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Long-term proactive management of psoriasis vulgaris with fixed-dose combination of 0.005% calcipotriene and 0.064% betamethasone dipropionate foam: Results of a phase III randomized controlled trial

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Patients received once-daily Cal/BD during the four-week open-label phase (NCT02899962). Patients achieving success (physician's global assessment of disease severity [PGA] score 'clear'/'almost clear' with ≥2-grade improvement from baseline) were randomized 1:1 in a double-blind fashion to twice-weekly Cal/BD or vehicle for 52 weeks. Eligibility criteria: ≥18 years; truncal and/or limb psoriasis, involving 2%-30% of body surface area; PGA ≥ 'mild' and modified psoriasis area and severity index score ≥2 at visit 1. Primary end point: time to first relapse (PGA ≥ 'mild'). Secondary end points: number of relapses; proportion of days in remission (PGA 'clear'/'almost clear'). 545 patients were randomized to Cal/BD or vehicle (safety set); 521 achieved treatment success in the open-label phase, (Cal/BD n = 256; vehicle n = 265 [full analysis set]); 251 (46.1%) randomized patients completed the study. Disease characteristics at randomization were similar between groups; 82% of randomized patients had PGA score 'moderate' at baseline. Median time to first relapse was 56 days vs 30 days, Cal/BD and vehicle, respectively. Risk of first relapse was 43% lower with Cal/BD vs vehicle (HR, 0.57, 95% CI, 0.47-0.69; $P < .0001$). Rate of relapse over one year was 46% lower (95% CI, 37%-54%; $P < .001$), Cal/BD group versus vehicle. Predicted mean number of relapses over one year was 4.0 vs 7.5, Cal/BD and vehicle, respectively. Cal/BD group had 11% more days in remission than vehicle ($P < .0001$), 41 extra days over 1 year. Cal/BD was well tolerated during the study. This is the first demonstration of long-term proactive psoriasis management with a twice-weekly topical regimen.

Commercial disclosure: This study was funded by LEO Pharma.

18261

One-point change in glabellar lines wrinkle severity from three phase 3 studies of daxibotulinumtoxinA for injection

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Background: DaxibotulinumtoxinA (DAXI) is a novel botulinum toxin A in clinical development for the treatment of glabellar lines (GL). A 1-point change from baseline on a 4-point scale represents a clinically measurable outcome and has been widely reported in GL studies. Here we present 1-point change results for DAXI from two pivotal phase 3 randomized, controlled trials (RCTs) and one repeat-treatment open-label study (OLS).

Methods: In the two RCTs, subjects with moderate or severe GLs were randomly assigned (2:1) to receive DAXI (40U) or placebo. GL severity was assessed up to 36 weeks. In the OLS study, a cohort of subjects were assigned to receive up to 3 repeat treatments over an 84-week period.

Results: In the two RCTs (n = 303; n = 306), the proportion of subjects with at least 1-point improvement from baseline based on investigator assessment was higher among DAXI-treated patients than among placebo-treated subjects (all $P \leq .0001$ through week 24). At week 4, 99.0% and 99.0% of DAXI subjects achieved at least a 1-point improvement. At week 28, DAXI responder rates were 45.2% and 48.3%. It took a median of 27.9 and 27.4 weeks for subjects to return to baseline wrinkle severity in the RCTs. Similar responder rates and duration were seen in the substantially larger OLS (n = 2691) for up to 3 treatments.

Conclusions: The 1-point responder rate with DAXI was statistically significantly greater than placebo, with a duration of 24 weeks or longer. Consistency of these findings was confirmed in the OLS.

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Particulate matter <2.5 μm as a model of pollution induces hyperpigmentation in melanocytes potentially via oxidative stress

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Background: There is increasing evidence that pollution causes premature skin aging, including loss of elasticity and hyperpigmentation. Multiple clinical studies have demonstrated a link between air pollution and skin hyperpigmentation, or age spots. Particulate matter with a diameter <2.5 μm (PM2.5) is one of the main components of air pollution that carries harmful heavy metal and toxic chemical compounds such as polycyclic aromatic hydrocarbons. The current study used cultured melanocytes to demonstrate PM2.5-induced hyperpigmentation and investigate the effect of a known potent antioxidant, a purified feverfew extract.

Methods: Melanocytes were challenged by PM2.5 (50 to 200 μg/mL) to evaluate the impact of pollution on melanogenesis in the presence or absence of a purified feverfew extract. Changes in cell viability, reactive oxygen species (ROS) and melanin content induced by PM2.5 were evaluated. Whole-genome RNA sequencing was used to assess the effect of PM2.5 in melanocyte gene profiling.

Results: PM2.5 at tested concentration didn't significantly impact the cell viability. PM2.5 significantly increased melanin content in a dose-dependent manner. PM2.5 also induced an increased level of ROS in melanocytes. The presence of a purified feverfew extract significantly reduced both ROS and melanin content induced by PM2.5. RNA sequencing revealed that PM2.5 caused broad changes in melanocyte gene expression.

Conclusions: Our study demonstrated a causative effect of PM2.5 in terms of increased melanin content and broad changes in gene expression in melanocytes, potentially via overproduction of ROS.

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18277

Development of a patient decision aid for hidradenitis suppurativa: Facilitating informed shared decision making

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Background: Shared decision making (SDM) incorporates patient values and preferences, health care provider expertise, and best evidence to facilitate optimal choices for patients. Recent North American guidelines for HS management provide treatment guidance for dermatologists but not patients.

Objective: To develop a PDA for hidradenitis suppurativa (HS) with an emphasis on HS patient values and preferences based on recent guidelines.

Methods and Results: PDA development consisted of: 1) content development whereby North American HS guidelines were translated into patient-friendly language; 2) focused discussion where 7 diagnosed HS patients completed an online survey addressing patient values, preferences, and trade-offs relevant to treatment, as well as PDA content, format, and accessibility (participants found the PDA easy to use and indicated that information was clearly presented. All stated they would use the PDA when choosing a treatment option and would recommend its use); and 3) health care provider assessment where feedback on PDA content and applicability was collected from 5 HS experts/dermatologists (participants generally agreed that content was accurate, steps were in a logical order, and amount of detail was appropriate. Four indicated they would recommend the use of the PDA). Efficacy evaluation of the PDA against an informational resource will be evaluated by a randomized controlled trial.

Conclusions: In partnership with HS experts and patients, we have developed an HS patient decision aid. This should assist in education on HS and its' treatment, clarify patient values and preferences and facilitate informed shared treatment decision making.

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