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Title: Elderly patients: NBTXR3 as a novel treatment option in locally advanced HNSCC

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Purpose/Objectives

As the incidence of head and neck squamous cell carcinoma (HNSCC) increases with age, elderly patients represent 25% of the affected population with an expected increase in the next 20 years. Being more vulnerable to treatment-induced toxicities, the elderly cannot be treated like younger patients, hence requiring innovative therapies. A new treatment option is currently clinically evaluated, NBTXR3. These first-in-class hafnium oxide nanoparticles are activated by radiotherapy and can physically destroy cancer cells. A phase I study [NCT01946867] was implemented for the treatment of locally advanced HNSCC of the oral cavity and oropharynx, focused on elderly patients (65 years and older) not eligible for cisplatin, the non-surgical standard of care, or intolerant to cetuximab.

Materials/Methods

Currently, 14 patients (pts) eligible for exclusive radiotherapy were included. A single intratumoral (IT) injection of NBTXR3 was followed by intensity-modulated radiation therapy (IMRT; 70 Gy/35 fractions/7 weeks), and a follow-up period until disease progression or study cut-off date. The study was designed as a 3 + 3 escalation dose with tested dose levels at 5%, 10%, 15% and 22% of baseline tumor volume. Primary endpoints included the determination of recommended dose and early dose limiting toxicity (DLT). Presence of NBTXR3 in the surrounding healthy tissues and efficacy per RECIST 1.1 response are also evaluated.

Results

No early DLT nor SAE related to NBTXR3 or injection procedure were observed for volume dose levels 5% (3 pts), 10% (3 pts), 15% (5 pts) and 22% (3 pts). So far, one AE (asthenia, grade 1) related to NBTXR3 was reported. Additionally, three AE related to the injection procedure (tumor hemorrhage, grade 1; oral pain, grade 2; asthenia, grade 1) occurred at 15% and 22%.

The injection feasibility was confirmed for all patients, and persistence of NBTXR3 over time and absence of leakage in the surrounding tissues were verified by CT scan comparison between post IT injection and post radiation images in evaluable patients.

For 5 out of 8 patients treated with NBTXR3 at doses >10%, the best response observed was a complete response (RECIST 1.1, local assessment).

Conclusions

Even at the highest doses, NBTXR3 is associated with a positive safety profile. Recruitment in the fourth and last dose level at 22% is ongoing. Preliminary results tend to highlight NBTXR3 benefit as a novel treatment option for elderly patients in locally advanced HNSCC. Considering the challenges brought by the population of interest, this study could lead to new perspectives in the support of frail patients with advanced age. This study answers a major medical need, as most HNSCC clinical trials do not focus on elderly patients.

In parallel, NBTXR3 is evaluated in 5 other clinical trials, including a phase II/III in soft tissue sarcoma (STS) [NCT02379845] and phases I/II for prostate [NCT02805894], liver [NCT02721056] and rectum cancers [NCT02465593].

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