First-in-class hafnium oxide nanoparticles NBTXR3 in the treatment of liver cancers.

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Abstract Disclosures

Abstract:

Background: Hafnium oxide nanoparticles, NBTXR3, increase the effect of radiotherapy (RT) by enhancing local energy dose deposit within tumor cells, resulting in increased cell death compared to the same dose of RT alone. NBTXR3 efficacy was demonstrated in a phase II/III study in soft tissue sarcoma (NCT02379845) and is currently evaluated in other solid tumors including liver cancers. The use of this radio enhancer is particularly relevant in liver cancer management, a difficult to treat heterogenous population, due to the presence of underlying liver dysfunction. **Methods:** Phase I/II study of NBTXR3 activated by RT in patients (pts) with HCC (with/without portal vein tumor thrombus) or liver metastasis (mets) [NCT02721056]. The dose escalation part followed a 3+3 design with tested dose levels equivalent to 10%, 15%, 22% and 33% of baseline tumor volume. Patients were treated with a single intralesional injection (ILI) of NBTXR3 followed by Stereotaxic Body RT (SBRT: 45 Gy/3 fractions/5 to 7 days). Determination of recommended dose(s) and early dose limiting toxicities (DLT) were primary endpoints. 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:** The 4 levels of ILI dose escalation were finalized (n = 17): 6 pts at 10% (2 SBRT doses tested due to organs

constraints), 4 pts at 15% and 22% (due to fiducial displacement and ILI shift) and 3 pts at 33% were included. ILIs were successful and SBRT was delivered as planned with no observed DLT or NBTXR3-related SAE at all levels. Only one grade 1 AE (fatigue) related to NBTXR3 was reported at dose level 33%. No relevant change of CPS or APRI was observed over time. Among 7 evaluable HCC pts the best target lesion responses by mRECIST were: 3 CR and 4 PR and among 5 evaluable mets pts: 2 PR, 1 SD and 2 PD. **Conclusions:** This study demonstrated the feasibility and good tolerance of the first in class NBTXR3 ILI. These results have supported a protocol amendment adding a higher dose of NBTXR3 (42% of the tumor volume). This innovative approach might constitute a valuable solution for patients with unresectable liver tumors and liver dysfunction. Clinical trial information: NCT02721056