TITLE: NBTXR3, an innovative treatment option for elderly, frail, head and neck squamous cell carcinoma patients: a phase I trial.

Authors:

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Rationale:

In the treatment of head and neck squamous cell carcinoma (HNSCC), elderly and frail patients (pts) are ineligible for chemoradiation with cisplatin, the non-surgical standard of care. Consequently, innovative research tends toward a new treatment option, NBTXR3. These first-in-class hafnium oxide nanoparticles are activated by radiotherapy and physically destroy cancer cells. They are currently evaluated in a phase I clinical trial [NCT01946867] for locally advanced HNSCC in the population of interest.

Materials and Methods:

So far, 12 pts, aged over 70, with stage III or IV HNSCC of the oral cavity or oropharynx, ineligible for surgery and for cisplatin, but eligible for exclusive radiotherapy were included. NBTXR3 was injected on Day 1, as a single intratumoral (IT) injection, followed by IMRT (70 Gy / 35 fractions / 7 weeks) on Day 2, with a follow-up of 24 months. Tested dose levels were by a 3+3 design at 5%, 10%, 15% and 22% of baseline tumor volume. Determination of the Recommended Doses and the early Dose Limiting Toxicities (DLT) were the primary endpoints and secondary objectives included IT residency (presence of leakage) and efficacy per RECIST 1.1 response.

Results:

No grade 3 or 4 adverse events (AE) related to NBTXR3, nor DLT were observed for volume dose levels 5% (3 pts), 10% (3 pts), 15% (5 pts), and 22% (1 pt). Two AE (tumor hemorrhage, grade 1, and oral pain, grade 2) related to intra-tumoral injection were reported at 15% and 22%. CT scan comparison between 24h post IT injection and post 7 weeks-radiation did not highlight any leakage of NBTXR3 in the surrounding tissues, and confirmed its persistence over time. 7 complete responses (CR) out of 11 (1 pt was not evaluable) were observed, mostly at the higher doses levels: 10% (2 pts), 15% (4 pts), 22% (1 pt). Among these 7 pts, at the data lock point, 6 CR persisted after 3 to 10 months of follow-up.

Conclusion:

NBTXR3 is safe and well tolerated even at the highest tested doses. Preliminary efficacy analysis suggests a promising perspective for the treatment of HNSCC in the elderly, with confirmed CR. These findings are consistent with preliminary outcomes from clinical trials in other oncological indications, supporting that NBTXR3 might be efficient at enhancing radiotherapy's efficacy in many types of solid tumors.