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

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Background: Atopic dermatitis (AD) is a chronic, intensely pruritic, inflammatory skin dermatosis. Janus kinases (JAKs) act downstream of proinflammatory cytokines and itch mediators involved in AD pathogenesis. Ruxolitinib (RUX) cream is a topical selective inhibitor of JAK1 and JAK2. In two phase 3 AD studies of identical design, RUX cream demonstrated rapid antipruritic and anti-inflammatory action.

Objectives: To evaluate efficacy and safety of RUX cream using pooled data from these studies in adolescent and adult patients with AD.

Methods: Two phase 3, randomized 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 0.75% RUX cream, 1.5% RUX cream, or vehicle cream (all twice daily) for 8 weeks of double-blind treatment. Patients on RUX subsequently continued treatment for 44 weeks; patients initially randomized to vehicle were re-randomized 1:1 to either RUX regimen. The primary endpoint was the proportion of patients achieving IGA treatment success (TS) at Week 8 (IGA of 0 or 1 and 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, a ≥4-point improvement in itch Numerical Rating Scale score (NRS4), a ≥6-point improvement from baseline in the Patient-Reported Outcomes Measurement Information System (PROMIS) Short Form – Sleep Disturbance (8b) score (24-hour recall), and safety. Results of pooled analyses from the 8-week vehicle-controlled period of both studies are presented.

Results: Of 1249 randomized patients, 130 (10.4%) discontinued treatment. The median (range) age was 32.0 (12–85) years; 19.6% were adolescents and 61.7% were female. The efficacy population consisted of 1208 patients (vehicle, n=244; 0.75% RUX, n=483; 1.5% RUX, n=481). All randomized patients were included in the safety population. Significantly more patients treated with either RUX cream regimen achieved IGA-TS at Week 8 (44.7% and 52.6% for 0.75% and 1.5% RUX, respectively) vs vehicle (11.5%; all $P<0.0001$). EASI-75 at Week 8 was achieved by 53.8% and 62.0% of patients who applied 0.75% RUX and 1.5% RUX vs 19.7% on vehicle (all $P<0.0001$). Substantially greater itch reduction was observed within 12 hours of first RUX cream application (mean change from baseline, –0.4 and –0.5 for 0.75% RUX and 1.5% RUX) vs vehicle (–0.1; all $P<0.02$). At

Week 8, more patients who applied RUX cream achieved NRS4 (41.5% and 51.5% for 0.75% RUX and 1.5% RUX) vs vehicle (15.8%; all $P<0.0001$). Considerable improvement in PROMIS 8b was achieved with both RUX cream regimens at Week 8 (20.9% and 23.8% for 0.75% RUX and 1.5% RUX) vs vehicle (14.2%; all $P<0.05$). Treatment-related adverse events (AEs) were reported in 4.7% of patients who applied RUX cream (combined) vs 11.2% of patients who applied vehicle. No AEs indicative of systemic activity of RUX were observed. No serious AEs related to RUX were reported.

Conclusion: RUX cream exhibits both anti-inflammatory and antipruritic effects in AD. In a pooled analysis from two large phase 3 studies, RUX cream demonstrated superior efficacy vs vehicle for IGA-TS, EASI-75, itch NRS4, and PROMIS 8b. The AE profile was similar to vehicle; the rate of application site reactions was low. These results demonstrate the potential of RUX cream as an effective and well-tolerated topical treatment for AD.

Author Disclosures

KP has received honoraria or clinical research grants as a consultant, speaker, scientific officer, advisory board member, and/or steering committee member for AbbVie, Akros, Amgen, Anacor, Arcutis, Astellas, Bausch Health/Valeant, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite, Celgene, Coherus, Dermira, Dow Pharmaceuticals, Eli Lilly, Galderma, Genentech, Gilead, GSK, InflaRx, Janssen, Kyowa Hakko Kirin, LEO Pharma, MedImmune, Meiji Seika Pharma, Merck (MSD), Merck Serono, Mitsubishi Pharma, Moberg Pharma, Novartis, Pfizer, PRCL Research, Regeneron, Roche, Sanofi-Aventis/Genzyme, Sun Pharmaceuticals, Takeda, and UCB.

JCS has served as an advisor for AbbVie, LEO Pharma, Novartis, Pierre Fabre, Menlo Therapeutics, and Trevi; has received speaker honoraria from AbbVie, Janssen-Cilag, LEO Pharma, Novartis, Sanofi-Genzyme, Sun Pharma, and Eli Lilly; and has received clinical trial funding from AbbVie, Almirall, Amgen, Galapagos, Holm, Incyte Corporation, InflaRX, Janssen-Cilag, Menlo Therapeutics, Merck, Novartis, Pfizer, Regeneron, Trevi, and UCB.

LK has served as an investigator, consultant, or speaker for AbbVie, Amgen, Anaptys, Arcutis, Dermavant, Eli Lilly, Glenmark, Incyte Corporation, Kamedis, LEO Pharma, L'Oreal, Menlo, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and Taro.

DT has served as an investigator for AbbVie, Avillion, Amgen, Arcutis, Astellas, Astion, Boehringer Ingelheim, Celgene, Dermira, DS BioPharma, Dow Pharmaceuticals, Eli Lilly, F. Hoffmann-La Roche Ltd, Galderma, GlaxoSmithKline, Incyte Corporation, Isotechnika, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, and UCB Biopharma.

MEK, MEV, and KS are employees and shareholders of Incyte Corporation.

ELS is an investigator for AbbVie, Eli Lilly, Galderma, Kyowa Hakko Kirin, LEO Pharma, Merck, Pfizer, and Regeneron and is a consultant with honorarium for AbbVie, Eli Lilly, Forte Bio, Galderma, Incyte Corporation, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and Valeant.