

Potential Targeted Therapy for Pediatric Brain Cancer

A potential targeted therapy was identified by a team of Dana-Farber and Boston Children's Cancer and Blood Disorders Center researchers.

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An international team of clinical collaborators, led by physician scientists from [Dana-Farber/Boston Children's Cancer and Blood Disorders Center](#), performed a first-ever clinical test of the targeted therapy avapritinib in pediatric and young patients with a form of high-grade glioma. They found that the drug, already FDA-approved for certain adult cancers, was generally safe and resulted in tumor reduction visible on brain scans, as well as clinical improvement, in 3 out of 7 patients.

The study was published in [Cancer Cell](#).

Pediatric-type high-grade gliomas are currently incurable brain tumors with median survival times less than 18 months after initial diagnosis.

Avapritinib is a small molecule that crosses the blood-brain-barrier and targets platelet derived growth factor alpha (PDGFRA), which is overactive in some pediatric high-grade gliomas and leads to uncontrolled growth of cancer cells. The team is now designing a clinical trial of avapritinib treatment for newly diagnosed pediatric patients with PDGFRA-altered high-grade gliomas to evaluate it in a larger patient population.

"In a highly aggressive disease with no effective targeted treatment options currently available, we were excited to observe a radiographic and clinical response in a subset of mostly relapsed, highly treatment-refractory patients following monotherapy with an oral small-molecule inhibitor," says lead senior author [Mariella Filbin, MD, PhD](#), Jan Paradise Chair in Brain Cancer Research, co-director of the Brain Tumor Center of Excellence at Dana-Farber/Boston Children's Cancer and Blood Disorders Center and research director of the Pediatric Neuro-oncology Program at [Dana-Farber Cancer Institute](#).

Filbin's research team first identified that gene alterations activate PDGFRA in about 15% of pediatric high-grade glioma patients and contribute to the aggressive behavior of this disease, which is typically treated with surgery and radiation.

Efforts to target PDGFRA in high-grade glioma in the past were unsuccessful, most likely due to

suboptimal pharmaco-kinetics and -dynamics of the drugs used. Avapritinib is a next-generation, highly selective and brain penetrant PDGFRA inhibitor. In pre-clinical research, Filbin's team found that avapritinib reduced tumor growth in patient derived tumor models and animal models. Those results inspired them to collaborate with clinical partners at the University of Michigan and the Medical University of Vienna to treat patients a small group of patients with PDGFRA-altered high-grade glioma with avapritinib through a compassionate use program.

"It was truly inspiring to witness how our scientific research could be rapidly translated into clinical practice, directly benefiting patients," says co-first author Sina Neyazi, MD, a postdoctoral fellow in the Filbin lab. "This discovery was made possible by the dedication of our clinical collaborators and the immense trust from patients and their families."

Filbin's team will next investigate which genetic alterations in tumors can predict response to avapritinib treatment, aiming to develop personalized treatment. Additionally, the team is developing combination therapies that include avapritinib alongside other FDA-approved drugs to maximize therapeutic effects and prevent treatment resistance.

"As a physician it is heartbreaking to tell a family that their child's tumor has returned despite standard-of-care therapy," says Filbin. "Our latest findings with brain-penetrant PDGFRA inhibitor avapritinib are encouraging for a subset of our patients who have genetic alterations in PDGFRA, and I am hopeful it will pave the way for developing innovative combination treatments that include avapritinib."

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