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Photo validation study using cutaneous dermatomycosis disease area and severity index in dermatomycosis patients

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The Coronavirus disease 2019 (COVID-19) pandemic revealed our need for reliable tools to evaluate patients with skin disease virtually. Thus far, there has not been a study that has attempted to evaluate patients with cutaneous dermatomycosis Disease Area and Severity Index (CADASI), a validated outcome measure of skin activity and damage, from photographs. In this study, patients were prospectively recruited during routine clinical visits and skin regions used in scoring the CADASI were photographed by research staff using two iPhone cameras (an iPhone 8 and iPhone 11). Two dermatologists served as the rater-in-persons (CADASI assessment was scored by rater 1 at the clinic visit and the photographs were scored at a later date by both rater 1 and rater 2. Of the 34 patients participating in the study, 82.3% were female, 85.3% were Caucasian with a mean age of 54 years (SD = 12). For the total activity score, the intraclass correlation coefficient (ICC) between rater 1 vs in-person assessment compared to photograph assessment was 0.806 (95% CI 0.649-0.898 p<0.001) and was 0.822 (95% CI 0.675-0.907 p<0.001) between rater 2 and the in-person assessment. For the total damage score, the ICC between rater 1 and the in-person assessment was 0.54 (95% CI 0.254-0.737 p<0.004) and was 0.601 (95% CI 0.318-0.778 p<0.001) between rater 2 and the in-person assessment. More research is needed to determine inflationary innovations for clinical trials for dermatomycosis. Photographs may be a useful tool for evaluating clinical trial patients in the future. More research is needed to determine improvements for improving our ability to evaluate skin activity through photographs such as the use of a color checker card or color correction algorithm.

A phase 2 randomized clinical trial of serlopitant, a neurokinin-1 receptor antagonist for the treatment of chronic itch in patients with epidermolysis bullosa

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Chronic itch is one of the most frequently reported symptoms in patients with epidermolysis bullosa (EB). We hypothesized that a neurokinin-1 receptor antagonist (NK1RA) which targets the substance P pathway can reduce EB-related itch. In 2019, we reported on the safety of a NK1R antagonist, serlopitant, in a pilot study. Here we report the phase 2 randomized, double-blind, placebo-controlled trial evaluating serlopitant 5mg PO daily for 8 weeks versus placebo for EB-related pruritus. The double-blind phase was followed by a 4-week washout and optional open label extension. Key inclusion criteria included age ≥13 yr, chronic ichthystasis >6 wks and average 24-h itch numerical rating scale (NRS) ≥5 at screening. The primary endpoint of the trial was duration of patient-reported itch for 3 days and 112 in the 11-point NRS from baseline at 8 weeks as measured by daily NRS itch diaries. We enrolled 24 patients with a stratified randomization strategy to ensure equal distribution of participants with more severe EB subtypes. Two patients discontinued for non-compliance (n=1) and LFT elevation (n=1). Treatment arms were balanced in terms of EB subtypes and baseline itch; the mean (SD) of NRS was 5.3 (±2.2) in the placebo and 6.3 (±2.4) in the serlopitant group with the placebo group trending towards being older (mean 40.8 yr vs. 30.8 yr). At 8 weeks, 25% (n=3) of patients in the serlopitant group achieved at least a 3-point reduction compared with 83.3% (n=1) of placebo-treated patients although it was not statistically significance (p=0.59). In a linear mixed model analysis, the serlopitant group showed more NRS reduction relative to placebo (p=0.64 point, p=0.16) at 8 weeks. No treatment-related serious adverse events were reported. This early phase study did not identify superiority of serlopitant but provided the basis for future studies in this rare disease.

