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TITLE: NBTXR3 TREATMENT INDUCES ANTITUMORAL IMMUNE RESPONSE IN HUMAN SOFT TISSUE SARCOMA

PRESENTATION TYPE: Poster

CURRENT CATEGORY: Soft Tissue Sarcoma

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ABSTRACT BODY:

Objective: NBTXR3 is an aqueous suspension of functionalized hafnium oxide nanoparticles, undergoing seven clinical trials for enhancing radiation therapy (RT). They were designed for high dose energy absorption/deposition within the cancer cells when exposed to radiotherapy (NBTXR3 + RT), leading to tumor cell death and possible improved outcomes. In preclinical studies, NBTXR3 + RT also proved to cause immunogenic cell death and activate immune response. Here, we discuss the hypothesis that NBTXR3 + RT induces a specific adaptive immune response compared to RT alone in patients with STS.

Methods: Tumor tissues pre-(biopsy) and/or post-treatment (resection) were collected from patients (pts) with locally advanced STS, who received either NBTXR3 as intratumor injection and RT (14 pts) or RT alone (12 pts), as preoperative treatment (NCT02379845). Immunohistochemistry and Digital Pathology for immune biomarkers and for Immunoscore® (CD3/CD8) were analyzed. Gene expression profiling and pre-optimized immune-gene signatures called Immunosign® were also used.

Results: NBTXR3 + RT showed a significant increase of T cells (CD3/CD8) and a pronounced increase of CD103+ immune cell infiltration post vs pre-treatment ($P<0.01$), which were not seen for RT alone, and an increase in Immunoscore (CD3 + CD8 cell densities) compared to RT alone ($P<0.07$). Additionally, up-regulation of immune system gene expression, especially adaptive immunity genes expression, between pre- and post-treatment was marked for NBTXR3 + RT when compared to RT alone. Indeed, a functional analysis of genes up-regulated in NBTXR3 + RT demonstrated enhanced cytokine activity (IL7, IFNA, IL16, IL11, IFNG), adaptive immunity (RAG1, GZMA, TAP1, TAP2, TBX21, STAT4, IFNG, LCK, LTK, CD37, CD22) and T cell signaling pathway (CD28, CTLA4, CD274, BTLA, TIGIT, CD40LG, CD5, CD3E, ZAP70).

Conclusion: NBTXR3 + RT triggers an enhanced adaptive immune response and contributes to transform “cold” tumor into “hot” tumor. These findings support the idea of NBTXR3 + RT being efficiently combined with immunotherapeutic agents, although further evaluations are needed to reinforce these results.

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Confirmation: I agree

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