Improving patient outcome through personalized radiation immuno-oncology approaches

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Statement of the Problem: New immuno-oncology approaches have emerged, to improve outcome for cancer patients. These approaches involve the use of immune-checkpoint inhibitors (CTLA-4, PD-1, PD-L1, etc), agonists (4-1BB, Ox 40-L), and cytokines (IL2, IL-15), some of which have received FDA clearance. Future direction, now involves using these agents in combination with other approaches. One approach may involve the use of radiotherapy. Radiotherapy has been shown to have "immuno-genic" effects on tumor cells, T cells, APCs, as well as the tumor micro-environment. Post radiotherapy, abscopal effect, has been previously described, and can lead to immune-mediated control of distant sites of disease, when one site of tumor deposit is irradiated. The purpose of our efforts is to improve outcome in our melanoma mouse model, and translate these findings into ongoing clinical trials, involving radiation and immunotherapy.

Methods: We have developed a B16F10GP melanoma human syngeneic mouse model to evaluate the immunological effects of radiation, in combination with various immune-checkpoint modulators and cytokines (Figure 1). In addition, our work also involves the development of tumor exosomes as potential biomarkers of post radiation abscopal response.

Findings: We demonstrate that several elements are needed to maximize the optimum post radiation abscopal response, and that the response is CD 8 T cell mediated. Considerations, such as radiation dose, radiation fractionation, and timing of radiation with various immune-checkpoint inhibitors are important factors to consider when designing clinical trials. Furthermore, tumor exosomes may play an important role as biomarkers in abscopal response.

Conclusion & Significance: Our data suggest that radiation may be one strategy that could improve outcome in patients, when combined with emerging immunotherapeutics, such as PD-L1/PD-1, CTLA-4, 4-1BB, and others. Future clinical trials are needed to translate this, into the clinic, as part of multi-disciplinary approach in the future.

Speaker Biography

Mohammad K Khan has expertise as Radiation Oncologists, and as a Translational Physician Scientist. He treats variety cancer patients, with expertise in skin cancers and hematological malignancies. His research focuses on translating post radiation abscopal effect into the clinic, to improve outcome for cancer patients. In particular, he is interested in developing multi-disciplinary approaches involving radiation and immuno-oncology to improve outcome for cancer patients. He currently leads several efforts that span patient outcomes work, basic sciences work, as well as ongoing clinical trials.

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