Abstract for ASCO 2018, section – Developmental Therapeutics—Immunotherapy

Title:

Hafnium oxide nanoparticle activated by radiotherapy generates an anti-tumor immune response.

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Background:

Radiotherapy (RT) can prime an anti-tumor immune response. Unfortunately, this response is not sufficient to allow tumor destruction and abscopal effect (effect on a distant untreated lesion) is hardly obtained. Hafnium oxide nanoparticle (HfO2-NP) is composed of high electron density material. After intratumoral injection (i.t.), HfO2-NPs are taken up by cancer cells and, when activated by RT, locally increase the radiation dose deposit, destroying more cancer cells than RT. We hypothesized that HfO2-NP + RT could enhance anti-tumor immune response, compared to RT alone, both in animal and human.

Methods:

Mouse CT26 cells were injected in both flanks of mice. When tumor volume is 50-120mm3, HfO2-NP (or vehicle) was injected by i.t. in the right flank tumors only, then irradiated (3x4Gy). Tumor growth was followed and animals sacrificed when a tumor reached 800mm3. Alternatively, tumors were collected 3 days after last RT fraction and immune cell infiltrates were analyzed by immunohistochemistry (IHC). Patients with locally advanced STS (NCT02379845) received either HfO2-NP + RT or RT alone. Pre- and post-treatment (biopsy and resection, respectively) tumor tissues for each patient are analyzed by immunohistochemistry and Digital Pathology for immune biomarkers and Pan-Immune gene expression profiling (> 16 patients per arm).

Results:

In mouse, an abscopal effect was observed with HfO2-NP but not with RT alone. IHC analyses show that a significant increase of CD8+ cells is present in treated and untreated tumors, but no effect was observed for RT alone. IHC analysis (post- vs pretreatment) show a marked increase of the biomarkers for patient treated with HfO2-NP + RT, particularly for CD8+ and PD1. No differences are seen for RT alone. The profile of gene expression HfO2-NP + RT differs from RT alone. Functional analysis of genes expression up-regulated in HfO2-NP + RT shows an increase of the cytokine and immune checkpoints expression, as T cell activation markers, compared to RT alone.

Conclusions:

HfO2-NP + RT bring marked changes to the tumor immune profile both in mouse model and in patients with STS, compared to RT. So far, these results show that HfO2-NP + RT induces a specific adaptive immune pattern.

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