

**FAST FACTS AND CONCEPTS #350**  
**PALLIATIVE CARE ISSUES IN GLIOBLASTOMA**  
**Roshni Abee Patel MD, Elizabeth Neil MD, Sam Maiser MD**

**Background** Glioblastoma (previously known as glioblastoma multiforme or GBM) is the most common incurable primary brain malignancy in adults. This *Fast Fact* addresses symptom management, prognosis, and medical decision-making in glioblastoma patients.

**Prognosis** Median age at diagnosis is 64; median survival from diagnosis is 15 months. Extended survival may be seen with favorable genetic mutations (e.g. MGMT and IDH), age < 50 years, and a fully independent postoperative functional status (1,2). Two-year survival after diagnosis is 27%; 5-year survival is 10% (3). Its illness trajectory is associated with a rapid rate of cognitive decline preceding the steep functional decline indicative of the usual dying phase of cancer.

**Symptom Presentation and Management** Tumor size, tumor location, and cancer treatment side effects are the most common determinants of how symptoms manifest.

- **Focal deficits.** Hemiparesis, aphasia, paresthesias, dysarthria, dysphagia, visual changes, and neglect are common. Management includes physical, occupational and speech therapy, psychosocial support, and corticosteroids (e.g. dexamethasone 2-4 mg daily or twice a day) (2,4).
- **Cognitive changes.** Depression and anxiety are common; hence many glioblastoma patients are initiated on antidepressants. Memory loss, personality changes, fatigue, agitation, and delirium are also common. Management options include psychotropics, assessment of decision-making capacity, and off-label use of psychostimulants for depression, apathy, or drowsiness (see *Fast Fact #173*) (5,6). While corticosteroids can help with vasogenic-related symptoms such as headaches or nausea, they can exacerbate behavioral changes via psychiatric side effects (see *Fast Fact # 323*).
- **Seizures.** Even though seizures are a common presenting sign of glioblastoma, prophylactic antiepileptic drugs (AEDs) are not recommended. Instead, active seizures are treated with benzodiazepines, and AEDs are initiated thereafter. Consultation with a clinical pharmacist or a neurologist is advised to minimize drug interactions and identify appropriate routes of administration for AEDs. At the end-of-life, oral administration may not be feasible. See *Fast Fact #229* for more information on rectal, sublingual, subcutaneous, or intravenous routes (2,11,2).
- **Headache, nausea, and fatigue.** These symptoms can result from the effects of chemotherapy or radiation therapy or from a disease-related increase in the intracranial pressure (ICP). Beyond conventional treatments, corticosteroids may help if vasogenic edema is present; radiation therapy and ventriculoperitoneal shunts can help manage increased-ICP-related symptoms (2,4,7).

**Cancer-Directed Therapy** For newly diagnosed patients with a preserved performance status, standard treatment involves maximal safe surgical resection followed by concomitant temozolomide (TMZ) chemotherapy and 6 weeks of radiotherapy (2,3). Essentially all patients will experience disease recurrence for which no standard treatment exists (1,2). Instead, various strategies are individualized.

- Any combination of repeat surgical resection, re-irradiation, and chemotherapy (TMZ or other) (8).
- Bevacizumab: A monoclonal antibody that can yield radiographic improvement of the tumor and thereby reduce functional deficits and the need for corticosteroids. Although it may improve quality of life, current data shows it does not prolong survival and can precipitate strokes and cardiovascular events via side effects including bleeding and clotting (9,10).
- Tumor Treating Fields (TTF): A headpiece that is worn 24 hours per day and applies low-intensity alternating electric fields to disrupt cell division of cancer cells. TTF is a new treatment with relatively limited evidence to suggest it can prolong survival when combined with TMZ for newly diagnosed and recurrent glioblastoma (12). The cosmetic appearance and burden of wearing a device all day, is a considerable trade-off that may impact quality of life.
- Hospice is an appropriate care plan for any patient with recurrent glioblastoma, particularly those with comfort-based goals of care and/or a poor performance status.

**Medical-Decision Making** Deciding when to stop life prolonging treatment can be challenging in glioblastoma. As with any other type of cancer or life-limiting illness, this should be a shared-decision between patients and clinicians based on performance status, treatment expectations, and quality of life preferences. Below are additional medical-decision-making elements worth highlighting for glioblastoma:

- In most cases, patients will not be able to enroll in hospice if they are continuing anti-cancer treatments like radiation or chemotherapy. There is some controversy around abruptly stopping bevacizumab for fear of rebound vasogenic edema contributing to a faster decline. Despite these concerns, bevacizumab is associated with its own side effects (loss of appetite, nausea, constipation, bleeding, clotting) and burdens. Hence, most experts recommend its discontinuation in the event of tumor progression so that patients can maximize their access to hospice support (11).
- Close collaboration with treating oncologists is crucial when interpreting tumor status on radiologic imaging, as microscopic progression may make radiologic interpretation challenging (11).
- Given the high risk for early cognitive changes, early advance care planning (ACP), including identification of a surrogate decision-maker, is critical with glioblastoma. ACP discussions should begin at diagnosis, and be revisited at oncologic touch points such as completion of first-line treatment, disease recurrence, hospitalizations, and any decline in functional status (6,13,14).
- Disease-related behavioral and/or cognitive changes can lead to caregiver burden and make home hospice dispositions challenging. This can create caregiver guilt, especially for patients who expressed a wish to die at home. Clinicians may need to support surrogates by highlighting the patient care needs and the safety benefits of a more supervised care setting.

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**Author Affiliations:** University of Minnesota Medical School, Minneapolis, MN (RP, EN, SM), Hennepin County Medical Center, Minneapolis, MN (SM).

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