Antitumor immune response induced by NBTXR3 activated by radiotherapy.

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Abstract Disclosures

Abstract:

Background: Radiotherapy (RT) can prime an anti-tumor immune response. Unfortunately, this response rarely generates total tumor destruction and abscopal effect. When activated by RT, intratumorally (IT) administered hafnium oxide nanoparticles (NBTXR3) locally increase radiation dose deposit and tumor cell death compared to RT alone. We hypothesized that NBTXR3 + RT could enhance the anti-tumor immune response, both in mice and humans. **Methods:** Murine CT26 cells were injected in both flanks of immunocompetent mice. When tumor volume reached 50-120mm3, NBTXR3 (or vehicle) was injected IT in right flank tumors only, then irradiated (3x4Gy). Mice were sacrificed when tumors reached 800mm3. Alternatively, tumors were collected 3 days after last RT fraction and immune cell infiltrates analyzed by immunohistochemistry (IHC). Patients (pts) with locally advanced Soft Tissue Sarcoma (STS) (NCT02379845) received NBTXR3 + RT or RT alone. Pre- and post-treatment (biopsy and resection, respectively) tumor tissues from pts were analyzed by IHC and Digital Pathology for immune biomarkers (> 16 pts per arm). **Results:** In mice, IHC

analyses showed an increase of CD8+ T cells infiltrates in both flanks of mice treated with NBTXR3+RT, while this was not observed in animals treated with RT alone. Furthermore, ICH analysis of post- vs pre-treatment samples from STS pts showed a marked increase of CD8+ and PD1 biomarkers for pts treated with NBTXR3 + RT, while no differences were seen for pts treated with RT alone. **Conclusions:** NBTXR3 + RT markedly changes the tumor immune profile in a similar manner in mice and pts with STS. We hypothesize that this adaptive immune response could help convert a local tumor microenvironment to a “hot” phenotype and thus improve the efficacy of immune checkpoint inhibitors. These results led us to investigate the safety and systemic effect of NBTXR3 activated by stereotactic ablative RT (SABR) in combination with anti-PD-1 antibody in pts with locoregionally recurrent or metastatic (to lung or liver) Head and Neck squamous cell carcinoma HNSCC, as well as in metastatic non-small cell lung cancer (NSCLC) and liver metastasis patients [NCT03589339].