



**Abstract 407 Figure 1** Mean change from baseline in percentage of Ki67+ T-cell expression in peripheral blood during first two cycles of XmAb20717

ence of pancreatic metastases) and immune-mediated myocarditis (Grade 4) that contributed to respiratory failure. A complete response was reported as the best overall response for 1 patient (melanoma); partial responses were reported for 5 patients (2 melanoma, 2 NSCLC, 1 ovarian). The objective response rate was 13% overall and 21% at 10 mg/kg (6/46 and 6/29 evaluable patients, respectively). All responders had prior CI exposure. Responses were observed only at 10 mg/kg and, within the 10 mg/kg group, appeared to correlate with higher peak serum concentration and area under the curve.

**Conclusions** XmAb20717 induced T-cell proliferation in peripheral blood consistent with dual-checkpoint blockade. Preliminary data indicate XmAb20717 was generally well-tolerated and associated with evidence of antitumor activity in CI-pretreated patients with various types of advanced solid tumors.

**Trial Registration** NCT03517488

**Ethics Approval** The study was approved by each institution's IRB.

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**PHASE I, FIRST-IN-HUMAN TRIAL EVALUATING BI 1387446 (STIMULATOR OF INTERFERON GENES [STING] AGONIST) ALONE AND COMBINED WITH BI 754091 (ANTI-PROGRAMMED CELL DEATH [PD]-1) IN SOLID TUMORS**

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**Background** Activation of the STING pathway in intratumoral immune cells leads to increased type I interferon production, promoting recruitment and priming of T-cells against tumor antigens, and providing anti-tumor activity.<sup>1</sup> Intratumoral administration of STING agonists has resulted in notable therapeutic activity in animal models.<sup>1</sup> STING agonists have also shown clinical activity in patients, which was more pronounced when combined with an anti-PD-1 antibody.<sup>2,3</sup> BI 1387446 potently and highly selectively activates the STING pathway; BI 754091 is a humanized IgG4 anti-PD-1 monoclonal antibody. Intratumoral administration of BI 1387446

resulted in tumor regression, and enhanced the activity of anti-PD-1 therapy in syngeneic tumor models.<sup>4</sup>

**Methods** NCT04147234 is a first-in-human, Phase I, open-label, multicenter trial of BI 1387446 in patients aged  $\geq 18$  years with advanced, unresectable and/or metastatic malignant solid tumors. Patients (up to  $\sim 122$ ) will be enrolled from  $\sim$ six sites across Europe and the USA. The main objectives are to characterize safety and determine the maximum tolerated dose (MTD) for BI 1387446  $\pm$  BI 754091. BI 1387446 will be administered intratumorally at increasing doses as monotherapy in Arm A, and in combination with BI 754091 (240 mg every three weeks, intravenously) in Arm B. In both arms, BI 1387446 will be administered in superficial lesions. In a potential third arm, Arm C, BI 1387446 will be administered in deep/visceral lesions in combination with intravenous BI 754091. Dose escalation will be guided by a Bayesian Logistic Regression Model with overdose control. For trial eligibility, patients must have exhausted standard treatment options, have  $\geq 1$  tumor lesion suitable for injection,  $\geq 1$  additional tumor lesion amenable to biopsy, and ECOG performance status of 0/1. Treatment will continue until progressive disease, unacceptable toxicity, other withdrawal criteria, or a maximum treatment duration of 34 cycles (for cycle 19 and onwards, administration of BI 1387446 is applicable for patients with a partial response), whichever occurs first. Primary endpoints are the MTD based on number of dose-limiting toxicities (DLTs), and number of patients with DLTs in the MTD evaluation period. Secondary endpoints are objective response based on RECIST 1.1, and best percentage change from baseline in size of target and injected lesions. Paired pre- and post-treatment biopsies of injected- and non-injected lesions and peripheral blood will be collected to assess pharmacodynamic changes associated with treatment. The trial is currently open for recruitment.

**Results** N/A

**Conclusions** N/A

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**Trial Registration** NCT04147234

**Ethics Approval** Not applicable.

**Consent** Not applicable.

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**A PHASE I TRIAL OF TALIMOGENE LAHERPAREPVEC FOR THE TREATMENT OF PERITONEAL SURFACE MALIGNANCIES (TEMPO)**

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**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  $4 \times 10^6$  PFU, and the dosing will continue in a standard ‘3+3’ dose escalation scheme. If the starting dose is tolerated, higher doses of  $4 \times 10^7$  and  $4 \times 10^8$  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)- <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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## 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 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 naïve 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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