IGV-001

IGV-001 is a personalized, autologous cancer cell-based immunotherapy conceived to deliver a tumor-derived antigenic payload in the context of immunostimulatory signals to patients with glioblastoma (GBM). IGV-001 consists of patient-derived GBM cells treated with an antisense oligodeoxynucleotide against insulin-like growth factor 1 receptor (IGF1R) and placed in proprietary biodiffusion chambers (BDCs). The BDCs are then exposed to 5-6 Gy radiation and implanted at abdominal sites for ~48 hours. IGV-001 has previously been shown to be generally safe with promising clinical activity in newly diagnosed GBM patients.

Methods: Mouse (m) or human (h) variants of IGV-001 were prepared using GL261 mouse GBM cells or human GBM cells, respectively. BDCs containing vehicle or mIGV-001 were implanted in the flanks of C57BL/6 albino female mice in preventative and therapeutic experiments, optionally in combination with a programmed cell death 1 (PD-1) blocker. Bioactivity of the general approach was also measured against hepatocellular carcinoma Hepa 1-6 cells. Mice were followed for the growth of subsequently implanted or pre-existing tumors and survival. Draining lymph nodes from mice receiving mIGV-001 were immunophenotyped. mIGV-001 and hIGV-001 were analyzed for extracellular ATP and high mobility group box 1 (HMGB1) as indicators of immunogenic cell death (ICD), along with flow cytometric analysis of viability, surface calreticulin, and reactive oxygen species. Stress and cell death-related pathways were analyzed by immunoblotting.

Results: IGV-001 causes oxidative and endoplasmic reticulum stress in GL261 cells, resulting in a cytotoxic response that enables the release of antigenic material and immunostimulatory, ICD-associated molecules including ATP and HMGB1 from BDCs. Immunophenotyping confirmed that IGV-001 increases the percentage of dendritic cells, as well as effector, and effector memory T cells in BDC-draining lymph nodes. Consistent with these observations, preventative IGV-001 limited tumor progression and extended overall survival in mice intracranially challenged with GL261 cells, a benefit that was associated with an increase in tumor-specific T cells with effector features. Similar findings were obtained in the Hepa 1-6 model. Moreover, therapeutically administered IGV-001 combined with PD-1 delayed progression in GBM-bearing mice.

Conclusions: These results support treatment with IGV-001 to induce clinically relevant ICD-driven anticancer immune responses in patients with GBM [1)]

1)
Cultrara C, Uhl C, Kirby K, Abed Elrazaq E, Zellander A, Andrews DW, Scott CB, Galluzzi L, Exley MA, Zilberberg J. A biologic-device combination product delivering tumor-derived antigens elicits immunogenic cell death-associated immune responses against glioblastoma. J Immunother Cancer. 2023 Aug;11(8):e006880. doi: 10.1136/jitc-2023-006880. PMID: 37550054.

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