LUMINOS-103: A BASKET TRIAL EVALUATING THE SAFETY AND EFFICACY OF PVSRIPO AND PVSRIPO IN COMBINATION WITH ANTI-PD-1/L1 CHECKPOINT INHIBITORS IN PATIENTS WITH ADVANCED SOLID TUMORS

¹Brant Inman, ²Matthew Milowsky, ³Raj Pruthi, ⁴Marshall Posner, ⁵Melissa Polasek, ⁶Shannon Morris*, ⁷Lori Mixson, ⁸Kristin Orr, ⁹Elizabeth Woodson, ¹⁰Andrea Kelly, ¹¹Garrett Nichols, ¹²Arjun Balar. ¹Duke University Medical Center, Durham, NC, USA; ²University of North Carolina Lineberger, Chapel Hill, USA; ³University of California San Francisco, San Francisco, CA, USA; ⁴Icahn School of Medicine at Mount Sinai, New York, NY, USA; ⁵Istari Oncology, Morrisville, NC, USA; ⁶New York University Langone Health, New York, NY, USA

Background PVSRIPO, a novel intratumoral viral immunotherapy, infects cells via CD155, which is widely expressed on solid tumors and antigen-presenting cells (APC). Infection is lethal in malignant cells, but a unique, activating, nonlethal infection of local APCs yields type-I/III interferon (IFN)-dominant inflammation with subsequent anti-tumor T-cell priming and activation resulting in anti-tumor efficacy. In preclinical models, PVSRIPO-dependent inflammation upregulated the PD-1/L1 pathway, and greater anti-tumor response was observed with PVSRIPO + anti-PD-1/L1 (α PD-1/L1). Promising clinical activity with PVSRIPO monotherapy was observed in patients with recurrent glioblastoma and advanced α PD-1-refractory melanoma.^{1 2} Collectively, these results warrant further clinical investigation of PVSRIPO $\pm$ α PD-1/L1.

Methods LUMINOS-103 (NCT04690699) is a phase (Ph) 1/2, open-label, multi-center, single-arm basket trial evaluating repeat administration of PVSRIPO $\pm$ α PD-1/L1 in adults with solid tumors. Trial objectives are to assess the safety and tolerability of PVSRIPO monotherapy in each cohort in Ph 1 and the safety, tolerability, and antitumor efficacy of PVSRIPO + α PD-1/L1 in each cohort in Ph 2. The first two study cohorts include patients with muscle-invasive bladder cancer being treated in the neoadjuvant setting (A) and patients with metastatic bladder cancer being treated in the 1st/2nd line setting (B); these cohorts have been described previously.³ Cohort C includes patients with resectable, locally advanced head and neck squamous cell carcinoma (HNSCC) being treated in the neoadjuvant setting; Cohort D includes patients with recurrent/metastatic HNSCC with a PD-L1 Combined Positive Score ≥ 1 being treated in the 1st line setting. Eligibility: HNSCC patients must have histologically or cytologically-proven SCC of the oral cavity, oropharynx, hypopharynx, or larynx. All patients must have prior and boosted PV immunization and tumors amenable to injection and biopsy. Key exclusion criteria: Requirement for oxygen supplementation, systemic or intratumoral therapy ≤ 6 months prior to the first dose of study drug, CNS metastases requiring immediate treatment, systemic immunosuppressive medications ≤ 4 weeks prior to the first dose of study drug, and severe active comorbidities. Patients who are HIV+, HBV+ or HCV+ are eligible provided they meet certain criteria. Primary endpoints include safety (all cohorts), tolerability (all cohorts), surgical complication rate (A, C), pathologic treatment effect/response (A, C), and objective response rate (B, D). Secondary endpoints include overall survival (all cohorts), pathologic downstaging and relapse-free survival (A, C), duration of response and progression-free survival (B, D), and assessment of tumor/blood biomarkers (all cohorts).

Trial Registration ClinicalTrials.gov: NCT04690699

REFERENCES

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Ethics Approval The study has been approved by the central Institutional Review Board (IRB), WCG (Study# 1310534) and will be approved by all local IRBs and other required committees, as applicable. The study will be conducted in accordance with the provisions of the Declaration of Helsinki and the Good Clinical Practice guidelines of the International Conference on Harmonization. All patients will provide written informed consent.

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