PERSONALIZED IMMUNOTHERAPEUTIC PLATFORM WITH EVIDENCE OF CLINICAL ACTIVITY IN GLIOBLASTOMA PROTECTS MICE AGAINST OVARIAN LIVER AND BLADDER CANCER TUMOR CHALLENGES

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Background Imvax is developing a novel personalized immunotherapeutic platform combining irradiated, patient-derived tumor cells and Insulin-Like Growth Factor Type-1 Receptor antisense oligonucleotide (IMV-001) in biodiffusion chambers (BDC; 0.1-micron pores). The combination product IGV-001 was recently evaluated in a newly diagnosed glioblastoma (GBM) phase 1b clinical trial. Median overall survival of highest exposure IGV-001-treated ‘Stupp-eligible’ patients was 38.2 months compared with 16.2 months in recent standard-of-care-treated patients (P=0.044). We have now found activity with the equivalent murine approach in multiple cancer models, highlighting the transformative potential of this immunotherapeutic platform beyond glioblastoma.

Methods We utilized the ID8-luciferase (-Luc) intraperitoneal ovarian cancer, the orthotopic Hepa1-6-Luc hepatocellular carcinoma model and orthotopic MBT-2 urothelial murine cancer models. BDCs containing saline or 1x10^6 IMV-001-treated tumor cells (hereon IOC-001, IHC-001, and IUC-001 respectively) were implanted in flanks of mice and explanted 48 h later, as per glioblastoma clinical protocol. Primary tumor challenge was conducted 28d after chamber implantation. Intra-mammary rechallenge in the Hepa1-6 model was conducted 102 days after orthotopic challenge alongside naive controls, since no primary controls were still alive. Mice were monitored for survival and tumor growth. Cytokine analysis and immunophenotyping were conducted.

Results 60% of IOC-001-treated mice survived to end of study at 58d post-tumor challenge, compared to only 19% of mice in the saline control group (MST=37d, P=0.004). Circulating IFN? was significantly higher in IOC-001-treated mice compared to controls on 1d post-tumor challenge (p<0.001) and trended higher in those receiving IHC-001 14d after tumor challenge. In the Hepa1-6 model, 50% of IHC-001-treated mice survived beyond 110d post-tumor (MST = 60.5d at end of study); Hepa1-6 intramammary rechallenge at 102d demonstrated durable systemic immunity in survivors. There were no survivors in the primary control group beyond 28d (MST = 18d; P=0.004). In the MBT-2 model, 42% of IUC-001-treated mice survived up to 90d post-tumor challenge (MST=33d at end of study); all control mice expired by 37d (MST=21d; P=0.0163). Low end of life bladder weights in surviving IUC-001-treated mice suggested minimal tumor burden. Further Immunological and Pathology data will be provided.

Conclusions These data support the durable antitumor activity of Imvax’s immunotherapeutic platform in multiple cancers beyond glioblastoma. Results suggest that efficacy is associated with a systemic immunological response, resulting in generation of Th1 antitumor cytotoxic T cells. Future studies are seeking additional biomarkers of response using phenotypic evaluation of T cell activation/exhaustion markers and Th1/Th2 responses.

REFERENCES