Upadacitinib dose alterations in adolescent and adult patients with atopic dermatitis: a real-world multicenter retrospective review

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Introduction:
Currently approved dosing regimens of upadacitinib (UPA) for moderate-to-severe atopic dermatitis (AD) are 15 mg (UPA15) once daily (QD) and 30 mg (UPA30) QD based on clinical trial data. However, dose alterations may be required in the context of inadequate efficacy, adverse events (AEs), and patient preference.

Objectives:
Our multicenter retrospective study evaluated the effect of upadacitinib dose alterations on real-world effectiveness and safety outcomes in patients with AD at three practices in Canada.

Methods:
Among 119 patients with AD initiated on UPA with ≥23-week follow-up, we identified patients undergoing dose alteration (escalation or reduction). Reasons for dose alteration were collected along with effects of dose alteration on effectiveness outcomes including Investigator Global Assessment (IGA), mean Eczema Area and Severity Index (EASI), body surface area (BSA), Dermatology Life Quality Index (DLQI)/Children’s DLQI (CDLQI), and IGAxBSA. Impact of dose alteration on incidence and outcomes of AEs was additionally analyzed.

Results:
From 119 total patients with AD initiated on UPA (≥23-week follow-up), 26.9% (32/119) underwent dose alteration: 40.6% (13/32) with dose escalation and 59.4% (19/32) with dose reduction. The mean age of patients who underwent dose alteration was 44.8 (range: 12-79) years; 62.5% (20/32) were female and 15.6% (5/32) were adolescents. Initial doses were UPA15 (43.8%, 14/32) and UPA30 (56.3%, 18/32). The mean time from UPA initiation to dose alteration was 228.3 (range: 9-520) days.
Thirteen patients underwent dose escalation: 69.2% (9/13) from UPA15 QD to UPA30 QD and 30.8% (4/13) from UPA30 QD to 45 mg (UPA45) QD. At the time of dose escalation: mean EASI score was 2.8 (mean EASI improvement from baseline: 57.4%), with 53.8% (7/13) and 7.7% (1/13) having achieved 75% and 90% improvements in baseline EASI scores (EASI75 and EASI90), respectively, while IGA scores were 1 (n=5) and 2 (n=8). At follow-up (mean duration: 83.3 days) after dose escalation: mean EASI score was 1.6 (mean EASI improvement: 84.4% [from baseline] and 54% [from date of dose escalation]), with 69.2% (9/13), 61.5% (8/13), 38.5% (5/13), and 61.5% (8/13) of patients achieving EASI75, EASI90, 100% improvement in EASI (EASI100), and IGA 0/1, respectively. Two patients (15.4%) discontinued UPA due to lack of efficacy despite dose escalation. Only 2 AEs were noted with dose escalation: transaminitis (n=1) and elevated creatine phosphokinase (n=1); the patient with transaminitis subsequently discontinued UPA.

Nineteen patients underwent dose reduction: UPA30 QD to UPA15 QD (63.1%, 12/19), UPA30 QD to UPA30 every other day (QOD) (10.5%, 2/19), and UPA15 QD to UPA15 QOD (26.3%, 7/19). Reasons for dose reduction included AEs (57.9%, 11/19) and patient preference following clearance or near-clearance (42.1%, 8/19). EASI/IGA responses were maintained in 78.9% (15/19) patients. Following dose reduction, 21.1% (4/19) of patients flared and required re-escalation (mean duration: 147.3 days). AEs requiring dose reduction included acne (36.4%, 4/11), herpes simplex (18.2%, 2/11), transaminitis (18.2%, 2/11), folliculitis (9.1%, 1/11), and recurrent respiratory tract infections (18.2%, 2/11). AEs improved in 54.5% (6/11) patients with dose reduction (mean follow-up: 164.1 days).

**Conclusions:**

Our real-world data suggests dose escalation from UPA15 to UPA30 and UPA30 to UPA45 (off-label) can result in higher skin clearance without any short-term safety concerns. Comparable to a Japanese real-world study (n=23), we noted incremental benefits with dose escalation, including
comparable and superior achievement of EASI75 (69.2% vs. 66.7%) and EASI90 (61.5% vs. 38.1%), respectively. Furthermore, we identified AEs at higher UPA doses can improve through dose reduction with majority of patients (78.9%) maintaining initial effectiveness response. Study limitations include its small sample size and retrospective nature.

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