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756P Phase I/II trial of NBTXR3 activated by SBRT in patients with hepatocellular carcinoma or liver metastasis

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Background: Treatment of hepatocellular carcinoma (HCC) and liver metastasis (mets) is challenging due to presence of underlying disease, e.g. cirrhosis. Stereotactic body radiation therapy (SBRT) is a well-tolerated alternative for inoperable patients (pts), yet maximal dose to the tumor is limited by potential toxicity to surrounding healthy tissues. Otherwise inert, NBTXR3 (hafnium oxide nanoparticles) when activated by ionizing radiation (RT) augments dose deposit within tumor cells, increasing tumor cell death compared to RT alone. A phase I/II clinical trial is underway to evaluate NBTXR3 activated by SBRT in pts with HCC or liver mets [NCT02721056].

Methods: A 3 + 3 dose escalation was utilized in the phase I. Pts received a single intralesional injection (ILI) of NBTXR3 followed by SBRT (45 Gy/3 fractions/5-7 days), with tested NBTXR3 dose levels of 10, 15, 22 and 33% of baseline tumor volume. Primary endpoints included recommended phase II dose(s) identification and DLT. Secondary endpoints included global safety profile assessment, liver function by Child-Pugh score (CPS), AST to Platelet Ratio Index (APRI), and response rate (mRECIST/RECIST v1.1).

Results: Four dose escalation levels are finalized (n = 17): 6 pts at 10% (2 SBRT doses tested due to organ constraints), 4 pts at 15 and 22% (due to fiducial displacement and ILI site shift) and 3 pts at 33%. No NBTXR3 related DLTs were observed. Related AEs observed: one malaise (G2, 10%); 2 abdominal pain, (G3, 15%); one bilateral pleural effusion (G1, 22%), one bile duct stenosis (G3, 22%) with associated disease recurrence and SBRT; one fatigue (G1, 33%). There were no clinically meaningful changes to CPS or APRI and CT-scan demonstrated absence of NBTXR3 in surrounding healthy tissues. In 7 evaluable HCC pts, best mRECIST target lesion responses were: 3 CR, 4 PR. In 5 evaluable mets pts, best target lesion responses were: 2 PR, 1 SD, 2 PD.

Conclusions: NBTXR3 was well tolerated and showed preliminary anti-tumor activity, supporting a protocol amendment to evaluate an additional NBTXR3 dose level (42%). This innovative approach has the potential to address an unmet medical need in pts with unresectable primary or metastatic liver lesions.

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