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 PD 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 oncolimmunotherapies 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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