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A Phase 3 Study of Ruxolitinib Cream in Children Aged 2–<12 Years With Atopic Dermatitis (TRuE-AD3): 8-Week Analysis

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Introduction & Objectives:

Ruxolitinib cream, a selective Janus kinase (JAK) 1/JAK2 inhibitor, is approved in the United States for the treatment of atopic dermatitis (AD) in adolescents/adults based on results from 2 phase 3 studies (TRuE-AD1/TRuE-AD2 [NCT03745638/NCT03745651]). In a pediatric pilot pharmacokinetics (PK)/safety study (NCT03257644), ruxolitinib cream was well tolerated in patients ≥2 years old (y/o) with AD; efficacy was consistent with TRuE-AD1/TRuE-AD2 results. This phase 3 pediatric study (TRuE-AD3 [NCT04921969]) evaluated efficacy, safety, and PK of ruxolitinib cream in patients 2–<12 y/o with mild to moderate AD.

Materials & Methods:

Patients 2–<12 y/o with an AD diagnosis for ≥3 months, Investigator's Global Assessment (IGA) of 2 (mild) or 3 (moderate), 3%–20% affected body surface area (BSA), and (for 6–<12 y/o) mean itch Numerical Rating Scale (NRS) score ≥4 were randomized 2:2:1 to twice-daily 0.75%/1.5% ruxolitinib cream or vehicle for 8 weeks of double-blind treatment; rescue therapy was not permitted. The primary endpoint was percentage of patients achieving IGA treatment success (IGA-TS; IGA 0/1 with ≥2-grade improvement from baseline) at Week 8. Secondary endpoints included percentage achieving ≥75% improvement in Eczema Area and Severity Index (EASI75) at Week 8, ≥4-point improvement in itch NRS score (NRS4) at Week 8 in patients 6–<12 y/o, time to achieve NRS4, and safety; PK was an exploratory endpoint.

Results:

Of 330 randomized patients, 288 (87.3%) completed the 8-week vehicle-controlled period; all 330 were included in the efficacy population (vehicle, n=65; 0.75%/1.5% ruxolitinib cream, n=134/n=131). Median (range) age was 6 (2–11) years; 54.2% were female; 54.5% White; 32.1% Black; 6.4% Asian. Mean (SD) affected BSA was 10.5% (5.40%); EASI was 8.6 (5.40); 76.4% of patients had IGA 3; 67.3% had AD therapy in the prior 12 months. A clinical effect was observed in patients applying 0.75%/1.5% ruxolitinib cream vs vehicle at Week 2, increasing through Week 8 for IGA-TS (36.6%/56.5% vs 10.8%; $P \leq 0.0001$ for both) and EASI75 (51.5%/67.2% vs 15.4%; $P < 0.0001$ for both). In patients 6–<12 y/o, NRS4 at Week 8 was achieved by 37.5%/43.4% vs 29.7%; median time to NRS4 was

11.0/13.0 days vs 23.0 days (hazard ratio, 1.74/1.77; *P*<0.05 for both). Treatment-related adverse events (AEs) during the vehicle-controlled period were reported in 5.3% of patients applying ruxolitinib cream (combined; 2.7% reported application site pain) vs 3.1% of patients applying vehicle (0% reported application site pain). No AEs suggestive of systemic JAK inhibition, serious AEs, or deaths were reported. No substantial changes in mean hematology values were observed. Mean (SD) steady-state plasma concentrations (Css) of ruxolitinib at Week 8 for 0.75%/1.5% ruxolitinib cream were 15.8 (30.4)/28.4 (59.2) nM, well below that required to inhibit thrombopoietin phosphorylation of STAT3 (half-maximal inhibitory concentration, 281 nM).

Conclusion:

In patients 2–<12 y/o with mild to moderate AD, ruxolitinib cream achieved significant efficacy at Week 8 vs vehicle for IGA-TS and EASI75. Patients 6–<12 y/o had improved itch in NRS4 at Week 8 and reduced time to NRS4 vs vehicle. Ruxolitinib cream was well tolerated. Low mean ruxolitinib plasma Css and a safety profile similar to vehicle suggest physiologically meaningful systemic JAK inhibition is highly unlikely. These results were similar to the phase 3 results in adolescents/adults.