Title

Phase I/II trial: NBTXR3 activated by SABR for patients with advanced HNSCC or NSCLC in combination with an anti-PD1 treatment

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Abstract body:

Hafnium oxide nanoparticles (NBTXR3) increase radiation dose deposit within the cancer cells when activated by radiotherapy (RT). NBTRX3 activated by RT is currently evaluated in 7 clinical trials including a phase I/II study in locally advanced HNSCC elderly patients [NCT01946867]. So far, no dose limiting toxicities (DLTs) were observed. In addition, animal studies showed that NBTXR3+RT can induce an abscopal effect which was not observed with RT alone. These results led us to investigate the safety and the systemic effect of NBTXR3 activated by SABR in a more advanced population of HNSCC i.e. locoregionally recurrent or metastatic (to lung or liver) HNSCC as well as in metastatic NSCLC and liver metastasis patients in combination with anti-PD1 [NCT03589339].

Recent clinical studies have demonstrated the efficacy of anti-PD-1 in recurrent/metastatic HNSCC and upfront metastatic NSCLC patients. However, most patients with recurrent/metastatic HNSCC demonstrate innate (primary) resistance to checkpoint inhibition and do not respond to initial therapy and only a subset of metastatic HNSCC/NSCLC patients benefits from this treatment. There is thus an important unmet medical need for a curative treatment of this population. We hypothesized that intratumoral/intralesional injection of NBXTR3 in the tumor or in one metastasis in lung or liver, followed by SABR may be a powerful mechanism to convert the local immune microenvironment to a “hot” phenotype and thus help to reverse resistance to immune checkpoint inhibition.

We thus designed an open label Phase I/II, non-randomized clinical study of NBTXR3 activated by SABR in combination with approved anti-PD1 in patients with advanced HNSCC or NSCLC*. The primary objective of the phase I is to determine the maximum tolerated dose/s, the early DLTs and the recommended dose/s of NBTXR3. The primary objectives of the phase II part are complete response of target lesion/s by RECIST v1.1 for the locoregional recurrent group, objective Response Rate by RECIST v 1.1 for the metastatic group and incidence of adverse events in both groups with a complete safety assessment.

The first-in-class NBTXR3 mode of action was demonstrated in a phase II/III randomize trial in locally advanced soft tissue sarcoma patients. NBTXR3 activated by RT showed a significant superiority meeting both primary and secondary endpoints and clinical benefits compared to RT alone [NCT02379845].

*Metastatic patients must have received an approved anti-PD1 with SD for at least for 12 weeks or with confirmed PD at 12 weeks