According to Dr Patel, clinicians should keep in mind that zongertinib was approved for patients with unresectable or metastatic NSCLC and *HER2* tyrosine kinase domain mutations who have received prior systemic therapy.

"Additional cohorts of the Beamion LUNG-1 study evaluated the activity of zongertinib in previously untreated patients," she says. "It is also important to remember that the recommended dose for zongertinib is based on body weight."

Specifically, the FDA approval noted that patients weighing less than 90 kg should receive 120 mg once daily; patients weighing 90 kg or more should receive 180 mg once daily.[1]

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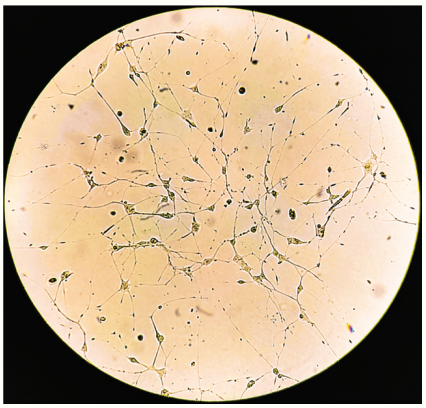
Diffuse midline gliomas get first FDA-approved drug

Patients with diffuse midline gliomas now have a US Food and Drug Administration (FDA)-approved treatment option. In August 2025, the FDA granted accelerated approval to the protease activator dordaviprone for patients aged 1 year or older with diffuse midline glioma with an *H3 K27M* mutation that has progressed after prior therapy.[1] This is the first FDA-approved systemic therapy for this rare brain tumor.



"Diffuse midline gliomas are devastating tumors that have no effective treatment options," says Ryan Merrell, MD, an associate professor of neuro-oncology at Vanderbilt University Medical Center in Nashville, Tennessee. "Radiation is the only treatment, but it usually only delays growth of the tumor for months."

Diffuse midline gliomas are unique, Dr Merrell says, because they occur in both children and adults.

"The childhood prototype tumor is diffuse infiltrating pontine glioma, or DIPG," Dr Merrell says. "This tumor is associated with a survival of 15 months; the adult tumors have similar survival."

The FDA's approval of dordaviprone was based on results from 50 patients (four pediatric patients and 46 adults) with recurrent *H3 K27M*-mutant diffuse midline glioma from five open-label, nonrandomized clinical trials.[2] Isabel Arrillaga-Romany, MD, PhD, director of neuro-oncology clinical trials at Massachusetts General Hospital in Boston, was the lead author of an article on the integrated analysis.

Adult patients received 625 mg of dordaviprone as oral capsules (125 mg each). For pediatric patients, the adult dose was allometrically scaled by body weight. The studies had different administration frequencies and treatment cycle lengths. The primary endpoint was the overall response rate by Response Assessment in Neuro-Oncology criteria for high-grade glioma.

One in five of the included patients responded to dordaviprone. One patient had a complete response, and nine patients had partial responses to therapy. The disease control rate was 40%.

Responses appeared durable, with a median duration of response of 11.2 months. The progression-free survival rate at 6 months was 35.1%. The overall survival (OS) rate was 57.3% at 12 months and 34.7% at 24 months. The median OS was 13.7 months.[2]

"There are no drug therapies for diffuse midline glioma, and dordaviprone is the first drug to show favorable results," Dr Merrell says. "Even though the results are modest, it is a breakthrough. The fact that results were seen in multiple studies is significant, even though the studies were non-randomized."

The study researchers noted that although the median time to response was 8.3 months, clinical benefits could occur before patients achieved an objective response. For example, corticosteroid responses occurred at a median of 3.7 months, and Karnofsky/Lansky performance status responses occurred at a median of 3.5 months.

All but one patient experienced at least one treatment-emergent adverse event (TEAE), the most common of which were fatigue (46%), nausea (36%), and headache (32%). There were no grade 4 treatment-related TEAEs or treatment-related deaths.

Continued approval for dordaviprone will be contingent on the verification of its safety and efficacy in the phase 3 ACTION trial.

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