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'First-in-human' drug for malignant glioma available in experimental trial

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The UC Cancer Institute is one of three centers internationally approved to test an experimental drug's safety and pharmacokinetics and also assess the clinical benefit against recurrent malignant glioma, an aggressive form of brain cancer.

The "first-in-human" phase-1 trial is expected to enroll up to 60 patients at clinical sites in the United States and Australia.

Led by Olivier Rixe, MD, PhD, this experimental drug trial uses antibody-drug conjugate (ADC) technology, a new drug delivery concept currently being investigated in the treatment of various cancers. ADC molecules consist of an antibody linked to a specific cytotoxic drug that is intended to target, bind and disperse only in malignant cells.

The experimental drug (called AMG 595) is intended to target a specific mutated cell receptor (EGFRvIII) which exists on the surface of tumor cells in up to 30 percent of patients with malignant gliomas. Preliminary studies in animals have shown that ADC molecules can effectively find these specific cancer cells, then enter them and release an active cytotoxic agent with the aim of killing the tumor cells while minimizing damage to the surrounding normal tissue.

"This allows us to use a highly cytotoxic drug targeted to the cancer cells in the brain based on a specific cellular marker," explains Rixe, John and Gladys Strauss Chair in Cancer Research at the UC College of Medicine and director of the Experimental Therapeutics/Phase 1 Clinical Trials

Program. "Until recently, primary brain tumor patients have traditionally been excluded from phase-1 oncology studies, so finding drugs to effectively target and make real advances against this particular type of very aggressive cancer has been virtually impossible."

Patients who have failed first- and second-line therapies for malignant glioma may qualify to participate in this trial. Potential candidates will be screened for the EGFRvIII mutation using tumor samples obtained during their original surgery prior to enrollment.

Each patient's response to the treatment and overall health will be clinically monitored through blood, urine and imaging tests at regular intervals through the trial. Patients may be involved in the study for about eight months, including a pre-study assessment period and safety follow-up visit.

This is a paradigm shift in the way we look at gliomas, because the ADC model has the potential to revolutionize the way we deliver chemotherapy to cancer cells while sparing the surrounding healthy tissue." adds Rixe.

"Our goal is to improve the benefits-risk ratio of treatment by increasing anti-tumor activity while reducing the side effects of toxicity on healthy tissue."

The clinical trial of AMG 595, the experimental drug being used in the study, is sponsored by Amgen, a biotechnology company based in Thousand Oaks, California.

More than 22,000 people in the United States are diagnosed with a primary malignant brain tumor every year, according to the National Cancer Institute, and the majority of these are malignant gliomas which have a poor prognosis.

In 2011, the UC Cancer Institute partnered with the UC Neuroscience Institute's Brain Tumor Center to launch a translational research program aimed at understanding the biological mechanisms of cancer's spread to the brain and developing more effective ways to treat the condition.

Both programs are part of the Cincinnati Cancer Center, a joint cancer program involving the UC College of Medicine, Cincinnati Children's Hospital Medical Center and UC Health. The collaborative initiative brings together interdisciplinary research teams of caring scientists and health professionals to research and develop new cures, while providing a continuum of care for children, adults and families with cancer.

Provided by University of Cincinnati Academic Health Center