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Real world studies for local skin reactions with the use of ingenol mebutate 0.015% and 0.05% to predict treatment efficacy

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Background: Ingenol mebutate (IMB; 0.015% or 0.05%) is an FDA-approved treatment that acts by disrupting atypical keratinocytes and initiating a proinflammatory response, and has been demonstrated to be efficacious in treating actinic keratosis (AK). Prior data from randomized, multicenter, vehicle-controlled phase 3 trials failed to demonstrate a correlation between local skin reactions (LSRs) and IMB efficacy outcomes, however, clinical interest in the potential association remains.

Objective: We summarized the literature using LSRs in predicting treatment efficacy for IMB in clinical practice, with the goal of expanding the current understanding of this effect.

Methods: We systematically searched PubMed and Medline to identify all relevant records until July 24, 2019. Search terms included "actinic keratosis," "local skin reactions or local skin response," "efficacy or treatment response," "factors and efficacy," "correlation and efficacy," and "ingenol mebutate." Relevant articles for humans in English language were reviewed.

Results: Six studies with 593 patients were included by reading title, abstract or full text: 3 were retrospective studies reviewing AKs on the face, scalp, and trunk/extremities. One was a prospective study looking at AKs on face/scalp; another was a single arm, open label, split-face study; and 1 regression analysis of data from the phase 3 trials. Three of the studies suggested a potential association between LSR and efficacy, while the other 3 showed no definitive association between LSRs and efficacy.

Conclusions: While promising, the use of LSRs to predict efficacy remains to be validated in real world studies.

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Health status, work productivity, and health care resource utilization in patients with moderate to severe atopic dermatitis: Analysis of the 2017 United States National Health and Wellness Survey

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Background: Moderate to severe atopic dermatitis (AD) exerts a significant burden on patients. This analysis examines the relationship between Dermatology Life Quality Index (DLQI) scores and health outcomes.

Design: Cross-sectional real-world study.

Methods: Data were analyzed from the 2017 US National Health and Wellness Survey. Respondents who reported physician-diagnosed AD/eczema and were considered moderate to severe based on DLQI ≥6 were included. The relationships between DLQI categories and health outcomes were examined using generalized linear models controlling for demographic and health history covariates. Outcomes included health status (Short Form-36 v2 [SF-36v2]), work productivity (Work Productivity and Activity Impairment questionnaire), and self-reported HCRU (emergency room [ER] visits and hospitalizations) in the past 6 months.

Results: n = 1017 respondents were included (73.6% female, overall mean age 37.4 years). The distribution of DLQI categories were as follows based on level of impact on patient's life: moderate (M; 6-10) = 56.5%, very large (VL; 11-20) = 32.7%, and extremely large (EL; 21-30) = 10.7%. After covariate adjustment, increasing DLQI score categories were associated with lower health status and increasing work-related impairment and HCRU. Least square means for M, VL, and EL groups, respectively, were as follows: SF-36v2 mental component summary = 37.7, 33.7, 29.8; SF-36v2 physical component summary = 44.3, 40.9, 38.0; SF-36v2 bodily pain domain = 41.3, 37.3, 34.1; overall work impairment = 47.4%, 62.4%, 81.3%; ER visits = 0.99, 1.85, 2.94; and hospitalizations = 0.57, 1.21, 2.70. All comparisons $P < .05$ relative to the M reference group.

Conclusions: The greater the impact of AD on the quality of patient lives, as measured by the DLQI, the greater the reported burden on mental and physical health status, work-related impairment, and HCRU.

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Lebrikizumab, a high-affinity interleukin-13 inhibitor, improves clinical manifestations in moderate to severe atopic dermatitis: Time course of response from a randomized, double-blinded, placebo-controlled, dose-ranging, phase 2b study

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Lebrikizumab (LEB) is a novel, high affinity monoclonal antibody targeting interleukin (IL) 13 that selectively prevents formation of the IL-13Rα1/IL-4Rα heterodimer receptor complex and subsequent signaling. Adults (EASI ≥16, IGA ≥3, and chronic AD for ≥1 year) were randomized 3:3:3:2 to subcutaneous LEB 125 mg q4w (250 mg loading dose [LD]; n = 73); 250 mg q4w (500 mg LD; n = 80), 250 mg q2w (500 mg LD at week [wk] 0 and 2; n = 75), or placebo (n = 52) for 16 weeks. Outcomes included percent change from Baseline (cfB) in EASI to wk 16 (primary) and EASI50, EASI75, EASI90, IGA 0/1 and pruritus NRS change ≥4 points at wk 16 (secondary end points). All LEB arms showed dose-dependent, statistically significant improvement in the primary end point vs placebo (125 mg q4w [−62.3%; $P < .05$], 250 mg q4w [−69.2%; $P < .01$], 250 mg q2w [−72.1%; $P < .001$] vs placebo [−41.1%]) at wk 16. A greater proportion of LEB- vs placebo-treated patients showed improvement on EASI50, EASI75, EASI90, and IGA 0/1 at wk 16, with statistically significant differences with LEB 250 mg q2w and q4w. A greater proportion of LEB-treated patients achieved pruritus NRS change ≥4 points, with statistically significant differences with LEB 250 mg q2w; differences vs placebo were seen by day 2. Across additional end points, advantages over placebo were seen by wk 4, including percent cfB in EASI (−42.4%, −46.5%, −50.4% vs −25.4%). Most TEAEs were mild/moderate and did not lead to discontinuation. Rates of conjunctivitis and herpes infections were low. These data highlight that selective blockade of IL-13 with LEB leads to improvements in key AD disease severity scores and pruritus while maintaining a favorable safety profile.

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Effects of cleansing on skin barrier function in atopic dermatitis and healthy skin: A pilot study

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Introduction: Cleansers and bathing are known to worsen skin barrier function (SBF), especially in intrinsically barrier-compromised atopic dermatitis (AD). Many commercially-available cleansers are marketed for AD, but guidance for optimal product selection and direct comparison are lacking.

Methods: Seven cleansers marketed for "eczema"/"sensitive-skin" (Aveeno, CeraVe, Cetaphil, Dove, Eucerin, Free&Clear, MooGoo) and water control were lathered on randomized areas of subjects' arms, then rinsed. SBF parameters [transepidermal water loss (TEWL), hydration, pH] were measured before and immediately, 30, 60, and 90 min after cleansing.

Results: Eight AD subjects and 11 healthy controls (HC) participated. Median TEWL across cleansers increased in both groups post-wash, with recovery to lower than baseline by 30 min and maintained through 90 min (AD = 83.4% baseline TEWL, HC = 85.0%). At 90 min, cleansers were more detrimental to TEWL than water in AD, but less detrimental in HC. Median hydration increased drastically in both groups post-wash, with hydration better maintained in HC than in AD at 90 min (AD = 116% baseline hydration, HC = 139%). In AD, cleansers impaired hydration compared with water, but were more hydrating than water in HC. Cleansing increased median pH post-wash in both groups, plateauing but without return toward baseline at 90 min.

Conclusions: Although initially disruptive to SBF, cleansers marketed for AD improve TEWL and hydration, but to a lesser degree in AD than in HC. Cleansing with these products appears to be more beneficial than water alone. No significant differences between products were identified in either group, suggesting that cleanser selection can be guided by cost, availability and patient preference.

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