Dupilumab Treatment Restores Skin Barrier Function Measured by Transepidermal Water Loss (TEWL) in Adults and Adolescents With Moderate-To-Severe Atopic Dermatitis

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Background: Atopic dermatitis (AD) is associated with immunological and skin barrier dysfunction. Current scientific evidence shows that type 2 inflammation, especially mediated by interleukin-4 and interleukin-13 cytokines, influences keratinization, integrity of tight junction, composition of lipids, microbiome diversity, filaggrin expression, and natural moisturizing factors. Dupilumab has been shown to suppress cellular and molecular cutaneous markers of type 2 inflammation and to reverse AD-associated epidermal abnormalities in patients with AD, supporting the hypothesis that dupilumab-induced blockade of type 2 inflammation can repair skin barrier alteration in AD. We present the results of a study designed to assess the effect of dupilumab on skin barrier function in adults and adolescents with moderate-to-severe AD over 16 weeks of treatment.

Methods: The dupilumab skin BArrier function and LIpidomics STudy in Atopic Dermatitis (BALISTAD; NCT04447417) is an open-label, exploratory study. Transepidermal water loss (TEWL [g/m^2/h]) was measured after skin tape stripping (STS) in lesional and non-lesional skin of 26 adolescents or adults with moderate-to-severe AD and the skin of 26 matched healthy volunteers. TEWL was assessed repeatedly over 16 weeks of dupilumab therapy. Adjusted mean values of TEWL at Week 16 were estimated with analysis of covariance (ANCOVA) models, of log-transformed TEWL values that included log-transformed baseline TEWL, skin type, age, and gender.

Results: At baseline, the mean (95% confidence interval [CI]) TEWL after 5 STS in lesional skin of the AD patients was 62.5 (53.9, 71.1) g/m^2/h, in non-lesional skin of the same AD patients was 21.2 (15.7, 26.8) g/m^2/h, and in the matched anatomical region in skin of healthy volunteers was 12.1 (10.0, 14.1) g/m^2/h. At Week 16, there were no statistically significant differences in the adjusted mean TEWL distribution between lesional and non-lesional skin in AD patients and matched healthy volunteers (P = 0.950 and P =

0.129, respectively). The mean TEWL (95% CI) was 16.8 (11.0, 25.6) g/m^2/h in lesional and 16.0 (12.5, 20.6) g/m^2/h in non-lesional skin. In the skin of healthy volunteers, the mean (95% CI) TEWL after 5 STS at Week 16 was 16.4 (10.3, 26.0) g/m^2/h.

Conclusion: Dupilumab treatment leads to significant improvement in TEWL in lesional skin of patients with AD, demonstrating restoration and normalization of epidermal barrier function.

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