Bempegaldesleukin in combination with local radiation and systemic checkpoint blockade induces a robust systemic anti-tumor effect.

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BACKGROUND

Purpose: The majority of solid tumors diagnosed in patients qualify as immunologically “cold” tumors. Immune checkpoint inhibitors have a limited response rate in patients with these tumor types1. We wanted to explore if immune modulatory radiation and bempegaldesleukin alter the response rate to immune checkpoint inhibitors in an immunologically “cold,” solid tumor model. Additionally, we wanted to investigate this treatment regimen under conditions that more appropriately mimic the disease pattern we typically see in patients (i.e. locally advanced disease and/or metastatic spread).

Bempegaldesleukin circumvents the limitations of IL-2: Using IL-2 in a treatment regimen does not come without consequences. It has a short half-life in vivo, requiring frequent administration. IL-2 does not only activate immune “killer” cells (i.e. NK cells, CD4+ T cells, CD8+ T cells). Immune inhibitory T regulatory (Treg) cells, which are present in the tumor microenvironment and used by tumors to evade an immune response, are also activated by IL-2. Finally, IL-2 has dose limiting toxicity, which can become overwhelming in patients (i.e. locally advanced disease and/or metastatic spread).

External Beam Radiation and NKTR-214 Synergy: We have previously shown a synergistic interaction between local low dose radiation therapy (RT) and NKTR-214 in mice bearing moderate sized melanoma tumors 2. The anti-tumor effect elicited by RT+NKTR-214 is mediated through T cells and, to a lesser degree, NK cells. Mice cured of their initial tumor burden (~75% of those treated with RT+NKTR-214) demonstrate a strong, tumor specific immune memory when rechallenged with a second inoculation of B78 tumors. However, this combination (RT+NKTR-214) is less effective in the presence of larger tumors or systemic disease.

METHODS

Model 1: B78 Flank, B16 Metastatic Melanoma Model

Model 2: Large, Well Established B78 Flank Melanoma Model

RESULTS

CONCLUSIONS


REFERENCES AND CONTACT INFORMATION

1. We plan to explore the potential of this treatment regimen (RT + bempegaldesleukin + anti-CTLA-4) in other tumor models, including models that spontaneously metastasize.
2. We are planning to investigate the mechanism behind this strong anti-tumor response using flow cytometry and qPCR.

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