Hafnium oxide nanoparticles and radiotherapy for solid tumors: a promising new treatment strategy

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Technological advances in radiation oncology over the past decade has focused on high-precision radiotherapy to reduce unwanted irradiation of normal tissues, while fully covering the tumor.
Techniques in photon radiotherapy such as intensity-modulated radiation therapy (IMRT) and image guidance (image-guided radiation therapy; IGRT) have improved the delivery of the dose while particle radiotherapy with protons or heavier ions has emerged as an interesting technology in radioresistant tumors in close proximity to organ at risk, when it is desired to spare growing organs from irradiation. Still, there is a high unmet medical need to enhance the energy dose deposit within tumor cells without increasing the dose received by surrounding healthy tissues.
Hafnium oxide nanoparticle (NBTXR3), a high electron density nanoparticle, has been specifically designed to address this high unmet medical need. Monte Carlo simulations using either photons or particles (protons) radiotherapy have proved the fundamental concept of local enhancement of energy dose deposit using high electron density nanoparticles.
The designed NBTXR3 nanoparticles increase the probability of interaction with incoming radiations to enhance the energy dose deposition from within tumor cells. They present a favorable ratio of X-ray absorption for an efficient cell killing to toxicity.
NBTXR3 administered as a single intratumoral injection and activated by photon radiotherapy is currently evaluated in several clinical trials, including a phase II/III in soft tissue sarcoma (STS) [NCT02379845] and phases I/II for head and neck [NCT01946867], prostate [NCT02805894], liver [NCT02721056] and rectum cancers [NCT02465593].
So far, 142 patients treated with NBTXR3 received radiotherapy as planned, with a good local safety profile. All data generated showed interesting transferability across different cancer indications. These first-in-class nanoparticles show promising results in terms of antitumor efficacy in patients with locally advanced STS and head and neck squamous cell carcinoma.

Furthermore, in preclinical studies, NBTXR3 exposed to radiotherapy has demonstrated substantial enhancement of immunogenic cell death and improvement of the immune response when compared to radiotherapy alone suggesting it could function as an effective in situ tumor vaccine.

In conclusion, NBTXR3 intended use fit perfectly with existing and under development radiotherapy technologies offering unique opportunity to widen the therapeutic window of radiation oncology. Beyond, it may efficiently combine with immunotherapeutic agents across oncology.