Title: a phase I/II trial of NBTXR3 nanoparticles activated by SBRT in the treatment of liver cancers.

Authors:

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Background: A new class of material with high electron density, hafnium oxide, was designed at the nanoscale (NBTXR3) to efficiently enhance the energy dose deposit from within the tumor cells and increase lethality of tumors, when exposed to radiotherapy (RT). The physical mode of action of NBTXR3 may represent a breakthrough approach for the local treatment of liver cancers, as it does not engage liver and renal functions, i.e. nanoparticles are not metabolized and not excreted by kidney. A phase I/II trial has been implemented for the treatment of hepatocellular carcinoma and liver metastasis [NCT02721056]. The study is currently recruiting patients.

Methods: Patients (pts) receive a single intralesional (IL) injection of NBTXR3 (53.3g/L) at Volume levels equivalent to 10%, 15%, 22% and 33% of the baseline tumor volume, followed by RT (SBRT, 45Gy / 3 fractions / 5 to 7 days). For the Phase I part, primary endpoints include determination of the Recommended Dose and Dose Limiting Toxicities (DLT). The Phase II part will test three different groups of patients, HCC with portal vein thrombus, HCC without portal vein thrombus and a third cohort with liver metastases. Primary endpoints are complete response rate and safety.

Results: Enrollment was completed for Volume levels 10% (6 pts) and 15% (4 pts) and is currently recruiting patients at 22% level. The NBTXR3 injections were successful in all cases. Radiotherapy has been delivered as planned without any DLT occurrence. No serious adverse event (SAE) related to NBTXR3 or the treatment procedure occurred. Three adverse events related to the injection were reported and no adverse event related to NBTXR3. Importantly, NBTXR3 nanoparticles did not have any impact on the reliability of image-guided radiation therapy (IGRT).

Conclusion: The injection of NBTXR3 was safe and well tolerated at these levels. Patients received the planned RT. No DLT occurred. Enrollment is now opened at the 22% level. NBTXR3 shows promising results in terms of safety and antitumor activity and is also currently evaluated in other six clinical studies.

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