exhibiting a purely local failure and 18 (50%) having concomitant local and distant failure. Patients with greater total metabolic tumor volume had an increased risk of treatment failure (HR 2.0; 95%CI 1.0-3.9, p=0.039). There was no difference in treatment failure rates when comparing tumor histology or extranodal involvement.
Of the 469 pretreatment disease sites, most (71%) continued to demonstrate a complete response at time of treatment failure. Lesion-specific factors associated with a greater risk of local failure included increased SUV max (p< 0.001), cross-sectional area (p <0.001), metabolic volume (p = 0.001), as well as the presence of necrosis (HR 2.0; 95% CI 1.05-3.81, p=0.035) and clustered lesions (HR 2.5; 95% CI 1.78-3.52, p<0.001). There was no difference in local failure rates in nodal vs. extranodal disease (p=0.65).

Conclusion

CAR T cell therapy patients with an increased tumor burden are more likely to experience disease progression. Furthermore, individual disease sites that are 1) larger, 2) hypermetabolic, or 3) necrotic are most likely to experience local failure. By identifying which patients, and furthermore, which pretreatment disease sites are most likely to fail, we may begin to consider incorporating local bridging treatments, such as radiotherapy, to high-risk sites to improve the efficacy of CAR T.

OC-0560 RT-activated hafnium oxide nanoparticles in cisplatin-ineligible locally advanced HNSCC patients

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Purpose or Objective

Elderly and frail patients (pts) with head and neck squamous cell carcinoma (HSNCC) remain a challenging population to manage due to the lack of evidence-based recommendations. Despite representing approximately 20% of the HNSCC population no consensus exists on the optimal treatment for these pts with locally advanced (LA) disease, vulnerable to current standard of care treatment-induced toxicities. New approaches are thus needed to improve clinical outcomes without adding toxicity. NBTXR3 hafnium oxide nanoparticles injected intratumorally may represent such an option. Otherwise inert, this first-in-class radioenhancer augments the radiotherapy (RT) dose within tumor cells when activated by RT, increasing tumor cell death compared to RT alone. The results presented here demonstrate the feasibility and safety of NBTXR3 activated by RT in elderly patients, a population with few therapeutic options.

Material and Methods

Patients with Stage III-IV LA HNSCC of the oropharynx or oral cavity ineligible for platinum-based chemoradiation received a single intratumoral injection of NBTXR3 and intensity modulated radiation therapy (IMRT; 70 Gy/35 fractions/7 weeks). This is a 3+3 design dose escalation study to test NBTXR3 dose levels equivalent to 5, 10, 15, and 22% of baseline theoretical tumor volume, followed by a dose expansion. Primary endpoints include Recommended Phase 2 Dose (RP2D) determination and early dose limiting toxicities (DLT). NBTXR3 presence in surrounding healthy tissues and anti-tumor activity (RECIST 1.1) were also evaluated.

Results

Enrollment was completed at all dose levels: 5% (3 pts), 10% (3 pts), 15% (5 pts), and 22% (8 pts). No early DLT or SAE related to NBTXR3 or injection were observed. One G1 AE (asthenia; 22%) related to NBTXR3 and four AEs (G2 oral pain, G1 tumor hemorrhage, asthenia, and injection site hemorrhage) related to injection were observed. RT-related toxicity was as expected with IMRT. The RP2D was determined to be 22% by the DSMB. CT-scan assessment demonstrated localization of NBTXR3 intratumorally without presence in surrounding healthy tissues. At a median follow-up of 231 days, 9/13 (2 unconfirmed) evaluable pts receiving doses ≥10%, achieved a complete response of the treated tumors. The final dose escalation safety and efficacy results will be presented herein.

Conclusion

NBTXR3 was well tolerated at all tested doses and demonstrated preliminary anti-tumor activity. The dose expansion part at the RP2D is ongoing. These results highlight the potential of NBTXR3 as a novel treatment option for elderly pts with LA HNSCC and address an unmet medical need.

OC-0561 Nano-Rad first in man study: AGuIX nanoparticles as radiosensitizing agent for radiotherapy

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Purpose or Objective

The occurrence of multiple brain metastases is a critical evolution of many cancers with a major impact on overall survival. A new gadolinium-based nanoparticle, AGuIX, has recently demonstrated its efficacy as a radiosensitizer and MRI contrast agent in several preclinical studies. The objective of this first in man study named Nano-Rad (NCT02820454) is to determine the feasibility and tolerance of intravenous injection of AGuIX in combination with radiotherapy.

Material and Methods

A monocentric, open-label, 3+3 phase I clinical trial design was used to evaluate the maximum tolerated dose of escalating dose of AGuIX nanoparticles (15, 30, 50, 75 and