Eosinophil Count, Serum CCL17/18/26 and Immunoglobulin E Levels in Atopic Dermatitis: Upadacitinib Phase 2 Study Analysis

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Introduction Upadacitinib (UPA), a selective JAK1 inhibitor, is being investigated for the treatment of atopic dermatitis (AD).

Objective This analysis assessed the impact of UPA treatment on absolute eosinophil count (AEC), serum Type 2 biomarkers, and total and allergen-specific immunoglobulin E (IgE) levels in patients with AD.

Materials and methods Adults with moderate-to-severe AD were randomized to daily placebo or UPA 7.5, 15, or 30 mg in a 16-wk, phase 2 study. Wk 16 AEC, serum biomarkers, and total and allergen-specific IgE (ImmunoCap) levels were analyzed along with changes in Eczema Area and Severity Index (EASI) and pruritus numeric rating scale (NRS, weekly average of daily patient assessments). Statistical analysis was done using analysis of variance and Spearman correlation.

Results Mean percentage improvements from baseline to wk 16 in EASI (39.4%/61.7%/74.4% vs 23.0%; P<0.05/<0.001/<0.001) and pruritus NRS (39.6%/48.0%/68.9% vs 9.7%; P<0.01/<0.001/<0.001) were significantly greater with UPA 7.5/15/30 mg vs placebo. AEC was significantly lower with 30 mg UPA vs placebo (P=0.01) at wk 16; significant differences were observed as early as wk 2 in UPA 15-mg (P=0.003) and 30-mg groups (P<0.0001) vs placebo. Serum levels of the Th2 cytokines, CCL18 and CCL26, and the Th22 cytokine, IL-22, were significantly lower with 15 mg and 30 mg UPA vs placebo as early as wk 2 (P<0.01); these significant decreases were sustained at wk 16 in UPA 15-mg and 30-mg groups (P<0.01). CCL17 (TARC) showed similar trends (significant at wks 2 and 8 vs baseline) with the UPA 30-mg dose. There were no clear trends in Th17 cytokine levels (IL-17A, IL-17F, or CCL20). Baseline levels of AEC were significantly correlated with baseline EASI (r=0.39, P<0.0001); in addition, percentage change from baseline to wk 16 in AEC correlated with percentage change at wk 16 in EASI (r=0.62, P<0.0001) and pruritus NRS (r=0.66, P<0.0001). Baseline serum levels of Th2 and Th22 cytokines significantly correlated with baseline EASI scores (CCL17/18/26: r=0.44/0.43/0.41, P<0.0001; IL-22: r=0.43, P<0.001). Changes from baseline to wk 16 in Th2 and Th22 cytokines correlated with percentage changes in EASI (CCL18/26: r=0.58/0.57, P<0.0001; IL-22: r=0.48, P=0.0001) and pruritus NRS (CCL18/26: r=0.37/0.43, P<0.01; IL-22: r=0.38, P<0.001). While baseline levels of serum total IgE correlated with baseline EASI (r=0.35, P<0.001), no trends in allergen-specific or total IgE levels as a function of study duration were observed.
Conclusion Eosinophil counts and serum levels of Th2 (CCL18/26) and Th22 (IL-22)-attracting chemokines were significantly reduced with UPA treatment (15/30 mg) as early as wk 2, suggesting that UPA may have early and robust effects on the Th2, Th22, and eosinophil axes. No significant changes in total and specific IgE levels were observed, suggesting that UPA clinical efficacy is independent of IgE levels, and this observation coupled with the lack of clinical efficacy for anti-IgE strategies in patients with AD argues against the primary role of IgE in AD pathogenesis.

Topic: 5. Atopic Dermatitis/Eczema

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