Hepatobiliary Cancer

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Treatment of hepatocellular carcinoma and liver metastases with hafnium oxide nanoparticles activated by SBRT: A phase I/II trial.

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Abstract

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Background: Treatment of unresectable liver cancer or liver metastases (mets) by stereotactic body radiotherapy is well tolerated but limited by the need to preserve liver function. Increasing energy deposition in the tumor while at the same time maintaining the dose in healthy tissue remains a major challenge in radiation oncology that could be achieved by NBTXR3 (hafnium oxide nanoparticles) when activated by radiotherapy (RT). NBTXR3 augments energy dose deposit within tumor cells, increasing tumor cell death compared to RT alone, while sparing healthy tissues. Patients (pts) with hepatocellular carcinoma (HCC) or liver metastasis (mets) may benefit from the mode of action of NBTXR3. A phase I/II clinical trial has been conducted to evaluate NBTXR3 activated by SBRT in these pts [NCT02721056]. **Methods:** The Phase I used a 3+3 dose escalation scheme with 5 NBTXR3 dose levels: 10, 15, 22, 33, and 42% of baseline tumor volume. NBTXR3 was administered by intratumoral injection (ITI) followed by SBRT (45 Gy / 3 fractions / 5 to 7 days or 50 Gy / 5 fractions / 15 days). Primary endpoints were identification of the recommended Phase II Dose and early DLTs. Secondary endpoints included safety profile, liver function evaluated by Child-Pugh score (CPS), AST to Platelet Ratio Index (APRI), and early efficacy by response rate (mRECIST/RECIST 1.1). **Results:** The dose escalation levels of 10, 15, 22 and 33% are completed (n = 17): 6 pts at 10% (2 SBRT doses tested due to organ constraints), 4 pts each at 15% and 22% (due to fiducial displacement and ITI shift) and 3 pts at 33%. No early DLT was observed and only one SAE (bile duct stenosis) related to NBTXR3 and RT occurred. CPS and APRI did not show clinically meaningful changes post-treatment and CT-

scan showed no leakage of NBTXR3 into surrounding tissues. Best response for HCC (n = 8) were 5CR, 3PR and for mets (n = 6) the results were: 3 PR, 3SD. **Conclusions:** ITI of NBTXR3 is feasible, demonstrated a very good safety and tolerability profile up to the 33% dose level. Recruitment needs to be finalized at the 42% dose level. Based on early efficacy results NBTXR3 has the potential to address an unmet medical need in pts with unresectable primary or metastatic liver cancer. Clinical trial information: NCT02721056.

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