Outcomes reported in clinical trials of postinflammatory hyperpigmentation: A systematic review


1 Dermatology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, United States, 2 Dermatology, University of Minnesota, Minneapolis, United States, 3 Dermatology, University of Pennsylvania, Philadelphia, Pennsylvania, United States and 4 Dermatology, Penn State College of Medicine, Hershey, Pennsylvania, United States

BACKGROUND: Due to heterogeneity in outcomes measured in clinical trials of post-inflammatory hyperpigmentation (PIH), 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 PIH moving forward. The aim of this study is to identify outcomes that are commonly measured in clinical trials of PIH 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 PIH treatment published in the English language between January 2010 to August 2020. Reported outcomes were extracted into a standardized data abstraction tool. 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, 38.9%). CONCLUSION: There is considerable heterogeneity in outcomes reported in clinical trials of PIH. 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

J. Yeake, N. Hook, M. Yamamoto, A. Kannan, E. Sanzani, A. Alehin, J. Harris and L. Gao

1 University of California Irvine, Irvine, California, United States, 2 University of California, San Francisco, San Francisco, California, United States, 3 VA Long Beach Healthcare System, Long Beach, California, United States and 4 Southern California Institute for Research and Education, Long Beach, California, United States

Notwithstanding recent advances, Merkel cell carcinoma (MCC) persists as an often-lethal malignancy. Despite the introduction of new therapeutic options, there is a pressing need for new biomarkers to inform patient management, including post-operative risk stratification, early detection of relapse, biomarkers for treatment response and prognosis.

Therefore, we sought to investigate alteration of gene signature in peripheral blood of patients with MCC. Genomic DNA was isolated from peripheral blood mononuclear cells (PBMC) obtained from patients before any treatment and at six months post-treatment. Gene expression analysis was performed on whole blood using the Human RefSeq v10.1 Gene Expression BeadChip. Results were validated using mRNA sequencing. Overall, 1,070 differentially expressed genes were identified which were enriched in angiogenesis and cell adhesion pathways. These genes are likely involved in the early stages of MCC development and may prove useful in future biomarker development.

Altered gene expression following targeted therapy for vascular malformation

M. Teng Dermatology, Stanford University, Stanford, California, United States

Somatic mutations including MAP2K1, Tie2 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 angiogenesis 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 off label 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 six months. Raw counts were aligned using STAR and differential expression analysis using edgeR. Differential gene expression was analyzed using a wald chi-squared test. We have identified n=486 FC ≥ 1.3 p < 0.05, n=10 adjusted p value <0.05 upregulated and n=296 FC ≥ 1.3 p < 0.05, n=6 adjusted p value <0.05 downregulated genes post treatment. The vast majority of clinical phenotypes was 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, indicating that 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 indicated renin angiotensin and TGFb signaling. Computational drug repositioning using these gene signatures predicted other therapeutic agents with similar effects as sirolimus such as vincristine, sunitinib and cyclosporin. Some of these agents have previously shown efficacy in treating vascular anomalies, further validating our results. This pilot study has demonstrated the feasibility to study systemic drug effects on vascular malformations. There is no approved treatment for vascular malformation currently. Further studies are required to confirm these findings and to explore the potential of using these gene signatures to identify new therapeutic agents for the treatment of vascular malformations.

Altered gene expression following targeted therapy for vascular malformation

M. Teng
dermatology, stanford university, stanford, california, united states

Somatic mutations including MAP2K1, Tie2 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 angiogenesis 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 off label 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 six months. Raw counts were aligned using STAR and differential expression analysis using edgeR. Differential gene expression was analyzed using a wald chi-squared test. We have identified n=486 FC ≥ 1.3 p < 0.05, n=10 adjusted p value <0.05 upregulated and n=296 FC ≥ 1.3 p < 0.05, n=6 adjusted p value <0.05 downregulated genes post treatment. The vast majority of clinical phenotypes was 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, indicating that 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 indicated renin angiotensin and TGFb signaling. Computational drug repositioning using these gene signatures predicted other therapeutic agents with similar effects as sirolimus such as vincristine, sunitinib and cyclosporin. Some of these agents have previously shown efficacy in treating vascular anomalies, further validating our results. This pilot study has demonstrated the feasibility to study systemic drug effects on vascular malformations. There is no approved treatment for vascular malformation currently. Further studies are required to confirm these findings and to explore the potential of using these gene signatures to identify new therapeutic agents for the treatment of vascular malformations.