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26856 Proliferative nodule resembling angiomatoid Spitz with pronounced degenerative atypia arising within a giant congenital nevus

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26839

Dupilumab with topical corticosteroids results in rapid and sustained improvement in adults with moderate-to-severe atopic dermatitis across all anatomic regions over 52 weeks

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Background: Atopic dermatitis (AD) affects different anatomic regions; some adults may exhibit more localized AD, such as head and neck involvement. We analyzed the extent of improvement in AD signs across different anatomic regions at Week 52 using data from the phase 3 dupilumab trial, LIBERTY AD CHRONOS (NCT02260986).

Methods: Adults with moderate-to-severe AD were randomized 1:3 to dupilumab 300 mg with topical corticosteroids (TCS) every 2 weeks (q2w+TCS) or placebo+TCS for 52 weeks. Least squares mean percent change (standard error) in Eczema Area and Severity Index by anatomic region is reported.

Results: 421 patients were analyzed (q2w+TCS, n = 106; placebo+TCS, n = 315). Significant improvements in all signs in all body regions occurred as early as Week 4 ($P < .05$). Erythema improvement at Week 52 (q2w+TCS vs placebo+TCS) was: head and neck −65.1(4.9)/−35.1(2.9); trunk −72.7(4.1)/−41.7(2.5); upper extremities −70.5(4.1)/−39.2(2.5); and lower extremities −75.7(5.1)/−40.9(3.1). Infiltration/papulation improvement at Week 52 (q2w+TCS vs placebo+TCS) was: head and neck −66.0(5.9)/−40.0(3.5); trunk −78.1(4.4)/−44.2(2.6); upper extremities −76.6(4.2)/−41.1(2.5); and lower extremities −80.4(6.0)/−42.1(3.6). Excoriation improvement at Week 52 (q2w+TCS vs placebo+TCS) was: head and neck −73.4(5.9)/−48.0(3.6); trunk −85.5(4.6)/−45.2(2.8); upper extremities −80.6(4.9)/−42.0(2.9); and lower extremities −85.7(5.1)/−40.7(3.0). Lichenification improvement at Week 52 (q2w+TCS vs placebo+TCS) was: head and neck −74.0(6.1)/−39.8(3.6); trunk −81.1(4.5)/−45.4(2.8); upper extremities −75.5(4.5)/−43.3(2.7); and lower extremities −81.6(4.6)/−47.1(2.8). Improvements were significant ($P < .0001$) for all Week 52 comparisons. Dupilumab was generally well tolerated with an acceptable safety profile.

Conclusion: In adults with moderate-to-severe AD, dupilumab q2w+TCS showed rapid, significant, and sustained improvement in AD signs across all anatomic regions compared with placebo+TCS.

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26842

Long-term proactive management with Cal/BD foam is beneficial for all patients with psoriasis irrespective of baseline characteristics

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Introduction: The Phase III PSO-LONG study (NCT02899962) demonstrated superior efficacy of proactive (PM) vs reactive management (RM) using calcipotriene 0.005%/betamethasone dipropionate 0.064% (Cal/BD) foam in adults with psoriasis. Here we evaluate whether certain baseline parameters had an effect on time to first relapse (TTFR), number of relapses and assessed interactions between treatment effect and baseline parameters.

Methods: PSO-LONG included an initial 4-week open-label phase (once-daily Cal/BD foam) and a 52-week, maintenance phase where patients were randomized to twice-weekly Cal/BD (PM) or vehicle foam (RM), with 4-weeks once-daily Cal/BD foam rescue treatment for relapse. The following baseline parameters were analyzed using a stepwise variable selection procedure: body surface area, modified-Psoriasis Area Severity Index (mPASI), Physician's Global Assessment (PGA), body mass index, age, gender, dermatology life quality index and duration of psoriasis. Continuous variables were divided into groups based on standard criteria.

Results: Overall, the effect of treatment on TTFR did not vary across any baseline parameters. Variables with a significant effect on TTFR were: treatment group (Hazard Ratio [HR]: 0.56; $P < .001$); PGA (moderate vs mild HR: 1.42; $P = .07$; severe vs mild HR: 2.32; $P = .003$); mPASI moderate vs mild (HR: 1.19; $P = .16$; severe vs mild HR: 1.78; $P = .002$); gender (female vs male HR: 1.25; $P = .03$). The effect of treatment on total number of relapses will also be presented.

Conclusion: The effect of long-term PM vs RM with Cal/BD foam was not dependent on baseline parameters. Patients with more severe disease at baseline had greater benefit from PM than those with milder disease.

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26845

Toward novel depigmenting agents through repurposing existing drugs

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Inhibitors of the enzyme tyrosinase have found clinical utility as agents to treat disorders of hyperpigmentation of the skin. Potential cellular toxicity and carcinogenicity of currently available tyrosinase inhibitors motivates finding safer and more effective alternatives. "Repurposed" drugs have recently attracted attention due to the possibility of finding safe and effective medical treatments with less time spent in early stage drug development. We report the identification and characterization of potent tyrosinase inhibitors that are "repurposed" existing drugs. Para-acetaminophenols, exemplified by the anti-inflammatory agent acetaminophen, displayed inhibitory activity against mushroom tyrosinase. Detailed analysis of enzyme kinetics in the presence of acetaminophen showed that it acts as a noncompetitive inhibitor. Further, acetaminophen behaved as an alternative substrate of the enzyme. Substituted analogs of acetaminophen were also effective inhibitors, but behaved as competitive inhibitors. Another class of approved drugs that inhibited the enzyme were found to display very potent inhibition of tyrosinase, with a Ki of 900 nanomolar. Kinetic analysis revealed this class of molecules acted as competitive inhibitors, with no evidence of undergoing chemical transformation by tyrosinase or enzyme inactivation. This class of molecules likely inhibits tyrosinase by coordinating with a copper ion in the enzyme active site. This type of strong and specific interaction with tyrosinase may make drugs of this class clinically useful as skin whitening agents.

Commercial Disclosure: None identified.

26856

Proliferative nodule resembling angiomatoid Spitz with pronounced degenerative atypia arising within a giant congenital nevus

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Proliferative nodules arising within congenital melanocytic nevi present a diagnostic challenge for dematopathologists given their close resemblance to melanoma. In difficult cases, ancillary molecular tests can be used to better exclude the possibility of malignancy. We report case of a biopsy and subsequent excision of an unusual proliferative nodule with overlapping features of angiomatoid Spitz tumor and ancient melanocytic nevus which demonstrated normal findings on both chromosomal microarray and a gene expression profiling assay. Our case is noteworthy given its striking resemblance to what has been reported for an angiomatoid Spitz tumor. To our knowledge, this particular morphologic subset of Spitz has been described primarily in the context of spontaneous melanocytic tumors arising de novo outside the context of a congenital lesion. The pathology showed bizarre cytological features along with a myxoid and highly vascularized stroma which is thought to represent degenerative atypia characteristic of an "ancient nevus." The lesions described as ancient nevi have some overlapping stromal features with angiomatoid Spitz tumors. A low proliferation index and paucity of mitotic figures is characteristic of these neoplasms. We hypothesize that continued host response to the lesion may be responsible for inducing the observed cytological and stromal derangement. Interestingly, these changes increased from the time of biopsy to the excision. Future studies should aim to define the genetic and immunologic signature of these lesions to help predict prognosis. The relationship between angiomatoid Spitz tumor, ancient change, and regressing nevi should also be investigated.

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