

AMERICAN BRAIN TUMOR ASSOCIATION

Glioblastoma and Malignant Astrocytoma



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ACKNOWLEDGEMENTS

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Founded in 1973, the American Brain Tumor Association (ABTA) was the first national nonprofit advocacy organization dedicated solely to brain tumor research. For nearly 45 years, the Chicago-based ABTA has been providing comprehensive resources that support the complex needs of brain tumor patients and caregivers, as well as the critical funding of research in the pursuit of breakthroughs in brain tumor diagnosis, treatment and care.

To learn more about the ABTA, visit www.abta.org.

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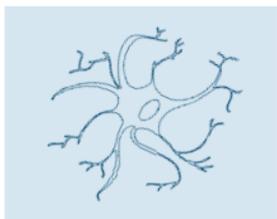
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Glioblastoma and Malignant Astrocytoma

ABOUT THIS PUBLICATION

This brochure is about glioblastoma (also called grade IV astrocytoma) and malignant astrocytoma (grade III astrocytoma). Collectively, these are both “high-grade” astrocytomas.

INTRODUCTION



Astrocyte

Any tumor that arises from the glial (from the Greek word for “glue”), or supportive tissue, of the brain is called a “glioma.”

One type of glioma is the

astrocytoma. Astrocytomas are named after astrocytes, the star-shaped cells from which they grow.

Astrocytomas are graded to describe their degree of abnormality. The most common grading system uses a scale of I to IV. Tumors also may be grouped by their rate of growth: low-grade (slow growth), mid-grade (moderate) and high-grade (rapid). On that scale, a grade I glioma is accurately considered benign, in that complete surgical excision is considered curative. These tumors, however, are diagnosed almost exclusively in childhood. Grade II gliomas are often designated “low-grade,” as the label “benign” fails to reflect the common tendency of these tumors to recur. Many patients with

grade II gliomas are done a great disservice by being told that their tumors are benign. Patients with grade II gliomas require serial monitoring by MRI or CT scan for surveillance of tumor recurrence every 6-12 months. The terms “malignant glioma” and “high-grade glioma” encompass both grade III and IV gliomas, and reflect the fact that management of these tumors is fairly similar, with some important exceptions. The word “anaplastic” means malignant. An anaplastic astrocytoma is a grade III or mid-grade tumor and diffusely infiltrating neoplasm that demonstrates focal or dispersed anaplasia (abnormal irregular shape) cells and an increased growth index compared with grade I and II astrocytoma. The pathological diagnosis is based on appearance of cells (nuclear atypia) and growth rate (mitotic activity).

Glioblastoma is still often abbreviated “GBM” is the highest grade glioma (grade IV) tumor, is the most malignant form of astrocytoma, and is synonymous with a grade IV glioma. The histologic features that distinguish glioblastoma from all other grades are the presence of necrosis (dead cells) and increase of abnormal growth of blood vessels around the tumor. Grade IV tumors are always rapidly growing and highly malignant tumors.

In this new era, 2016 World Health Organization classification has incorporated molecular information into diagnoses in the past. Diagnosis of central nervous system (CNS) tumor diagnoses is made by both identifying and characterizing the physical appearance and growth rate as well as genetic features. The use of “integrated” phenotypic and genotypic parameters for CNS tumor classification adds a level of objectivity and narrowly defined diagnostic entities than in prior classifications, which in turn should lead to greater diagnostic accuracy as well as improved

patient management and more accurate determinations of prognosis and treatment response.

For example, tumors with methylated MGMT (inactive gene) have been found to predict a longer length of survival, and responds better to chemotherapeutic agents in the treatment of glioblastoma.

The IDH1 gene encodes for a metabolic enzyme called isocitrate dehydrogenase 1, which catalyzes the conversion of isocitrate to alpha-ketoglutarate as part of normal function of brain metabolism. A mutation in this gene was discovered in a small percentage of glioblastoma samples in 2008, and has since been found in a majority of low-grade gliomas and secondary high-grade gliomas. This mutation was present in 12% of GBM. These markers are beginning to be used as a diagnostic test for predicting longer survival and for evaluating the efficacy of new targeted molecular drugs. There are two subtypes of glioblastoma: 1) glioblastoma, IDH-wild type (90%), frequently defined as primary or de novo predominated in patients over 55 years of age; 2) glioblastoma, IDH mutant (10%) which called secondary with malignant transformation from low grade glioma, common in younger patients under 45 years old.

