Efficacy and Safety of Ruxolitinib Cream for the Treatment of Atopic Dermatitis: Results From Two Phase 3, Randomized, Double-Blind Studies

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Background: Atopic dermatitis (AD) is a chronic, inflammatory skin disease that can greatly impact patients' quality of life. Janus kinases (JAKs) act downstream of key proinflammatory cytokines and itch mediators, including interleukin (IL)-4, IL-5, IL-13, and IL-31, that are involved in AD pathogenesis. Ruxolitinib is a selective inhibitor of JAK1 and JAK2. In an earlier phase 2 study in adult patients, ruxolitinib cream significantly reduced skin inflammation and substantially decreased itch vs vehicle in up to 8 weeks of treatment. There were no notable safety findings.

Objective: To evaluate the efficacy and safety of ruxolitinib cream in a large population of adolescent and adult patients with AD

Methods: Two phase 3, randomized, double-blind studies (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651]) enrolled patients aged ≥12 years with AD for ≥2 years, an Investigator's Global Assessment (IGA) score of 2 or 3, and 3%–20% affected body surface area. In both studies, patients were randomized (2:2:1) to either of two ruxolitinib cream dose regimens (0.75% BID, 1.5% BID) or vehicle cream for 8 weeks of double-blind treatment. Patients on ruxolitinib cream could subsequently continue treatment for 44 weeks; patients initially randomized to vehicle were re-randomized 1:1 to either ruxolitinib cream regimen. The primary endpoint was the proportion of patients achieving IGA treatment success at Week 8, defined as an IGA score of 0 or 1 with a ≥2-grade improvement from baseline. Secondary endpoints at Week 8 included the proportion of patients achieving ≥75% improvement in Eczema Area and Severity Index (EASI-75) vs baseline, the proportion of patients with a ≥4-point improvement in itch Numerical Rating Scale score (NRS4), as well as safety and tolerability assessments. This analysis includes the primary results from both studies at Week 8.

Results: In TRuE-AD1, 631 patients were randomized (vehicle, n=126; 0.75% BID, n=252; 1.5% BID, n=253); the median (range) age was 32.0 (12–85) years, 62.0% of patients were female, and 19.5% were adolescents. Seventy-three patients (11.6%) discontinued from the study. In TRuE-AD2, 618 patients were randomized (vehicle, n=124; 0.75% BID, n=248; 1.5% BID, n=246); the median (range) age was 33.0

(12–85) years, 61.5% were female, and 19.7% were adolescents. Fifty-seven patients (9.2%) discontinued from the study. The efficacy population consisted of 631 patients for TRuE-AD1 (all randomized patients), and 577 patients for TRuE-AD2 (vehicle, n=118; 0.75% BID, n=231; 1.5% BID, n=228). All patients who received ≥1 dose of treatment (same as all randomized patients) were included in the safety population in both studies. In TRuE-AD1 and TRuE-AD2, respectively, significantly more patients treated with either dose regimens of ruxolitinib cream achieved IGA treatment success (0.75% BID, 50.0% and 39.0%; 1.5% BID, 53.8% and 51.3%) vs vehicle (15.1% and 7.6%; all P<0.0001). EASI-75 was achieved by 56.0% and 51.5% of patients applying ruxolitinib cream 0.75% BID, as well as 62.1% and 61.8% on 1.5% BID vs 24.6% and 14.4% on vehicle (all P<0.0001) in TRuE-AD1 and TRuE-AD2, respectively. In both studies, significantly greater itch reduction was observed within 12 hours of first application of ruxolitinib cream 1.5% BID vs vehicle (P<0.05). At Week 8, clinically meaningful reduction (itch NRS4) was achieved by more patients who applied ruxolitinib cream (0.75% BID, 40.4% and 42.7%; 1.5% BID, 52.2% and 50.7%) vs vehicle (15.4% and 16.3%, all P<0.001). The overall rate of treatment-emergent adverse events in both studies after 8 weeks of treatment was comparable between the ruxolitinib cream regimens (0.75% BID, 29.4%; 1.5% BID, 26.3%) and vehicle (33.6%). The frequency of application site reactions was low; no clinically significant application site reactions were observed, including areas of sensitive skin (eg, the face). The rate of serious adverse events was comparable in all treatment groups (0.75% BID, 0.8%; 1.5% BID, 0.6%; vehicle, 0.8%). Long-term safety is currently being evaluated in the 44-week extension period of both studies.

Conclusion: Ruxolitinib has been shown to have both anti-inflammatory and antipruritic effects. In two large phase 3 studies of identical design, ruxolitinib cream demonstrated superior efficacy vs vehicle for endpoints including IGA treatment success, EASI-75, and itch NRS4. The safety profile was similar to vehicle and consistent between the two studies; the rate of application site reactions was low. These results support the potential of ruxolitinib cream as an effective and well-tolerated topical treatment for AD.

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