ATOPIC ECZEMA/DERMATITIS

CHANGES IN SKIN BIOMARKERS FOLLOWING CRISABOROLE TREATMENT CORRELATE WITH CLINICAL IMPROVEMENT IN ATOPIC DERMATITIS

Emma Guttman-yassky [1] - Ana B. Pavel [1] - Aisleen Diaz [1] - John L. Werth [2] - Chuanbo Zang [3] - Ivana Vranic [4] - Vivek S. Purohit [5] - Michael A. Zielinski [2] - Bonnie Vlahos [2] - Yeriel D. Estrada [1] - Etienne Saint-cyr Proulx [6] - William C. Ports [5] - Robert Bissonnette [6]

Icahn School Of Medicine At Mount Sinai, Dermatology, New York, United States [1] - Pfizer Inc., Inflammation And Immunology, Collegeville, United States [2] - Pfizer Inc., Biostatistics, Collegeville, United States [3] - Pfizer Inc., Safety, Walton Oaks, United Kingdom [4] - Pfizer Inc., Inflammation And Immunology, Groton, United States [5] - Innovaderm Research, Dermatology, Montreal, Canada [6]

Introduction: Crisaborole ointment, 2%, is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild-to-moderate atopic dermatitis (AD).

Objective: A single-center, vehicle-controlled, intra-patient, phase 2a study (NCT03233529) was conducted to evaluate the efficacy and characterize the mechanism of action of crisaborole. This correlation analysis examines the relationship between clinical improvements and changes in skin hyperplasia, barrier function, and immune biomarkers.

Materials and Methods: Adults (N=40) with mild-to-moderate AD and 2 target lesions ≥3×3 cm with identical lesion Investigator's Static Global Assessment (ISGA) of at least moderate were enrolled. Lesions were randomized intra-patient (1:1) to double-blind crisaborole:vehicle, applied twice daily at the investigational site for 14 days. Punch biopsy specimens were collected at baseline (lesional and nonlesional) and day 15 (lesional). Clinical measures and skin biomarkers were quantified. The relationship between changes in biomarkers and improvement in lesion Total Sign Score (TSS), ISGA, and Transepidermal Water Loss (TEWL) from baseline to day 15 were analyzed using Spearman correlation coefficients.

Results: TSS, ISGA, and TEWL improvements were correlated with each other (ρ=0.328-0.701, $P<0.05$). Correlations (ρ=0.316-0.601, $P\leq0.05$) were found between improvement in lesional efficacy scores (TSS and/or ISGA) and skin biomarkers, including hyperplasia-related biomarkers (KRT16, epidermal thickness, Ki67+ cells, and IL-17/IL-22-induced S100As), cellular infiltrates (CD3+ T-cells, CD11c+ and FCεR1+ dendritic cells), and Th2 and Th17-related measures (IL-5, PI3). TEWL improvement was

positively correlated with KRT16 and PI3 (ρ=0.376-0.397, P<0.02) and negatively correlated with FLG (ρ=-0.379, P<0.02).

Conclusions: Clinical improvements with crisaborole were significantly associated with changes in hyperplasia, barrier function, and inflammation-related biomarkers in AD lesional skin samples.