WHO grade III anaplastic astrocytomas are now each divided into IDH-mutant, IDH-wildtype. Grade III gliomas without mutant IDH could be considered “pre-glioblastomas”, having a poorer prognosis than IDH mutant tumors. IDH mutations tend to occur in younger brain tumor cases, most commonly between the ages of 20 and 40, with a median age at diagnosis in the 30s. The mutation is also associated with tumors of the frontal lobe as approximately 70% of IDH-mutated gliomas are located there. IDH1 mutations may serve as a predictive biomarker to guide aggressive surgical resection. Patients with IDH1-mutant astrocytomas were found to have a

better overall prognosis than those with wild-type IDH1 astrocytomas.

Incorporating molecular techniques into a patient's tumor analysis will allow for the promise of precision medicine by combination of targeted cancer drugs.

INCIDENCE

An estimated 24,790 new cases of primary malignant brain tumors are expected to be diagnosed in the US in 2016. About 50% of gliomas are glioblastomas with 12,120 new cases predicted. They are most common in adults ages 45–65, and affect more men than women. Glioblastomas arise from normal brain tissue. They may invade and migrate away from the main tumor within the brain; however, glioblastoma will rarely spread elsewhere in the body.

Anaplastic astrocytomas occur more often in younger adults ages 30 -50 and account for 17% of primary malignant brain tumors. Only 9% of childhood brain tumors are glioblastomas.

Between 1% and 7% of people with glioblastomas and about 4% of people with anaplastic astrocytomas are found to have multiple tumors at the time of diagnosis.

CAUSE

Brain tumors cannot be prevented. The cause of these tumors and other types of brain tumors is unknown. Genes are the fundamental building blocks found in all body cells. Scientists have identified abnormalities in the genes of different chromosomes which may play a role in the development of tumors. However, what causes those abnormalities is still uncertain.

Scientists are conducting environmental, occupational, familial and genetic research to identify common links

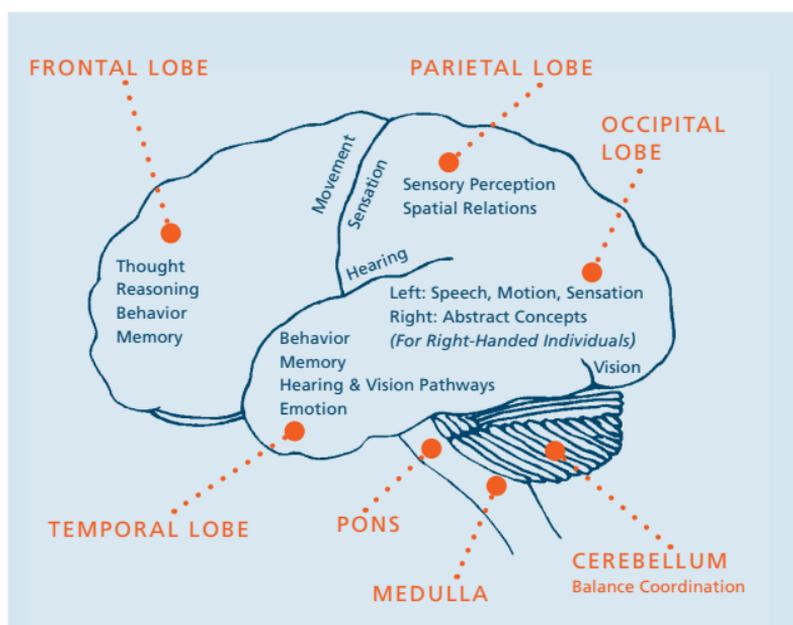
among patients. Despite a great deal of research on environmental hazards, no direct causes have been found.

The majority of brain tumors are not hereditary. Brain tumors can be caused by a genetically inherited syndrome, such as Neurofibromatosis, Li-Frameni, Von Hippel-Lindau, Turcot and Tuberous Sclerosis, but these only affect 5% of patients.

SYMPTOMS

As a brain tumor grows, it may interfere with the normal functions of the brain. Symptoms are an outward sign of this interference.

