Hafnium oxide nanoparticles as a promising emergent treatment for head and neck cancer

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In the treatment of head and neck cancer, tumor response has been improved by combining radiotherapy (RT) with chemical agents, radiosensitizers and monoclonal antibodies. However, these associations come with challenging limitations in terms of pharmacology, local control, clinical outcome benefits or patient quality of life. In addition, high doses of radiation may result in several undesired reactions which underline the need for new therapeutic approaches.

A new class of material with high electron density, hafnium oxide, was designed at the nanoscale in the form of crystalline 50nm-particles (HfO_2-NP) to efficiently absorb ionizing radiation and increase the radiation dose deposited - "hot spots" of energy deposit - from within the tumor cells to more focused and efficient cell killing.

Preclinical studies have demonstrated increase of cancer cells death *in vitro* and marked antitumor efficacy *in vivo* in presence of these nanoparticles (HfO_2-NP) exposed to RT, when compared to RT alone. Hafnium oxide nanoparticles efficacy was assessed in cancer epithelial and mesenchymal tumor models and on patient-derived tumor xenografts in nude mice, showing superior anti-tumor effects over radiation therapy alone in terms of complete response and overall survival.

HfO_2-NP (NBTXR3), administered as a single intratumoral injection and activated by radiotherapy, is currently evaluated in a phase I clinical trial for head and neck cancer [NCT01946867]. So far, patients treated in phase I showed good local and systemic tolerance to the product up to the highest dose level and received radiotherapy as planned, confirming a very good local safety profile.

Regarding the patients, the durability of response so far is superior to 13 months, with some patients at 16 and 22 months follow-up without recurrence.

NBTXR3 nanoparticles constitute a rising hope for head and neck cancer patients as it could lead to a decrease in the long-term adverse effects of RT and an improvement in quality of life, associated with strong locoregional control.

Besides, NBTXR3 + RT is also evaluated in clinical trials for soft tissue sarcoma, prostate, liver and rectum cancer and is showing promising results in terms of benefit-risk ratio assessment and efficacy, leading to believe in bright perspectives for the treatment of head and neck cancer.

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