Hafnium oxide nanoparticles (NBTXR3), a novel radiation enhancer achieves marked antitumor efficacy across five tumor types

Short Title:
In vivo NBTXR3 efficacy

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Abstract:
NBTXR3 are hafnium oxide nanoparticles (NPs) used for a single intratumor administration as radioenhancer in combination with radiation therapy (RT) as part of multi-modality of cancer treatment. The size, shape and surface of the NPs have been designed to develop strong interactions with cancer cells - effective cell binding and uptake - and to persist within the tumor mass during the whole RT treatment. The high electron density of the NPs is responsible for an increased probability of interaction with incoming ionizing radiations (when compared to tumor tissues with low electron density) and an increased energy dose deposition within the cancer cells which results in an enhanced tumor destruction when compared to RT alone. NBTXR3 works similar to the physical mode of action of RT, it does not rely on any biological system or target and constantly amplifies the radiation dose deposition ("on/off" activation). Here we present the transferability of the approach from one type of cancer to the other evaluating (i) the feasibility of the intratumor injection (intratumor availability of NBTXR3 nanoparticles by Computed Tomography (CT) or µCT) and (ii), the antitumor efficacy of NBTXR3 exposed to radiation. NBTXR3 NPs demonstrated a good intratumor availability and persistence across all tested tumor models (epithelial or mesenchymal origin), including human PDX tumor models. Notably, in PAC-120 tumor model the persistence of NBTXR3 NPs within the tumor mass was observed for more than 50 days which is equivalent to the entire duration of RT treatment. The antitumor efficacy was systematically enhanced in terms of tumor growth delay for animals treated with NBTXR3 and exposed to RT when compared to RT alone. NBTXR3 is currently in clinical trials in seven cancer indications including: soft tissue sarcoma, head and neck (H&N), liver, rectal and prostate. These preclinical studies support the rationale for the development of NBTXR3 across all cancer indications where radiation treatment is used.

NBTXR3 intratumor availability and antitumor efficacy

Tumor model		X-ray sources (antitumor efficacy)	CT or µCT
Sarcoma	HT1080	200kV, Ir192	
	LPS80T3 (PDX)	200kV, Co60	x
	A673	Co60	
Prostate	PC3	150kV	x
	DU145	200kV	x
	PAC120 (PDX)		x
H&N	CAL33	200kV	x
	FaDu	200kV	x
Colorectal	HCT116	Ir192	x
Lung	NCI-H460-luc2	200kV	x

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