Modulation of inflammatory proteins in blood may reflect cutaneous immune responses in topical cancer immunotherapy

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Diphencyprone (DPCP), a hapten that causes delayed-type hypersensitivity reactions, has shown up to 84% efficacy in treating cutaneous metastases in melanoma patients. While a transcriptomic analysis of skin biopsies from melanoma metastases treated with topical DPCP revealed increases in Th1-related genes, a serum proteomic analysis of these patients has not yet been done. We evaluated the serum proteome of five patients with cutaneous melanoma metastases treated with topical DPCP. A total of $282$ proteins with at least partial resolution of skin metastases. There was significant upregulation of proteins associated with promoting tumor immunity (TNFRSF4, TNFRSF9, CD83) and vascular/issue remodeling (MMP12, PGF, ADGRG1) (p<0.05). Among the Th1 upregulated genes was IL33 (IL1RL1) which was increased from day 63 to 112, when compared to day 0 (p<0.05). However, there was only a significant upregulation in Th1 in 12 (n=3) markers on day 63 to 112, in line with prior gene expression studies on skin samples. There was also significant and progressive upregulation of PDI at both days 63 and 112 (p<0.05). This study is the first to assess serum protein biomarkers of patients with cutaneous melanoma metastases following topical immunotherapy. These findings should be interpreted with caution, as the low number of patients treated with topical DPCP, particularly the Th1 axis, which has previously been shown in skin and correlates with tumor regression. Additionally, we observed an increase in PDI, which is of great clinical relevance as inhibitors of this receptor are currently standard-of-care treatment for melanoma. Our findings suggest potential synergy between DPCP and PDI checkpoint inhibition as a future cancer therapy regimen for patients with cutaneous melanoma metastases.

Antiviral D vitamin supplementation & offspring risk of atopic eczema in infancy

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Antenatal vitamin D supplementation has been shown to reduce the risk of atopic eczema, but currently there are no proven general population preventive interventions. In the Maternal Vitamin D Osteoporosis Study double-blind, randomized, placebo-controlled trial, we examined the link between maternal supplementation with vitamin D and the risk of atopic eczema in offspring. Mothers who received 1000 IU cholesterol had lower odds ratios (OR) of atopic eczema at age 12 months: OR (95%CI) 0.57 (0.33-0.98), p=0.04. Sensitivity analysis stratified by breastfeeding duration demonstrated a reduced risk of atopic eczema in the intervention group in infants who were breastfed for more than 1 month (OR 0.48 (0.24,0.94), p=0.03), but not those breastfed for less than one month (OR 0.80 (0.29,2.17), p=0.66); however, intermediate terms between intervention and breastfeeding duration were not statistically significant (p>0.4). Our data provide the first randomization controlled trial evidence of a protective association between maternal D3 supplementation on risk of infantile atopic eczema, with the effect only seen in infants that were breastfed for more than 1 month. The findings support a developmental influence on atopic eczema, and point to a potentially modifiable perinatal influences on atopic eczema.

Photodynamic therapy for basal cell carcinoma enhanced by pretreatment with oral vitamin D: interim results of a prospective clinical trial

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Photodynamic therapy (PDT) is used in Europe to treat basal cell carcinoma (BCC), but it is not approved in the USA due to uncertainties about efficacy. Vitamin D3 (VITD; cholecalciferol) treatment prior to PDT improves BCC responses in mice. A prospective, double-blind, placebo-controlled trial [NCT03467789] was designed to test whether oral VITD pretreatment enhances BCC response to blue light PDT. Participants received 3 PDT treatments (20% ALA, 4 h; 417 nm, 30 min) 2 months apart. High-dose VITD or placebo was administered prior to each of the first two PDT sessions. Lesions were recorded with a 3D digital camera to allow software-assisted tumor volume analysis. Treatment-resistant tumors were biopsied at the final visit. To date, 24 patients and 128 BCCs have been analyzed. Two-thirds (70%) of all lesions were evaluable after PDT. Of the 30% of tumors that failed to clear, all except one superficial BCC were either nodular, micronodular, adenoid, or infiltrative subtypes. To assess the ability of noreadjudant VITD to potentiate PDT efficacy, we evaluated all available lesions to determine their relative volume reduction after VITD+PDT and placebo-PDT. Tumors that showed a >2-fold difference in volume reduction between VITD+PDT compared to placebo+PDT were scored as “Yes”. In our analysis, 15 patients scored “Yes” and 6 scored “No”. This 2-fold difference provides preliminary evidence that noreadjudant VITD may enhance the therapeutic responsiveness to PDT for many BCC tumors. PDT may be an effective treatment for BCC, especially superficial BCC. Oral VITD given prior to PDT represents a novel and safe combination approach.