Long-Term Safety and Disease Control With Ruxolitinib Cream in Patients With More Severe Atopic Dermatitis: Pooled Results From Two Phase 3 Studies

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Atopic dermatitis (AD) is a highly pruritic inflammatory skin disease. The severity of AD is often stratified using objective (Investigator’s Global Assessment [IGA], Eczema Area and Severity Index [EASI], body surface area [BSA]) and subjective (eg, itch numerical rating scale [NRS]) assessment tools. Topical therapies are the standard of care for most patients with AD. For patients with more severe AD, systemic therapies may be considered as monotherapy or in combination with topical therapies. Ruxolitinib cream is a Janus kinase (JAK) 1 and JAK2 inhibitor in development for the treatment of AD. In two phase 3 randomized studies of identical design (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651]), 1249 patients aged ≥12 years with AD for ≥2 years with an IGA score of 2 or 3 and 3%–20% affected BSA were randomized (2:2:1) to twice-daily 0.75% ruxolitinib cream, 1.5% ruxolitinib cream, or vehicle cream for an 8-week double-blinded vehicle-controlled (VC) period followed by a double-blinded long-term safety (LTS) period up to Week 52. Patients initially randomized to ruxolitinib cream remained on their regimen; patients initially on vehicle were rerandomized (1:1) to either ruxolitinib cream strength. During the VC period, patients were instructed to continue treating lesions regardless of lesion improvement. During the LTS period, patients were to treat skin areas with active AD only and stop treatment 3 days after clearance of lesions. Patients were to restart treatment with ruxolitinib cream at the first sign of recurrence. Here, we evaluated the long-term safety and disease control of ruxolitinib cream in the subpopulation of patients with more severe AD at baseline. The definition of more severe AD was based on the inclusion criteria for clinical trials of systemic therapies (ie, dupilumab and oral JAK inhibitors). Among patients with a baseline IGA score of 3,
EASI ≥16, and BSA ≥10% in the pooled population, 31 and 28 patients continued in the LTS period in the 0.75% and 1.5% ruxolitinib cream arms, respectively, and were evaluated for disease control. The proportion of patients who had no AD lesions or only minimal AD lesions (IGA score of 0/1) ranged from 48.4%–82.8% from Weeks 12 through 52 in patients who applied 0.75% ruxolitinib cream and from 62.5%–91.3% in patients who applied 1.5% ruxolitinib cream. During the LTS, measured mean total affected BSA ranged from 3.0%–5.5% among patients who applied 0.75% ruxolitinib cream and from 2.5%–4.8% in patients who applied 1.5% ruxolitinib cream. A safety analysis included patients who received 0.75% (n=39) or 1.5% (n=36) ruxolitinib cream in any period of the TRuE-AD studies. Treatment-emergent adverse events (AEs) were reported in 28 (71.8%) and 24 (66.7%) patients who applied 0.75% and 1.5% ruxolitinib cream, respectively. Application site reactions remained infrequent during the LTS period (0.75% ruxolitinib cream, n=1; 1.5% ruxolitinib cream, n=2). Treatment-related AEs were reported in 6 patients in each ruxolitinib cream group (15.4% for 0.75% ruxolitinib cream; 16.7% for 1.5% ruxolitinib cream); none were serious. No patient in either ruxolitinib cream arm discontinued from the study because of an AE. In summary, patients with more severe AD achieved long-term disease control with ruxolitinib cream monotherapy during the 52-week study period. Ruxolitinib cream was well tolerated in the long-term setting in this subset of patients who may be eligible for both systemic and topical therapies. Taken together, these data suggest that ruxolitinib cream may delay or prevent the need for systemic therapy in a subset of patients with more severe AD.

Author Disclosures
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.
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.
AB has served as a scientific advisor and/or clinical study investigator for AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Aslan, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Evommune, Forte, Galderma, Incyte Corporation, Janssen, Landos, LEO Pharma, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma.

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LFE has served as an investigator, consultant, speaker, or data safety monitoring board member for AbbVie, Almirall, Arcutis, Asana, Dermavant, Eli Lilly, Forte Biosciences, Galderma, Ichnos/Glenmark, Incyte Corporation, Janssen, LEO Pharma, Novartis, Ortho Dermatologics, Otsuka, Pfizer, Regeneron, and Sanofi Genzyme.