Abstracts

Background Peritoneal surface dissemination (PSD) of gastrointestinal and ovarian cancers carries a poor prognosis. Although cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy has emerged as a treatment option for this patient population, only a minority of patients benefit from this approach. This finding highlights the need for novel approaches to this disease. Previous data have shown that the local treatment of orthotopic tumors in syngeneic murine models with the oncolytic virus talimogene laherparepvec (TL) converts 'cold' immunosuppressive tumor microenvironments into 'hot' immune microenvironments that support the regression of tumors. We hypothesize that intraperitoneal (IP) delivery of TL will be safe and tolerable and demonstrate clinical activity in patients with PSD of gastrointestinal (GI) and ovarian cancers.

Methods We are conducting the TEMPO Trial (NCT03663712), a non-randomized, open-label Phase I trial of IP TL in patients with stage IV PSD from GI or ovarian tumors enrolled at University of Illinois College of Medicine at Chicago, Duke Cancer Institute, and Wake Forest University School of Medicine. There will be two stages in this study, a Dose Escalation Cohort, and a Dose Expansion Cohort. In the Dose Escalation Cohort, three subjects will be enrolled at the starting dose of 4 × 106 PFU, and the dosing will continue in a standard '3+3' dose escalation scheme. If the starting dose is tolerated, higher doses of 4 × 107 and 4 × 108 PFU will be evaluated. Once the MTD is determined, six subjects will be enrolled in the Dose Expansion Cohort at the MTD. All subjects will be dosed with IP TL once every two weeks for up to 4 doses (in addition to the initial seroconversion dose). The primary objective is to evaluate the toxicity profile. The statistical analyses will be only descriptive and performed on the intent to treat, per protocol, and safety populations.We hypothesize that IP TL leads to coordinated interactions between resident peritoneal innate and adaptive immunity. We will delineate these interactions by evaluating peritoneal exudates to assess a) treatment-related changes in peritoneal cytokine levels using multiplex cytokine analysis and b) resident peritoneal immune cell phenotype and function with flow cytometry methods. Plasma and urine fluid samples will be analyzed for viral load.

Results N/A

Conclusions This study will test the safety, tolerability, and preliminary clinical activity of IP TL; the results will be relevant to inform future investigations of local oncoimmunotherapies in patients with PSD, a highly unmet need population that currently has limited therapeutic options.

Acknowledgements N/A

Trial Registration Registered at clinicaltrials.gov- https://clinicaltrials.gov/ct2/show/NCT03663712. The identifier is NCT03663712

Ethics Approval This study was approved by the Institutional Review Boards at the University of Illinois College of Medicine at Chicago, Duke Cancer Institute, and Wake Forest University School of Medicine.

Consent N/A

REFERENCES

1. N/A

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410 PHASE I STUDY OF INTRATUMORAL NBTXR3 IN COMBINATION WITH ANTI-PD-1 IN PATIENTS WITH ADVANCED CANCERS

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Background Cancer immunotherapies have shown promising clinical outcomes; however, the majority of patients are non-responders or will develop resistance during the course of treatment. One of the current challenges is to increase the response rate to immune checkpoint inhibitors (ICIs). Combining immunotherapy with radiation therapy (RT) is emerging as a valuable strategy to prime the immune response. However, RT dose and ultimate efficacy are limited by toxicity related to exposure of healthy tissues. First-in-class radioenhancer NBTXR3, administered by one-time direct intratumoral injection, is designed at the nanoscale to increase RT dose deposit with subsequent increase in tumor cell killing, without increasing toxicity to normal tissue. Preclinical and early clinical data suggest NBTXR3/RT can prime the immune system and act as an in situ vaccine leading to an anti-tumor immune response, producing both local and systemic (abscopal) effects. We hypothesize NBTXR3/RT in combination with anti-PD-1 (NBTXR3/RT/PD-1), will act synergistically to increase the proportion of ICI responders or convert ICI non-responders to responders.

Methods A multicenter, open-label, phase I trial [NCT03589339] evaluating safety and tolerability of NBTXR3/RT/PD-1 in three cohorts: (1; H&N) Locoregional recurrent or recurrent and metastatic head and neck squamous cell carcinoma (HNSCC) amenable to re-irradiation of the HN field, (2; lung) lung or (3; liver) liver metastases from any primary cancer eligible for approved anti-PD-1 treatment. NBTXR3 injected volume is based on a percentage of baseline tumor volume. Stereotactic body RT (SBRT) is delivered as per standard practice. The primary objective is to determine NBTXR3/RT/PD-1 recommended phase II dose in each cohort. Secondary objectives are to evaluate anti-tumor response (objective response rate), safety and feasibility of NBTXR3 injection, and NBTXR3 body kinetic profile.

Results To date 6 patients have been treated: 3 in H&N (2 anti-PD-1 naïve) and 3 in lung (all anti-PD-1 non-responders. No DLT or SAE has been observed. Grade 2 nausea related to NBTXR3 or injection procedure was observed in H&N. 2 H&N patients and 3 lung patients have completed RT and initiated anti-PD-1 treatment. RT-related safety profile was as expected. Tumor shrinkage was observed in 1 anti-PD-1 naive and 2 anti-PD-1 non-responders and additional preliminary efficacy and updated safety results will be presented.

Conclusions To date, NBTXR3 administration activated by SBRT in combination with anti-PD-1 treatment has been safe and well tolerated in patients with advanced cancers. Promising early signs of efficacy in anti-PD-1 naïve, as well as in patients having progressed on previous anti-PD-1 therapy will be presented.

Trial Registration NCT03589339

Ethics Approval This study was approved by local institution's review board

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