Since the skull cannot expand in response to the growth of a tumor, the first symptoms are usually due to increased pressure in the brain. Headaches, seizures, memory loss and changes in behavior are the most common symptoms.



Functions of the lobes of the brain

Loss in movement or sensation on one side of the body, language dysfunction and cognitive impairments are also

common. Other symptoms may also occur depending on the size and location of the tumor.

DIAGNOSIS

To obtain an accurate diagnosis, your doctor will begin with a neurological examination followed by an MRI or CT scan. The scan may be done with a contrast dye that makes the border and details of the tumor more visible. If you have a tumor, the scan will help your doctor determine the size, location and probable type of tumor. Some physicians may also request an MRS (magnetic resonance spectroscopy) scan which measures chemical and mineral levels in a tumor. Those measurements may give a suggestion as to whether a tumor is malignant or benign. It may also help distinguish a brain tumor from other medical problems, such as infection (tuberculosis, parasite, bacterial and fungus), demyelination (a disease that damages the myelin, or protective sheath, of a brain's neurons) or a stroke. On MRI with contrast, high grade gliomas show brightly (this is called enhancement); low grade gliomas frequently do not enhance with contrast, or slightly enhance. However, only the examination of a patient's tumor tissue under a microscope and molecular analysis can confirm an exact diagnosis.

TREATMENT

SURGERY

Generally, the first step in the treatment of glioblastomas is surgery. With today's modern techniques, surgery is generally safe for most patients. The goals of surgery are to obtain tumor tissue for diagnosis and treatment planning, to remove as much tumor as possible, and to reduce the symptoms caused by the presence of the tumor. In some circumstances, such as certain medical conditions or concerns about the location of the tumor, a biopsy may be done in place of the surgery. The tissue obtained during the biopsy is then used to confirm

the diagnosis. Diagnosis is based upon the most visible cell structure change and growth activity seen in the tissue, even if the features are found in only a few cells. Performing a surgical resection provides a larger number of cells, leading to a more accurate diagnosis, which can greatly influence management and treatment options.

Optimally, the neurosurgeon would like to remove as much of the tumor as possible. However, due to the location of the tumor – where movement, sensation or speech would be affected – some tumors cannot be completely removed. Partial tumor removal may be performed to decrease the amount of swelling in the brain or to reduce seizure activity.

Surgery to remove a brain tumor is carried out by making an opening in the skull over the tumor in what is known as a craniotomy. Several specialized pieces of equipment are available to the neurosurgeon. Brain mapping, MRI tractography (photo) and functional MRIs help the neurosurgeon determine and avoid eloquent areas of the brain during surgery. Stereotactic computerized equipment, image-guided techniques or an intra-operative MRIs can be used by the surgeon as navigational tools – much like a GPS system. These tools help to guide the neurosurgeon's access into some of the difficult or deep areas in the brain. Lasers may be used during surgery to vaporize tumor cells. Ultrasonic aspirators are tools which break apart and suction out the tumor. High-powered microscopes help the neurosurgeon to better see the tumor.

Because the tentacle-like cells of an astrocytoma grow into the surrounding tissue, these tumors cannot be totally removed. Surgery is helpful, however, as partial removal can help decrease symptoms and the tissue obtained

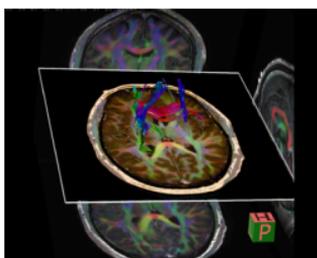


Image courtesy of Surasak Phuphanich, MD, FAAN.

during the surgery confirms the type of tumor.

Radiation, chemotherapy and/or immunotherapy are then used to treat the remaining tumor.

RADIATION

In adults, radiation therapy usually follows a biopsy or surgery. There are different types of radiation which may be given using various doses and schedules.

Conventional fractionated external beam radiation is “standard” radiation given five days a week for five or six weeks. External beam radiation is actually the same radiation you get with a simple chest X-ray. Conventional radiation for high-grade astrocytomas is usually aimed at the tumor site and the area around the tumor.

