# New drug shrinks brain tumors, reduces seizures in children with tuberous sclerosis

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A drug used to treat advanced kidney cancer has now been shown to reduce a particular kind of brain tumor by at least 30 percent in patients with tuberous sclerosis-a genetic disease that causes tumors to grow on vital organs. In addition, patients in the study with active epilepsy had an 86 percent reduction in seizure frequency.

The phase 2 study of everolimus, marketed by Novartis under the tradename Afinitor, is published in the *New England Journal of Medicine*.

Based on the data from the Cincinnati Children's Hospital Medical Center study, the U.S. Food and Drug Administration on Oct. 29 granted accelerated approval of everolimus for patients with these tumors, known as subependymal giant cell astrocytomas, or SEGAs. Prior to FDA approval, surgery was considered standard therapy for SEGAs.

Every patient in the Cincinnati Children's study experienced a decrease in size of their tumor, and no patient required surgery for their tumor after treatment with everolimus, says David Franz, MD, a neurologist at Cincinnati Children's and the study's senior author.

Franz is a professor of pediatrics and neurology at the University of Cincinnati (UC) College of Medicine.

"This is a potential alternative to neurosurgical resection and the first targeted medical therapy for this disorder," says Franz. "Children and teens may not only avoid surgery and have improved seizure control, but they also may see improvement in other aspects of this disease, including a reduction or even elimination of hydrocephalus-a buildup of fluid inside the skull leading to increased intracranial pressure."

Seventy-eight percent of patients with tuberous sclerosis and astrocytomas achieved a 30 percent or greater reduction in tumor volume at six months after treatment, according to Franz, director of the Tuberous Sclerosis Clinic at Cincinnati Children's and associate director of clinical affairs in the division of neurology. Everolimus also was associated with a clinically relevant reduction in overall seizure frequency. Of 16 patients for whom EEG data were available at baseline and after six months, nine experienced decreases in seizure frequency.

Franz and his colleagues evaluated 28 patients with tuberous sclerosis as young as 3. Most were less than 18 years old. The median age was 11. Tumor volume was measured by MRI assessment of the brain.

Hydrocephalus is commonly associated with these tumors because they are located deep within the brain in spinal fluid pathways, or ventricles. The researchers found that evererolimus not only resolved hydrocephalus but also improved malformations of the brain tissue itself. These malformations, called parenchymal dysplasia or hamartomas, are found in the brains of 90 percent of tuberous sclerosis patients. Patients reported their quality of life, as measured by a validated quality of life and neuropsychological assessments,

improved at three months and six months.

The drug is an mTOR inhibitor that works by slowing down the mTOR protein that is overactive in patients with tuberous sclerosis. This same pathway is implicated in other cancers and neurological conditions, such as Alzheimer's disease, Parkinson's disease and Huntington's disease, as well as autism, making everolimus a potential candidate to treat these mTOR-associated disorders, according to Franz.

The Tuberous Sclerosis Clinic at Cincinnati Children's follows more than 600 children and adults with tuberous sclerosis and manages every aspect of the disorder with a multidisciplinary approach.

**More information:** Novartis provided drug and financial support for the study. In addition, Tarek Sahmoud, MD, PhD, one of the study's co-authors, is an employee of Novartis.

Provided by University of Cincinnati