14393

Real world experience using cyclosporine in psoriasis: Efficacy and toxicity in the Australasian Psoriasis Registry

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Background: Cyclosporine is a calcineurin inhibitor that is approved for short-term use to treat moderate to severe chronic plaque psoriasis. In Australia it is a requirement to have trialed and failed, or have a valid contraindication to, at least two of cyclosporine, methotrexate, acitretin, or nbUVB therapy to be eligible for subsidised biologic therapy for chronic plaque psoriasis in adults. Therefore, it is important in clinical practice throughout Australia that cyclosporine efficacy and safety is well understood.

Methods: Retrospective cohort analyses on all patients in the Australasian Psoriasis Registry (APR) with moderate to severe psoriasis who had been treated with cyclosporine until July 2019. Results In the APR there are a total of 851 patients treated with cyclosporine for chronic psoriasis from the commencement of the registry in 2008 until July 2019. The majority of these patients had moderate to severe psoriasis. The majority of patients ceased cyclosporine was ceased due to lack of efficacy compared with toxicity in 62.8% and 36.8% cases, respectively. The most common toxicity events were hypertension (14.3%), renal impairment (8%), nausea (4.9%), and headache (3.1%). Interestingly, toxicities such as gastrointestinal upset and nausea occurred most commonly in the first 6 weeks of treatment, whereas renal impairment typically occurred much later (mean time to toxicity 278 days). Conclusion This study observes the real world experience of cyclosporine use in chronic psoriasis, and highlights the patterns and timings of adverse events and treatment failure due to lack of efficacy in this Australian population.

Commercial disclosure: None identified.

14407

The Cancer Risk Among MITF E318K Mutation Carriers

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The microphthalmia-associated transcription factor (MITF) E318K variant has been identified as a moderate-risk allele for melanoma. However, there is conflicting published data regarding the relationship of this variant with various types of cancers. Our goal was to perform a systemic review and meta-analysis of the published data and analyze two additional patient populations: published data from the Cancer Genome Atlas (TCGA) database and small cohorts of patients at Massachusetts General Hospital with cutaneous melanoma, early-onset breast cancer and colon cancer. Our systemic review and meta-analysis of previous publications confirmed a significant association of the variant with melanoma (6 published papers, n = 272 patients; odds ratio (OR) = 2.33; 95% confidence interval (CI) = 1.82-2.99; I^2 = 34%). TCGA analysis demonstrated a significant correlation of the variant with incidence of cancer (OR 2.56; *P* value = 6.82E-07) and developing cancer other than melanoma (OR 2.24; *P* value = 6.53E-05). Among 25 cancers tested in the TCGA and MGH datasets, cancers most strongly associated with the variant compared with European non-cancer controls included uterine carcinosarcoma (OR 7.34; *P* value = 0.034), colon cancer (OR 2.739; *P* = .044), and melanoma (OR 2.14, *P* value = 0.062). In conclusion, the germline E318K variant contributes to cancer susceptibility in multiple cancers beyond cutaneous melanoma. Our analysis may have identified novel associations of the variant with colon cancer and uterine carcinosarcoma. Since the variant abolishes a SUMOylation site on MITF, it may induce a pro-carcinogenic transcriptional program in colon cancer and uterine carcinosarcoma. Further work needs to be done to better characterize this relationship before cancer screening recommendations are updated.

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14409

Successful treatment of calcinosis cutis of fingertip in the setting of CREST syndrome with topical 20% sodium thiosulfate

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A 67-year-old woman with a 20-year history of limited scleroderma (CREST syndrome), presented to our clinic with a 6-month history of a painful and ulcerated lesion on the tip of the right index finger. Dermatologic examination revealed a 3×3 mm ulcer with extrusion of a little stony hard white material associated with significant tenderness. The diagnosis of calcinosis cutis (CC) was made. In this patient, antinuclear antibody and anticentromere antibody were positive while anti-topoisomerase I (anti−Scl-70) antibody was negative. For the treatment of CC, she was started on topical sodium thiosulfate (STS) 20% in petrolatum base. She applied the medication three times a day and covered it with a bandage during night. After two months of treatment her pain was relieved and after three months of initiation of treatment her CC lesion was resolved. She tolerated the medication well without any significant adverse effect. Finally, the site of CC remained well healed over the 3.5 years of follow-up. CC is a rare chronic process characterized by deposition of insoluble calcium salts in the skin and subcutaneous tissues. Treatment of CC is difficult and challenging and there is no consensus on the suggested treatments. STS in forms of intravenous, intralesional and topical has been reported to be helpful in treating calcinosis. Three mechanisms of action have been proposed for STS: increased calcium solubility, vasodilation and antioxidant effect that restores endothelial cell function. This case presentation suggests topical STS as an effective treatment modality for patients with limited numbers of superficial CC.

Commercial disclosure: None identified.

14418

The correlation of ultraviolet radiation-associated mutations with patient and tumor-specific factors in cutaneous squamous cell carcinoma

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Background: Affecting ~1 million Americans every year, squamous cell carcinoma (SCC) is the second most common skin cancer. Risk factors include an immunocompromised state and ultraviolet (UV) radiation. An immunocompromised state and certain anatomic areas of the face infer an increased risk of developing metastatic disease. The extent to which UV radiation contributes to SCC development in high-risk patients and tumors remains to be elucidated.

Objective: To compare the contribution of UV radiation in SCCs for immunocompetent versus immunocompromised patients and between different anatomic locations known to be high-risk versus medium/low-risk.

Methods: A cohort of 20 patients with high-risk SCC was developed from an academic medical center. We performed next-generation sequencing using a hotspot mutation panel covering 76 cancer-associated genes using formalin-fixed paraffin-embedded tissue (Vela Diagnostics). We categorized exon variants (excluding germline and synonymous mutations) as being caused by UVA/reactive oxygen species (ROS) or UVB.

Results: Sixty-four percent of mutations in immunocompetent patients (n = 12) were UVB-associated. This was significantly more than in immunocompromised patients (41.7%, n = 8, *P* = .04). The proportion of both UVB and UVA/ROS mutations were significantly different between SCCs in high-risk areas (n = 11) and medium/low-risk areas (n = 9), with high-risk area tumors having more UVA/ROS mutations and less UVB mutations (*P* = .034, *P* = .017).

Discussion: Overall, SCC from immunocompromised patients or high-risk areas were associated with less UVB mutations, suggesting additional mechanisms of pathogenesis, such as an altered tumor microenvironment. These findings support further research to better understand the pathogenesis with the goal of improving outcomes for patients.

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