/1. UPA monotherapy was utilized in 39.7% (71/179) of cases. Common concomitant therapies included topical corticosteroids (55.3%, 99/179), topical calcineurin inhibitors (6.7%, 12/179), and intramuscular triamcinolone acetonide (2.2%, 4/179). Statistically significantly higher achievement of endpoints was noted for patients using concomitant therapies (EASI75; EASI90; EASI≤1) and systemic biologic/JAKi-naïve patients (EASI75; EASI≤5; IGA 0/1; DLQI/CDLQI ≥4-point improvement). Outcomes were not significantly different between dosing regimens.

Frequent AEs included: acne (16.2%, 29/179), hypertriglyceridemia (14%, 25/179), elevated creatinine phosphokinase (10.1%, 18/179), herpes simplex virus (6.7%, 12/179), and transaminitis (4.5%, 8/179). Three patients (1.7%) discontinued treatment (myalgia/arthralgia [n=2]; gastrointestinal discomfort [n=1]). No serious infections, tuberculosis, venous thromboembolism, major adverse cardiovascular events, gastrointestinal perforation, or malignancy were observed in 44.7 patient-years of safety follow-up for the treatment period being analyzed.

**Conclusions:**

Our study included 75.4% (135/179) of patients with follow-up at weeks ≥12 to ≤16. Interestingly, we found more favourable results than Measure Up 1/2 and AD Up clinical trials at week 16 for
IGA 0/1, EASI75, EASI90, EASI100, and DLQI 0/1, likely owing to a patient population with less extensive baseline disease severity, while the safety profile was commensurate. Additionally, we noted higher achievement of IGA 0/1, EASI75, and EASI90 endpoints versus similar real-world studies. Study limitations include its retrospective nature and short follow-up duration. Nonetheless, our results support clinical trial findings suggesting UPA is effective and safe for AD.

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