Pruritus Response and Skin Biomarkers of Atopic Dermatitis With Crisaborole Versus Vehicle in Patients With Mild-to-Moderate AD

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Background: Crisaborole ointment, 2%, is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild-to-moderate atopic dermatitis (AD). The mechanism of action of crisaborole is not well defined. This phase 2a, single-center, vehicle-controlled, intrapatient study (NCT03233529) evaluated clinical efficacy and changes in skin biomarkers in adults with mild-to-moderate AD.

Objective: To assess pruritus response and its relationship with changes in key skin biomarkers with crisaborole versus vehicle.

Methods: Patients ≥18 years with clinical diagnosis of mild-to-moderate AD were included. Two moderate-to-severe target lesions were randomized intrapatient (1:1) to double-blind twice-daily crisaborole or vehicle for 15 days; thereafter, patients applied open-label crisaborole twice-daily to all affected areas for 28 days. Lesion pruritus severity was assessed daily by the patient for each target lesion during the double-blind period using a pruritus numeric rating scale (NRS). Pruritus NRS2, NRS3, and NRS4 responses were defined as ≥2-, ≥3 , and ≥4-point improvement from baseline in pruritus NRS score, respectively. Punch-biopsy specimens of each target lesion were collected for biomarker analysis at baseline (pre-dose), day 8 (optional), and day 15.

Results: 40 patients were included in the study, and 38 (95%) completed the study. Statistically significant differences for crisaborole versus vehicle in proportion of patients achieving target lesion pruritus NRS2, NRS3, and NRS4 responses were observed starting at days 4 (after 3 days of treatment), 5, and 8, respectively. On day 15, target lesion pruritus NRS2, NRS3, and NRS4 responses (95% CI) were reported for 84.6% (69.5-94.1) versus 51.3% (34.8-67.6), 77.1% (59.9-89.6) versus 48.6% (31.9-65.6), and 63.6% (45.1-79.6) versus 31.4% (16.9-49.3) of crisaborole- versus vehicle-treated lesions, respectively (P<0.01 for all). Compared with vehicle, crisaborole reduced the expression of pruritus-related interleukin-31 (IL 31) at day 8 (fold change, −1.99 vs 1.92, P=0.071) and day 15 (−3.12 vs −1.36, P=0.19) and thymic stromal lymphopoietin receptor (TSLPR) at day 8 (−1.71 vs 1.01, P=0.0086) and day 15 (−1.76

vs −1.14, P=0.013). However, Spearman correlation coefficients for change in pruritus biomarkers and change from baseline in target lesion pruritus NRS score across treatments at day 15 were −0.052 for IL-31 and 0.224 for TSLPR.

Conclusion: Crisaborole significantly improved lesion pruritus NRS score responses (≥2-point improvement) as early as day 4 compared with vehicle in patients with mild-to-moderate AD. Crisaborole reduced expression of key pruritus-related biomarkers without correlation with pruritus improvement. Further research is needed to elucidate the mechanism of the effect of crisaborole on pruritus.

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