Atopic dermatitis (AD) is a highly pruritic inflammatory skin disease. The pathogenesis of AD involves Janus kinases (JAKs) acting downstream of proinflammatory cytokines and itch mediators. Ruxolitinib cream is a JAK1/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 Investigator’s Global Assessment (IGA) score of 2 or 3 and 3%–20% affected body surface area (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-blind vehicle-controlled (VC) period, followed by a double-blind long-term safety (LTS) period up to Week 52. Patients initially randomized to ruxolitinib cream remained on their regimen during the LTS period; 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. The objective of this analysis was to evaluate the long-term safety and disease control of ruxolitinib cream in patients with AD in TRuE-AD1/TRuE-AD2 who continued in the 0.75% ruxolitinib cream arm (TRuE-AD1, n=222; TRuE-AD2, n=204) or the 1.5% ruxolitinib cream arm (TRuE-AD1, n=225; TRuE-AD2, n=221) from
the VC period into the 44-week LTS period. The proportion of patients with no AD lesions or only minimal AD lesions (IGA score of 0/1) with 0.75% and 1.5% ruxolitinib cream ranged from 62.4%–76.9% and 66.5%–77.3%, respectively, in TRuE-AD1 and 59.6%–76.7% and 72.0%–80.1% in TRuE-AD2 from Weeks 12 through 52. Measured mean total affected BSA was <3% throughout the LTS period in the 1.5% ruxolitinib cream arm in TRuE-AD1 (range, 1.5%–2.5%) and TRuE-AD2 (range, 1.4%–2.1%), and was <3% in the 0.75% ruxolitinib cream arm during most of the LTS period in both studies (TRuE-AD1 range, 1.5%–3.2%; TRuE-AD2 range, 2.2%–3.3%), attesting to a limited extent of disease. In a pooled safety analysis, treatment-emergent adverse events (AEs) were reported in 256 (60.1%) and 240 (53.8%) patients who applied 0.75% (n=426) and 1.5% (n=446) ruxolitinib cream, respectively, over the 44-week LTS period. The frequency of application site reactions remained low during the LTS period. Treatment-related AEs were reported in 20 patients (4.7%) who applied 0.75% ruxolitinib cream and in 13 patients (2.9%) who applied 1.5% ruxolitinib cream; none were serious. Treatment-emergent AEs resulted in discontinuation in 9 patients (2.1%) in the 0.75% ruxolitinib cream group, and no patients in the 1.5% ruxolitinib cream group. In summary, approximately 70% of patients maintained no or minimal lesions (IGA score of 0 or 1), and the extent of AD lesions (percent of affected BSA) remained low during the 44-week LTS period, indicating that patients achieved long-term disease control with ruxolitinib cream. Ruxolitinib cream was well tolerated in the long-term setting, with no serious treatment-related AEs.

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, Gilead, GlaxoSmithKline, Incyte Corporation, InflaRx, Janssen, Kyowa Hakko Kirin, LEO Pharma, 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, Eli Lilly, Janssen-Cilag, LEO Pharma, Novartis, Sanofi Genzyme, and Sun Pharma; 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, Amgen, Arcutis, Astellas, Astion, Avillion, 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.

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.

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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.