684 NBTXR3 ACTIVATED BY RADIOTHERAPY IN COMBINATION WITH NIVOLUMAB OR PEMBROLIZUMAB IN PATIENTS WITH ADVANCED CANCERS: RESULTS FROM AN ONGOING DOSE ESCALATION PHASE I TRIAL (STUDY 1100)

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Background Immune checkpoint inhibitors (ICIs) have changed how cancer patients are treated, still, most patients ultimately develop resistance. Overcoming or preventing this resistance is a major clinical challenge. NBTXR3, when injected intratumorally, has been shown preclinically to enhance RT energy deposition, subsequent tumor cell death, and tumor antigen release to effectively expand T-cell repertoire. NBTXR3/RT thus has the potential to trigger both a local and a systemic immune response to help improve ICI treatment.

Methods Study 1100 is a phase I dose escalation/expansion trial [NCT03589339] evaluating NBTXR3 activated by stereotactic body radiotherapy (SBRT) and followed by anti-PD-1 therapy (either nivolumab or pembrolizumab) in 3 cohorts of patients (pts) with advanced solid tumors. Pts are either resistant to prior ICI or naïve. Escalation cohorts were defined by site of injection: head & neck (H&N) lesions, lung, or liver metastases. SBRT was delivered as per standard practice. The primary objective of the escalation phase was to determine the NBTXR3/RT/anti-PD-1 recommended phase 2 dose for each cohort. Secondary objectives were feasibility, safety, and antitumor efficacy (objective responses).

Results 28 patients have been treated in the dose escalation phase in two escalating dose-levels for each cohort: 11 H&N, 10 lung, and 7 liver. Median age was 66.5 years. Two DLTs occurred in 1 pt at the first dose level in the H&N cohort. Grade $\geq$ 3 NBTXR3-related AEs occurred in 4 (14.3%) pts. SBRT+ ICI safety profile was in line to previously reported. Among 20 pts evaluable for efficacy, overall tumor responses were observed in 8/20 (40%) with disease control observed in 15/20 (75%) respectively, including durable complete responses. Objective tumor responses were observed in patients resistant to prior ICI. Updated safety and efficacy results will be presented.

Conclusions NBTXR3/RT/anti-PD-1 is feasible, predictable and safe in pts with recurrent HNSCC, lung, or liver metastases. The RP2D was defined. This new treatment shows promising early signs of efficacy. Subgroup analyses are ongoing and might help improve further results in specific populations. Overall, these results support evaluation of NBTXR3/RT/anti-PD-1 in the ongoing enlarged expansion phase.

Trial Registration NCT03589339

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