Abstract ASTRO 2018

Title:

Hafnium oxide nanoparticles activated by radiotherapy induce anti-tumor immunity in patients with advanced soft tissue sarcoma

Authors:

J. Galon[1], M. Laé[2], J. O. Thariat[3], S. Carrere[4], Z. Papai[5], M. Delannes[6], P. Sargos[7], P. Rochaix[6], L. C. Mangel[8], Z. Sapi[9], T. Tornoczky[8], I. Peyrottes[10], R. Tetreau[11], M. C. Château[4], M. P. Sunyach[12], P. Agoston[13], H. Brisse[2], C. Llacer[11], A. Lecesne[14], and S. Bonvalot[2];

[1]INSERM, Paris, France, [2]Institut Curie, Paris, France, [3]Centre Baclesse, Caen, France, [4]Institut du cancer de Montpellier, Montpellier, France, [5]Magyar Honvedseg Egeszsegugyi Kozpont, Budapest, Hungary, [6]Institut Universitaire du Cancer Toulouse, Toulouse, France, [7]Department of Radiation Oncology, Institut Bergonie, Bordeaux, France, [8]Pecs University, Pecs, Hungary, [9]Semmelweis University, Budapest, Hungary, [10]Centre Antoine Lacassagne, Nice, France, [11]Montpellier Cancer Institute, Montpellier, France, [12]Centre Léon Berard, Lyon, France, [13]National Institute of Oncology, Budapest, Hungary, [14]Institut Gustave Roussy, Villejuif, France

Objectives:

Soft tissue sarcoma (STS) is a rare type of cancer, which occurs in tissues connecting, supporting and/or surrounding other structures of the body, like muscle, fat, etc. More than 50 subtypes of STS exist, characterized by a strong propensity to local recurrence and metastatic spreading. Consistently, the immune microenvironment in sarcomas is highly variable. A new class of high electron density material, hafnium oxide, was designed at the nanoscale to efficiently absorb ionizing radiation from within the tumor cells and increase the dose deposition into the tumor. These nanoparticles (HfO_2-NP), delivered into the tumor by a single injection and activated by radiotherapy, have the ability to enhance immunogenic cell death and immune response in preclinical studies.

Here, we explore in a phase II/III trial in patients with locally advanced STS, the effects of nanosized hafnium oxide exposed to RT in terms of tumor immune profile changes in patients, when compared to RT alone.

Materials/Methods:

Patients with locally advanced STS (NCT02379845) received either HfO_2-NP activated by RT or RT alone. Pre- and post-treatment (biopsy and resection, respectively) tumor tissues for each patient were analyzed by immunohistochemistry and Digital Pathology for immune biomarkers (CD8+, CD3+, PD1+, CD103+) and Pan-Immune gene expression profiling by NanoString (>16 patients per arm).

Results

Immunohistochemistry analysis (post- vs pre-treatment) show a marked increase of the tested biomarkers for patient treated with HfO_2-NP + RT, particularly for CD8+ and PD1, while no differences are seen for RT alone. Interestingly, the profile of gene expression HfO_2-NP + RT differs from those obtained with RT alone. Functional analysis of genes expression up-regulated in HfO_2-NP + RT (post- vs pre-treatment) shows an increase of the cytokine/interleukine and immune checkpoints expression, and T cell lymphocyte activation markers, compared to RT alone.

Conclusions

Regarding immune cells infiltrates (post- vs pre-treatment), promising results are reported for patients treated with HfO_2-NP activated by RT, when compared to RT. So far, these results show that HfO_2-NP + RT induces a specific adaptive immune pattern. As such, it may convert immunologically “cold” tumor into “hot” tumor and be effectively combined with immunotherapeutic agents across oncology. More tissue samples are under evaluation to reinforce these findings.

https://doi.org/10.1016/j.ijrobp.2018.07.109