Metabolic activity, hypoxia response elements and induced angiogenesis, biomarkers for overall survival in solid tumors

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Patients with cancer are evaluated through different oncology laboratory markers, aiming at translation to clinical findings, both to evaluate progression of disease as well as translating to overall survival, as surrogate markers. This effort has been revolutionized as the traditional measurements of the tumor size in CT scans, and identifying cancer response by RECIST criteria, has failed to effectively translate into patient survival. Therefore establishing the prognosis in majority of patients, especially with heterogeneous tumors, has been extremely challenging. One area of most recent attention in identifying surrogate markers has been the vasculogenesis and its related serum markers. Different stages of carcinogenesis and metastasis is greatly dependent on tumor angiogenesis, as a result of vascular endothelial dysfunction. Novel ways to assess vascular function in cancer include measuring levels of circulating endothelial cells (CEC) or circulatory tumor cells (CTCs). The presence of circulating endothelial cells (CEC) has recently been recognized as a useful marker of vascular damage. That said, as of today, there is not a single biomarker used clinically for assessing vasculogenesis, or intratumoral hypoxia and the correlation between FDG-PET findings and survival has not been strong, especially in more heterogenous cancers (such as breast and lung cancer). Here we hypothesize that serum/plasma VEGF measurements, as a biomarker for vasculogenesis (and possible intratumoral hypoxia), before and after therapy independently, or in addition to, circulatory tumor cells assay, can be used as a prognostic marker correlating with FDG-PET findings. Altogether, it is a meaningful companion diagnostic tool to translate to clinical outcome, and overall survival. This is also important in therapeutic areas, as traditional chemotherapies in general (all anthracyclines, Alkylators, Platinum based chemotherapies, etc.) increase the serum circulatory tumor cells, as well as serum VEGF, by several mechanisms, including proinflammatory cytokines, disrupting the tumor vessels by disrupting endothelial dysfunction and causing tumor cell leaks. This necessitates new tools to overcome such negative measurable impact on potential survival. Accordingly, here, we present a summary of 150 cases of advanced disease and in detail, we present six cases of heterogenous stage four breast cancer who had failed several lines of chemotherapy, and were treated using a novel antiangiogenic therapy, consisting of natural and off label drugs. These are known to inhibit hypoxia induced pathways, in a protocol called multi targeted epigenetic therapy (MTET), resulting in independent and synergistic response identified by serum VEGF/CTC/ and FDG-PET combo findings, and translated to improved progression free, or overall survival. We conclude that this sample, although small, presents considerable effect size and can impact the current practice of oncology by providing better prognostic and therapeutic tools targeting angiogenesis in refractory heterogeneous disease.

Biography

M A Nezami is a Board Certified Physician graduated from USC and UCSF residencies and fellowship and trained in Integrative Cancer Therapy. He serves as Researcher and national and international Speaker, in Oncology and Epigenetic field. He has been involved in many research projects and publications/presentations. He is an Inventor and Innovator and has designed a new method of treating advanced cancer, called Multi Molecular Targeted Epigenetic Therapy (MTET). With this method, over the last 7 years, he has successfully treated many patients, mostly with advanced cancer who had failed conventional methods.

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