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

Taylor Braunberger
M Adelman
Tor Shwayder
L E. Clarke
Ben J. Friedman

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Improvements were significant (P/C0 75.5(4.5)/100% is paid for by LEO Pharma.

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 improvements (q2w+TCS vs placebo+TCS) was: head and neck –70.4(1.1)/–41.7(2.5); upper extremities –75.4(1.1)/–42.0(2.9); and lower extremities –81.0(3.0)/–47.2(2.6). Lichenification improvement at Week 52 (q2w+TCS vs placebo+TCS) was: head and neck –66.0(5.9)/–42.2(2.6); upper extremities –76.6(4.2)/–41.1(2.5); and lower extremities –80.4(6.0)/–42.3(6.0). Excoriation improvement at Week 52 (q2w+TCS vs placebo+TCS) was: head and neck –73.4(5.9)/–48.0(5.6); trunk –85.3(5.6)/–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)/–43.5(2.7); and lower extremities –81.6(4.6)/–47.2(2.6). 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.

Commercial Disclosure: None identified.

26842 Long-term proactive management with Cal/BD foam is beneficial for all patients with psoriasis irrespective of baseline characteristics
Mark Lebwohl, MD, Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY; Marie Holst Morch, MS, LEO Pharma Research, Denmark
Introduction: The Phase III PSO-LONG study (NCT02889962) 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 foam (PM) or vehicle foam (RM) over 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 = .05). 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.

Commercial Disclosure: 100% is paid for by LEO Pharma.

26845 Toward novel depigmenting agents through repurposing existing drugs
Jurius Germanas, MD, PhD, Department of Dermatology, University of Maryland School of Medicine; Kyounghee Kim, PhD, Maryland Dermatology Associates; Tomas Germanas, Maryland Dermatology Associates
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-aceetaminophen, 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.

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