When standard treatment fails: Jefferson to start unique immunotherapy for brain tumor patients

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Physicians at the Jefferson Hospital for Neuroscience (JHN), the region's only dedicated hospital, are tackling a particularly aggressive brain cancer that even surgery, chemotherapy and radiation often fail to treat with a promising new immunotherapy to attack a patient's tumor with their own cancer cells.

Starting as early as January, the first of 12 patients diagnosed with a malignant astrocytoma from a clinical trial led by David W. Andrews, M.D., Co-Director of the Brain Tumor Center of the Kimmel Cancer Center at JHN, will receive a "cancer Trojan horse" that could significantly shrink their tumor and possibly extend their life.

Considering patients with malignant astrocytomas rarely live past four months, a new treatment method is highly needed.

Here's how the immunotherapy works. The patient's cancer cells are removed during surgery and then treated with a type of therapy that turns off a growth factor receptor, which plays a critical role in cell survival. Without it, cancer cells die.

Those same cells are then placed in a diffusion chamber (to keep the cells from spreading back into the body), re-implanted back into the patient within a day and then retrieved up to two days later-this is what makes it stand out from other immunotherapies. During their time in the

body, those reinserted, extracted tumor cells communicate a message to the other tumor cells to die-and tell the body's immune system to help do it.

Looking Back to Move Forward

The clinical trial comes off the heels of successful animal research and a pilot study at Jefferson that uncovered its benefits 10 years ago. In that study, eight of 10 patients treated with the immunotherapy had significant tumor shrinkage, with regression on a MRI. One man survived for eight years with no further treatment.

"The preclinical work and our own pilot study tell us that this novel treatment could have a significant impact on these cancer patients who don't have many options," Dr. Andrews said.

In the procedure, a patient's glioma cells are treated with an antisense therapy known as "18-mer type 1 insulin-like growth factor receptor antisense oligodeoxynucleotide" before they are placed back in the body. Antisense therapy is designed to target genes involved in cancer progression and came in to use 10 years ago.

Jefferson's approach differs from other immunotherapy strategies, with many advantages, Dr. Andrew said. In this design, the antigen (the treated cancer cells) is released slowly over a 24-hour period enabling many waves of immune cells known as dendritic cells to take up antigen and migrate to nearby lymph nodes, leaving no antigens for replacement dendritic cells. The most popular current approach involves injecting the patient's own dendritic cells as a single episode of inoculation-a one and done.

"We feel that our approach will yield a very successful immunotherapy for these patients and perhaps other cancer patients as we open this

trial," he said. "The previous data and our new Phase I clinical trial will hopefully guide us towards new standards of care."

Dr. Andrews will lead the new Phase I clinical trial, which will investigate the safety and feasibility of the immunotherapy, as well as progress in the 12 patients.

Leading the Way

Jefferson, which has an annual tumor volume that exceeds 1,000 cases, making it the busiest brain tumor practice in the tri-state area, is known for its leading clinical trials. That includes participation in a national tumor bank devoted to the genetic analysis of brain tumors (the TCGA project) and a slew of trials testing new combinations of chemotherapy and radiation therapy for the treatment of a variety of brain cancers.

As authors and lead accruers to the Radiation Therapy Oncology Group (RTOG) trial 9508, Jefferson established a new world standard of care for brain metastases in an article published in Lancet in 2004.

Currently, Jefferson is a leading participant in two RTOG trials, one investigating the use of Temozolomide, or TMZ, and radiation therapy with and without the chemotherapy drug bevacizumab in patients with newly diagnosed glioblastomas. The other is the RTOG spinal axis radiosurgery trial, which randomizes patients between conventional radiation and radiosurgery for treatment of symptomatic spinal axis metastases.

Maria Werner-Wasik, M.D., an Associate Professor of Radiation Oncology, also co-directs the Brain Tumor Center at Jefferson.

Taking research to bedside is also part of Jefferson's overall mission for better patient care. Last year, in a game-changing article published in the

Journal of Clinical Oncology, physicians discussed a treatment technique and results that extended the survival of patients with glioblastoma beyond any previously published results. That treatment, which is now available at Jefferson, delivers stereotactic boost radiotherapy to patients with malignant gliomas and has nearly doubled median survival time from 14 to 24 months.

"It's vital to this institution to constantly pursue new treatments for these very serious tumors where current treatments often have minimal impact with modest survival benefit," Dr. Andrews said. "It's just one example of how the multidisciplinary team at Jefferson, which includes neurosurgeons, neuropathologists, neuro-oncologists, radiation oncologists, and neuro-immunologists, tackles brain tumor research. We strive to apply new knowledge to take better care of the hundreds and hundreds of patients that come through our doors."

Provided by Thomas Jefferson University

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