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# Pediatric Astrocytoma Treatment & Management

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* Author: Lauren R Weintraub, MD; Chief Editor: Max J Coppes, MD, PhD, MBA  [more...](javascript:showModal('author-disclosures');)

## **Medical Care**

### **General**

Treatment of astrocytomas depends on the location and grade of the tumor. Tumor location and associated morbidity may limit resection or render the tumor inoperable.

Patients who develop significant obstructive hydrocephalus that does not resolve may require the placement of a ventriculoperitoneal shunt.

### **Chemotherapy**

Chemotherapy has had a limited role and limited success in the treatment of high-grade astrocytomas. Although there is no standard chemotherapy, the most commonly used regimen consists of temozolomide given concurrently with radiation therapy followed by maintenance temozolomide and bevacizumab. Investigational therapies include dendritic cell vaccines and immune checkpoint inhibitors.[[11](javascript:void(0);),[12](javascript:void(0);)]

For low-grade astrocytomas that are inoperable because of location or have demonstrated early recurrence or progression, chemotherapy with carboplatin and vincristine has been successfully used in an effort to avoid or delay irradiation. Other drug regimens may also be effective.

### **Targeted therapies**

Dabrafenib (Tafinlar), in combination with trametinib (Mekinist), is indicated in pediatric patients aged 1 year and older for low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy.

Approval was based on results from the phase 2/3 TADPOLE trial that showed patients randomized to receive dabrafenib plus trametinib experienced a statistically significant improvement in overall response rate (ORR) of 47% (CI: 35-59%), compared with 11% among those who were randomized to receive chemotherapy. At a median follow-up of 18.9 months, median progression-free survival (PFS) was 20.1 months with the immunotherapy combination, compared with 7.4 months with chemotherapy (P < .001).[[13](javascript:void(0);)]

Tovorafenib is is also indicated for relapsed or refractory pediatric LGG harboring a BRAF fusion or rearrangement, or BRAF V600 mutation in patients aged 6 months and older.[[14](javascript:void(0);)]

### **Low-grade astrocytoma**

Surgical resection is the primary treatment modality. If feasible, a complete resection is the goal of surgery in order to minimize the risk of local recurrence. However, long-term progression-free intervals may ensue even after partial resection. Low-grade tumors that recur or progress may be re-resected, and patients can undergo observation without further treatment if the risk of neurologic impairment from further growth is low and the tumor has undergone a significant interim period of dormancy.

Low-grade tumors that (1) are inoperable (diencephalic, brain stem), (2) are partially resected and posing a high risk of neurologic impairment if allowed to regrow, or (3) demonstrate early progression or recurrence may be treated with local radiotherapy to the area of the tumor plus a 2-cm margin. Radiotherapy is relatively contraindicated in children with neurofibromatosis type 1 (NF1) due to risks of radiation-induced secondary high-grade brain tumors, mutagenesis and intracranial vasculopathy. Alternatively, chemotherapy may be used in young children in whom the clinician wishes to avoid or to delay radiotherapy because of its potential neurologic sequelae in this age group. To date, the most active chemotherapy regimen for these tumors is carboplatin and vincristine. These agents show objective response rates of 50-80% and produce prolonged stable disease.

### **High-grade astrocytoma**

Following surgical resection, patients are treated with local irradiation to 50-60 Gy with a 2-cm to 4-cm margin around the area of edema defined by imaging.

The addition of single-agent or multiple-agent chemotherapy preradiotherapy and postradiotherapy has little or no impact on the overall survival rate (0-30%) in this group of patients, despite of producing response rates as high as 45%.

Biologic therapy targeting molecular markers in pediatric high-grade astrocytomas, such as tyrosine kinase inhibitors that inhibit epidermal growth factor receptor (EGFR), dendritic cell vaccines and immune checkpoint inhibitors are also being investigated.

### **Astrocytoma of the brain stem**

Surgery has no role in those patients with diffuse brainstem gliomas. Surgery is feasible for many patients with exophytic and cystic tumors, and extensive resection may prolong survival even without further treatment. However, a surgical approach to focal midbrain, medulla, and tectal plate regions is hazardous and resections are generally limited.

Local radiotherapy to 54 Gy is used for patients with inoperable tumors and for those who have high-grade lesions or early recurrence/progression of low-grade tumors. Radiotherapy for diffuse pontine lesions and high-grade tumors usually results in early and significant neurologic improvement, although the overall outlook remains dismal.

Despite ongoing clinical trials, a chemotherapeutic role in the management of patients with brainstem tumors has yet to be established.

Trials are underway using radiosensitizing chemotherapy and biologic therapy, concurrent with radiotherapy, in attempts to improve survival.

### **Astrocytoma of the visual pathway**

The natural history of visual pathway astrocytomas is erratic. Some patients experience long-term stabilization without treatment, whereas others develop progressive disease with neurologic deterioration culminating in death. This is especially true for children with neurofibromatosis. In contrast to those with chiasmatic lesions, patients with isolated optic nerve tumors rarely die of their disease; therefore, treatment efficacy must be based on visual outcome and freedom from treatment sequelae.

A period of observation without treatment is recommended in cases without severe proptosis, rapidly progressive visual decline, or extensive chiasmal tumors (with distortion or invasion of optic tracts, hypothalamus, or the third ventricular area).

Surgery is warranted only in those with chiasmatic or deeper intracranial involvement in order to rule out the possibility of an uncommon high-grade lesion.

Chemotherapy with carboplatin and vincristine is typically used as an initial therapy to avoid or delay irradiation in children. This combination chemotherapy has produced responses in the majority of newly diagnosed patients. Other regimens may also be effective.[[15](javascript:void(0);)]

### **Intramedullary spinal cord astrocytomas**

Complete surgical resections are difficult in astrocytomas because a distinct tumor-cord interface is often absent; however, nearly 80-90% of resections may be performed in most cases.

Treatment with radiotherapy is the same as that for other CNS astrocytomas. Lower radiation doses to 50 Gy are used because of radiation intolerance of the spinal cord. Treatment of low-grade tumors with radiotherapy yields 5-year survival rates of 65-70%. Patients with high-grade tumors generally die of their disease within months of diagnosis despite radiation and chemotherapy.

See [Brain Cancer Treatment Protocols](http://emedicine.medscape.com/article/2005182-overview) for summarized information.