

1122

RADIOTHERAPY-ACTIVATED NBTXR3 NANOPARTICLES INDUCE INTERFERON BETA SECRETION BY CANCER CELLSJordan Da Silva*, Sebastien Paris. *Nanobiotix, Paris, France*

Background The first-in-class radioenhancer NBTXR3 is composed of hafnium oxide nanoparticles, design to be delivered to patients by a single intratumor injection. When exposed to radiotherapy (RT), NBTXR3 nanoparticles increase radiation dose deposition from within the cancer cells. Results from a phase II/III clinical trial in patients with locally advanced Soft Tissue Sarcoma demonstrated significant superiority and clinical benefits of NBTXR3 activated by RT compared to RT alone, with a very good safety profile. Several preclinical studies have established the immunomodulatory capacities of NBTXR3 (e.g., increase of CD8 infiltrates in tumors, restoration of anti-PD1 sensitivity, induction of abscopal effect, etc.). Nonetheless, few data are currently available to understand the biological mechanisms triggered by NBTXR3+RT at the cancer cell level which could explain these results. Here, we investigated the impact of NBTXR3 activated by RT (NBTXR3+RT) on the interferon beta (IFN-beta) secretion by cancer cells.

Methods The impact of NBTXR3 activated by radiotherapy on IFN-beta production by cancer cells was evaluated by ELISA assay in the supernatant of CT26.WT cells (a murine colorectal cancer cell line). Six-wells plates containing plated cells were treated (or not) with 400µM of NBTXR3. The following day, cells were irradiated (or not) by a single dose of 4Gy. After 3 days, supernatants were collected, and the IFN-beta secretion was analyzed by ELISA assay. The efficacy of each treatment modality on cell viability was also measured by MTT assay.

Results ELISA analyses showed no effect of NBTXR3 without RT. In contrast, RT alone induced a significant increase of IFN-beta secretion. Interestingly, NBTXR3+RT significantly increased IFN-beta secretion by treated cells, compared to RT alone. MTT assay also show the superior capacity of NBTXR3+RT to destroy cancer cells, compared to RT alone.

Conclusions It has been previously reported that NBTXR3 +RT (3 fractions of 4Gy) produced a significant abscopal effect in competent mice bearing CT26.WT tumors. Our in vitro data show that NBTXR3+RT can significantly enhance the secretion of IFN-beta by these cells, with only a single dose of 4Gy. These results suggest that the immunomodulatory capacities of NBTXR3+RT measured in vivo could be explained, at least in part, by a greater secretion of IFN-beta, a cytokine known to play a central role in the priming of immune response.

<http://dx.doi.org/10.1136/jitc-2022-SITC2022.1122>