Outcomes reported in clinical trials of postinflammatory hyperpigmentation: A systematic review
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BACKGROUND: Due to heterogeneity in outcomes measured in clinical trials of post-inflammatory hyperpigmentation (PH), it is difficult to compare different treatment modalities. Reviewing the diversity in reported outcomes is a necessary step in developing a core outcome set (COS), or a minimal set of outcomes that should be reported in all clinical trials of PH to assist those interested in identifying outcomes or comparing PH as part of the development of a COS for future clinical studies. METHODS: A systematic review of the literature was conducted to identify clinical trials of PH treatment published in the English language between January 2010 to August 2020. Reported outcomes were extracted and synthesized. RESULTS: 36 studies were included, and 101 outcomes were identified and grouped into 6 domains: adverse events/effects, clinical assessment, clinical recurrence, perception of health, patient satisfaction, and quality of life. The most commonly reported outcome was “Erythema” as an adverse event (reported in 16 of 36 studies, 44.4%). Additional common outcomes were “Darkness/intensity of pigmentation” (15 of 36 studies, 41.7%) and “Global improvement of pigmentation” (14 of 36 studies, 38.8%). CONCLUSION: There is considerable heterogeneity in outcomes reported in clinical trials of PH. Development of a COS is necessary to standardize outcomes reporting in future clinical trials, which will help to facilitate later comparison of outcomes across multiple studies.

Circulating tumor DNA as a biomarker for treatment response in an advanced Merkel cell carcinoma patient
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Notwithstanding recent advances, Merkel cell carcinoma (MCC) persists as an often-lethal cancer for the majority of patients failing out of immunotherapy. There are unmet clinical demands for effective alternative therapies and novel sensitive methods for monitoring therapeutic response of immunotherapy and beyond. Recently, circulating tumor DNA (ctDNA) analysis using a next generation sequencing (NGS) platform has shown to be sensitive and effective in postoperative management, early detection of relapse, and predicting treatment response and prognosis in several human cancers. In the first case to our knowledge, we describe a case of Merkel cell carcinoma which initially recurred after surgery and progressed on pembrolizumab, with debilitating side effects. Six months after second surgery and adjuvant radiation, she developed in-transit metastases, leaving her limited treatment options. Over the course of combinational TVEC and HRT treatment, we found that ctDNA analysis performed using a personalized and tumor-informed (bespoke) NGS assay correlated with increased tumor burden, treatment response, and imaging findings. At three-month follow-up, ctDNA remains undetectable. As her MCC was extremely aggressive and had recurcated shortly after her previous treatment modality, this is a promising outcome. Our pioneer observation underpins future study to ascertain the transformative role of ctDNA in MCC management, including post-operative risk stratification, early detection of relapse, biomarkers for treatment response and prognosis.

Altered gene expression following targeted therapy for vascular malformation
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Somatic mutations including MAP2K1, TSC1 and PIK3CA were recently identified in endothelial cells of various vascular malformations. These small populations of genetically altered cells are believed to be crucial in promoting angiomatosis and tissue growth that leads to vascular malformations. There is no approved treatment for vascular malformation currently. Therefore, we sought to investigate alteration of gene signature in peripheral blood of patients treated with oral therapy. We performed RNA-Seq on blood samples of 9 patients with vascular malformations. Gene expression was analyzed before and after sirolimus treatment for an average of 6 months. Raw counts were aligned using STAR and differential expression analysis using deseq2. Differential gene expression was analyzed using a wald chi-squared test. We have identified n=498 (FC ≥3 p<0.05, n=10 adjusted p-value <0.05) upregulated and n=96 downregulated genes post therapy (FDR <0.05). The variance of clinical phenotypes of patients analyzed were reflected in their gene expression profiles in peripheral blood. Interestingly, the gene expression profiles became more clustered and exhibited resemblance post treatment. Therefore, the current study is the first to exhibit similar regulatory effects for different vascular malformations. Gene ontology pathway analysis demonstrated changes in addition to PI3K/ mTOR, β-catenin and WNT signaling, cell cycle regulation as well reported renin angiotensin axis and platelet signaling. Computational drug repositioning analysis using these gene signatures predicted other therapeutic agents with similar effects as sirolimus such as vincristine, sunitinib and glucocorticoids. Some of these agents have previously shown efficacy in treating vascular anomalies, further validating our results. This pilot study has demonstrated significant novelty and clarity and will stimulate future investigation into a simple yet comprehensive way that may enable noninvasive diagnosis and therapeutic intervention in the future.

Clinical risk factors associated with MRSA incidence in pediatric celluflis
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Background: Methicillin-resistant Staphylococcus aureus (MRSA) infection in pediatric cellulitis can be difficult to diagnose and treat with appropriate antibiotic coverage. Detection of methicillin resistance can be challenging as it requires isolation of the causative organism by microbial culture, and clinical characteristics alone have limited ability to distinguish MRSA infection. Objective: To identify predictive risk factors for MRSA infection in hospitalized pediatric patients. Methods: Single-center, retrospective chart review of 893 pediatric dermatology consultations over 17 months between August 2017 through February 2018. We included all inpatients with a diagnosis of cellulitis, MRSA, or non-MRSA cellulitis. We excluded patients who were previously excluded if guidelines for MRSA were not available at a surgical site. Multivariate logistic regression analysis was conducted using all independent variables that reached statistical significance in univariate testing. Results: MRSA was cultured in 266 patients (29.8%) and MRSA was isolated in 350 patients (39.2%). The risk factors for MRSA growth were: being in the intensive care unit (ICU; OR 2.17, 95% CI 1.38-3.39, p<0.014), nasal carriage (OR 2.17, 95% CI 1.49-3.18, p<0.001), and having a complicated MRSA infection (OR 2.22, 95% CI 1.44-3.44, p<0.001). Conclusions: MRSA was isolated in the majority of patients with cellulitis. Risk factors for MRSA growth were: ICU admission, nasal carriage, and having a complicated infection. The majority of MRSA-infected patients had non-complex cellulitis that required treatment with antibiotics. However, 1 in 4 patients had a high-risk cellulitis that required treatment with antibiotics. Therefore, patients with cellulitis should be assessed for MRSA infection, especially if they are in the ICU, have nasal carriage or a complicated cellulitis.