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Hepatocellular carcinoma and liver metastasis treated by hafnium oxide nanoparticles activated by SBRT: A phase I/II trial.

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Background: Hafnium oxide nanoparticles, NBXTR3, were developed to increase the tumor-localized high energy deposit once activated by ionizing radiation such as stereotactic body radiotherapy (SBRT) and thus to increase tumor cell death compared to the same dose of radiation. NBTXR3 is characterized by a single intratumor/intralesional (IL) administration and fits into standard RT schedule with no change in patient's flow, treatment protocol or equipment. Herein the preliminary results of a phase I/II clinical trial evaluating this combination in patients (pts) with hepatocellular carcinoma (HCC) or liver metastasis (mets). **Methods:** HCC and liver mets patients were treated with an IL injection of NBTXR3 followed by SBRT (15 Gy*3 fractions). The phase I part of the trial follows a 3+3 dose escalation design at dose levels of NBTXR3 corresponding to 10%, 15%, 22%, 33% of the baseline tumor volume. This study aims primarily to identify the Recommended Dose and the incidence of early Dose Limiting Toxicities (DLTs) of NBTXR3 activated by SBRT. Secondary endpoints include assessment of global safety profile, liver function evaluated by Child-Pugh score (CPS), AST to Platelet Ratio Index (APRI), and response rate (mRECIST/RECIST 1.1). **Results:** Enrollment is at the last dose level, 33%, and completed at 10% (6 pts), 15% (4 pts) and 22% (4 pts). So far, no early DLTs nor severe adverse events related to NBTXR3 were observed. Both CPS and APRI did not reveal important variations in accordance to NBTXR3 low toxicity. The best observed target lesions responses, among 7 evaluable HCC pts for response (mRECIST), were: 3 complete responses, 3 partial responses (PR) and 1 stable disease (SD) and among 5 evaluable liver mets pts: 1 PR, 3 SD and 1 progressive disease (RECIST 1.1). **Conclusions:** NBTXR3 is well tolerated at the 22% dose level with an overall positive safety profile. This innovative approach might constitute a valuable solution for pts with liver tumors beyond standard treatment lines. NBTXR3 was successful in a phase II/III in soft tissue sarcoma [NCT02379845] and is currently evaluated in head and neck [NCT01946867; NCT02901483], prostate [NCT02805894] and rectum cancers. Clinical trial information: NCT02721056.