A PHASE I SAFETY AND TOLERABILITY STUDY OF VAXINIA (CF33-HNIS), A NOVEL CHIMERIC ONCOLYTIC POXVIRUS, ADMINISTERED INTRATUMORALLY OR INTRAVENOUSLY IN ADULTS WITH METASTATIC OR ADVANCED SOLID TUMORS

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Background CF33 is a novel chimeric oncolytic poxvirus, encoding the human Sodium-Iodide Symporter (hNIS) transgene. The transgene is inserted in place of the viral thymidine kinase gene at the J2R locus, allowing in situ replication in normal cells. The engineered virus selectively replicates in tumor cells and leads to tumor cell lysis, releasing tumor- and virus-associated antigens and stimulating antitumor immunity. The expression of the transgene hNIS with CF33 allows for imaging of the CF33 virus with SPECT. In preclinical models of colon, lung, and pancreatic cancer, CF33-hNIS demonstrated a robust anti-tumor response and enhanced expression of PD-L1 in tumor cells.1-3 The combination of CF33-hNIS + anti-PD-L1 therapy showed a synergistic tumor killing, and increased survival in a preclinical triple negative breast cancer (TNBC) model.4 This study will evaluate the safety and recommended Phase 2 dose (RP2D) of intratumoral (IT) and intravenous (IV) CF33-hNIS alone or in combination with pembrolizumab in advanced or metastatic solid tumors, after progression following ≥2 prior lines of therapy.

Methods This is a dose-escalation, multi-center phase 1 study evaluating the safety of CF33-hNIS administered IT or IV alone, or in combination with pembrolizumab in patients with advanced or metastatic solid tumors (NCT05346484). CF33-hNIS is administered in 21-day cycles on C1D1 and C1D8; then D1 of each cycle thereafter. Pembrolizumab begins C2D1 for the combination groups and is administered Q3W. Up to 100 patients will be enrolled across study groups. Key inclusion criteria: age ≥ 18 years; ECOG 0–2; confirmed advanced or metastatic solid tumor; progression after ≥ 2 prior lines of therapy; ≥ 1 measurable lesion. Key exclusion criteria: previous treatment with an oncolytic virus; systemic steroid treatment; uncontrolled brain/CNS metastases. The co-primary endpoints are safety and RP2D. Secondary endpoints include objective response rate, viral shedding titers, and level of tumor infection by CF33-hNIS. Response is determined according to RECIST v1.1 and iRECIST criteria. Patients may receive treatment until disease progression. The dose-limiting toxicity (DLT) window is 28 days for CF33-hNIS monotherapy and 42 days for combination treatment. The study began enrolling patients in March 2022; IV monotherapy cohorts 1–3; IT monotherapy cohorts 1–2; and IV combination cohort 1 have been completed without DLTs. IV monotherapy cohort 4, IT monotherapy cohort 3, IV combination cohort 2, and IT combination cohort 1 are currently enrolling in the US.

Trial Registration NCT05346484

REFERENCES

Ethics Approval The study has been approved by the Institutional Review Board/Independent Ethics Committee at each site. All study participants provide written informed consent before enrollment.

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