Clinically meaningful improvements in patient-reported outcomes and itch: analysis of a phase 2 clinical trial in adults with moderate to severe atopic dermatitis treated with etrasimod, a novel, oral selective sphingosine 1-phosphate receptor modulator

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Background: Atopic dermatitis (AD) is a chronic and pruritic disease with a substantial patient burden. Etrasimod is a novel, oral, once-daily, selective sphingosine 1-phosphate 1,4,5 receptor modulator in development for multiple immune-mediated inflammatory disorders. We assessed the effects of etrasimod on patient-reported outcomes (PROs) and itch (assessed by Peak Pruritis Numerical Rating Scale [PP-NRS]) in a phase 2 clinical trial in adults with moderate-to-severe AD.

Methods: After a 1-week run-in with emollient, participants with chronic AD ≥1 year, Eczema Area and Severity Index ≥16, validated Investigator's Global Assessment (vIGA) score ≥3, and ≥10% affected body surface area were randomized 1:1:1 to once-daily etrasimod 1 or 2 mg or placebo for 12 weeks (NCT04162769). PROs included Dermatology Life Quality Index (DLQI), Patient-Oriented Eczema Measure (POEM), and office-based PP-NRS.

Results: Of 140 participants randomized, 80% completed 12 weeks. Most participants (82.9%) had moderate vIGA scores at baseline. A significantly greater proportion of participants receiving etrasimod 2 mg vs placebo had a ≥4-point improvement from baseline in POEM at Weeks 2 (56.5% vs 23.9%, *P*=0.0019), 4 (56.5% vs 34.8%, *P*=0.0316), 6 (60.9% vs 34.8%, *P*=0.0158), and 12 (58.7% vs 37.0%, *P*=0.0109); and in DLQI at Weeks 8 (65.1% vs 51.1%, *P*=0.0282) and 12 (69.8% vs 55.6%, *P*=0.0107). Percent changes from baseline in office-based PP-NRS were significantly improved at Weeks 4 (-25.9% vs -10.1%, *P*=0.0083), 8 (-35.8% vs -18.0%, *P*=0.0065), and 12 (-41.5% vs -24.0%, *P*=0.0166). The most common adverse events (AEs) in participants receiving etrasimod (≥5% and greater than placebo) were nausea, constipation, back pain, and dizziness. There were no serious AEs, or opportunistic or serious infections.

Conclusions: Etrasimod 2 mg resulted in clinically meaningful improvements in PROs and itch assessed vs placebo over 12 weeks in participants with moderate-to-severe AD and had a safety profile consistent with previous trials.

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