Enhanced Anti-tumor Activity of the Combination of Entinostat and NKTR-214 in Renal and Colon Cancer Tumor Models

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BACKGROUND
Combination strategies are required to improve outcomes for patients with cancer. Recent studies have shown that entinostat (ENT) and NKTR-214 are a novel HDACi-1B/2 inhibitor designed with potent safety, tolerability, and anti-tumor efficacy. In preclinical models, entinostat combined with high-dose entinostat 2 demonstrated synergistic effects against tumor growth and improved infiltration of immune cells. In this study, we investigated the anti-tumor efficacy and immune response of entinostat combined with NKTR-214 in syngeneic renal and colorectal cancer models.

RESULTS

- **Cell Lines:**
  - In the CT26 colorectal cancer cell line and BCA3 melanoma cell line, combined treatment with entinostat and NKTR-214 was associated with in vitro growth inhibition compared to untreated controls, with significant activity at higher doses.
- **Tumor Infiltrating Lymphocytes Analysis:**
  - Enhanced infiltration of CD8+ T cells in the tumor microenvironment in the CT26 model. Mice (n=3) were treated with drugs as described in materials and methods. On day 7 after drug treatment, the tumors were harvested, and single-cell suspensions were prepared. CD8+ T cells were then analyzed by FACS for PD-1+ and GranzymB+.
- **Anti-tumor activity:**
  - The combination treatment increased Th1 CD8 T cell infiltration in the RENCA model. Figure 4B. Figure 6.

CONCLUSIONS
The combination treatment significantly inhibited tumor growth in CT26 and RENCA models. Combination of entinostat and NKTR-214 significantly inhibited tumor growth in CT26 and RENCA models. The combination significantly enhanced T cell cytotoxicity by producing more IFNγ and granzyme B in CD8+ T cells. NKTR-214 alone or with higher dose entinostat also significantly decreased Tregs in CT26 cell models. Entinostat alone increased ADCC’s in the BCA3 model, and the addition of NKTR-214 to the BCA3 model.

*References:*