

# Early, encouraging data for glioblastoma treatment reported at ASCO

June 10 2022

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Glioblastoma (histology slide). Credit: Wikipedia/CC BY-SA 3.0

All of the newly diagnosed glioblastoma multiforme patients enrolled in a Phase 1 clinical trial at the University of Alabama at Birmingham have exceeded both their median and expected progression-free survivals. Two patients, to date, have exceeded their expected overall survival. Glioblastoma multiforme is the most aggressive type of cancer originating in the brain.

The data were presented at the 2022 American Society of Clinical Oncology Annual Meeting this month, and they highlight the intellectual

property INB-200—a proprietary drug-resistant immunotherapy, or DRI technology, using gamma-delta T [cells](#) and licensed from the UAB Research Foundation and two other institutions to the clinical-stage biopharmaceutical company IN8bio Inc.

The clinical trial is led by Burt Nabors, M.D., in collaboration with IN8bio. Nabors is a professor of Neurology at UAB and a senior scientist in the O'Neal Comprehensive Cancer Center. Gamma-delta T cells are a specialized population of T cells that possess unique properties, including the ability to differentiate between healthy and diseased tissue.

The open label study has fully enrolled the first two cohorts, and enrollment has initiated for Cohort 3, with additional clinical updates expected later in 2022, IN8bio announced in a [press release](#).

The Phase 1 trial tests for safety and durability. As of June 3, six patients had been dosed with INB-200, three in Cohort 1, each receiving a single dose, and three in Cohort 2, each receiving three doses, with the one additional patient in Cohort 2 still awaiting treatment, Nabors said in his poster session. There have been no treatment-related serious adverse events and no dose-limiting toxicities, cytokine release syndrome or neurotoxicity observed to date.

Adverse events have generally been tolerable, including grade 1/2 anemia, fevers, headaches, myelosuppression and nausea. Importantly, Nabors says, repeat dosing has not demonstrated a change in the toxicity profile. Patients in Cohorts 1 and 2 each received  $1 \times 10^7$  DRI gamma-delta T cells intratumorally on Day 1 of a 28-day treatment cycle for a total of one and three cycles respectively, along with standard of care chemotherapy with temozolomide, or TMZ.

The primary endpoint of this trial is safety, Nabors says. Secondary

endpoints include progression-free and overall survival.

DRI was developed based on two observations. First, when tumors are damaged by TMZ treatment, they develop stress-induced ligands on the [cell surface](#). Normally, these signals would incite the immune watchdog gamma-delta T cells to recognize and kill the damaged tumor cells, through their ability to differentiate between healthy and diseased tissue. However, the second observation reveals a problem—TMZ therapy kills lymphatic immune cells, including the gamma-delta T cells. This hinders the immune system's ability to leverage the TMZ-induced state of increased tumor vulnerability.

In DRI, peripheral blood mononuclear cells are collected from the patient. The gamma-delta T cells in that collection are purified, and then they are given a gene that makes them resistant to TMZ. Next, the drug-resistant gamma-delta T cells are expanded and reintroduced into the patient, concomitantly with TMZ chemotherapy. The resistant gamma-delta T cells should then be able to recognize the stress-induced ligands on the surface of TMZ-treated [tumor cells](#) and start to eliminate them.

"INB-200 continues to show promising activity in this challenging disease," said Trishna Goswami, M.D., chief medical officer of IN8bio. "All patients have exceeded their expected progression-free survival, and some have exceeded expected overall survival, even with poor prognostic factors such as MGMT unmethylated disease. We are particularly encouraged by patients in the repeated dose cohort who continue to do well, including one patient who has recently reached the one-year progression-free milestone, demonstrating durable stable disease and having returned to work."

MGMT, or O<sup>6</sup>-methylguanine DNA methyltransferase, is a prognostic biomarker used in glioblastoma; unmethylated tumors are unresponsive to treatment with chemotherapeutic agents such as TMZ.

Larry Lamb, Ph.D., former professor in the UAB Department of Medicine, and the scientific co-founder and current chief scientific officer at IN8bio Inc., helped develop the technology. IN8bio is a leader in gamma-delta T cell-product candidates for solid and liquid tumors, and INB-200 is the first genetically modified gamma-delta T cell therapy to enter clinical trials.

**More information:** Phase I study of drug resistant immunotherapy (DRI) with gene modified autologous  $\gamma\delta$  T cells in newly diagnosed glioblastoma multiforme (GBM) patients receiving maintenance temozolomide (TMZ), 2022 American Society of Clinical Oncology Annual Meeting.

Provided by University of Alabama at Birmingham

Citation: Early, encouraging data for glioblastoma treatment reported at ASCO (2022, June 10) retrieved 1 October 2023 from

<https://medicalxpress.com/news/2022-06-early-glioblastoma-treatment-asco.html>

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