A form of “local radiation” may be used to boost conventional radiation. Most forms of local radiation treat the tumor while protecting the healthy cells surrounding the tumor. They include:

- Conformal photon radiation, which can be delivered by several methods including intensity- modulated radiation therapy (IMRT) and 3-D Conformal radiation therapy, which contours the radiation beams to match a tumor’s shape and size.
- Image-guided radiation therapy (IGRT) is the technique of using imaging technology at the time of each treatment to verify that patients are in the right position within a millimeter.
- Proton beam therapy is an alternative to the standard radiation, which provides superior dose distribution for higher dose at the tumor and avoid healthy tissue and reduces overall toxicity.
- Interstitial radiation, in the form of solid or liquid radiation, may be implanted into the tumor during surgery.

- Stereotactic radiosurgery (SRS) and Fractionated stereotactic radiosurgery (FSRS) are special forms of precisely focused, high-dose radiation typically used for small, localized tumor as a single dose treatment or fractionated treatment over four to five days.
- Photodynamic therapy uses a sensitizing drug and laser light to destroy tumor cells during surgery.
- Boron neutron capture therapy releases radioactive compounds within the tumor.

CHEMOTHERAPY

For newly diagnosed GBM, a six-week course of temozolomide is given concurrently with radiation. Temozolomide is an alkylating agent with reasonable blood-brain barrier penetration. With recent data, older patient over 65 years old, a three-week course of radiation may be considered as a new standard care. Radiation treatment is given daily Monday through Friday. Oncologists recommend taking temozolomide one hour prior to radiation therapy to maximize its purported radiosensitizing effect, though for practical reasons nighttime administration may be more feasible for some patients. Similar treatment has been routinely applied to anaplastic astrocytoma (AA) patients because of no standard care. Early results from the ongoing clinical “CATNON” study showed benefit of concurrent radiation with temozolomide and monthly maintenance or radiation and followed by monthly temozolomide. For more information on temozolomide, visit the ABTA website at www.abta.org.

Researchers continue to look for new drugs to treat GBM and AA, and there are many drugs under investigation. Some of these drugs have proven useful in treating other types of tumors in the body, and still others are standard brain tumor drugs given in a different way. Because chemotherapy drugs can affect normal cells, patients can expect side effects such as low white blood cell or platelet count, fatigue, hair loss or lack of appetite from treatment.

Most chemotherapy drugs are cytotoxic drugs. Cytotoxic drugs are designed to destroy tumor cells. They work by making tumor cells unable to reproduce themselves. Carmustine (BCNU), Lomustine (CCNU), or Gleostine (Generic), Gliadel wafer (biodegradable discs infused with BCNU), Temozolomide (Temodar) Cisplatin, Carboplatin, Etoposide and Irinotecan are examples of cytotoxic drugs. They may be given as a single agent or in combination i.e. PCV (Procarbazine, CCNU, Vicristine), Carboplatin/ Etoposide.

Only BCNU/CCNU, Gliadel wafer and Temodar have been approved by the Food and Drug Administration (FDA) for the treatment of high-grade brain tumors. Others have received approval in the treatment of other cancers, and thus must be prescribed “off-label” for brain tumor use.

Researchers are also developing new ways of delivering drugs to the tumor. Convection-enhanced delivery, or CED, uses a pump to slowly “flow” a chemotherapy drug or biologic substances into the tumor site. In another method, a biodegradable carmustine wafer is left in the tumor cavity after surgery to release a chemotherapy drug into the remaining tumor tissue. Other researchers are working with nanoparticles which release drugs into the tumor at a pre-determined rate with good penetration through blood-brain barrier (BBB).

Chemotherapy may be used in infants and very young children to delay radiation therapy until the age of three or four. At that point, the child’s brain is more fully developed and better able to tolerate radiation therapy. Clinical trials are underway to evaluate the most effective ways of treating these tumors in infants and children.

MANAGEMENT OF SYMPTOMS WITH MEDICATION

There are several drugs used to relieve the symptoms of a brain tumor. Steroids are drugs used to decrease swelling (edema) around the tumor. The most

frequently prescribed steroid for brain tumor patients is dexamethasone. Steroids should be tapered to the lowest dose necessary to alleviate symptoms. In some cases, this can be done rapidly, though in other cases, it is necessary to maintain patients on a standing steroid dose. Many patients, particularly those with tumors associated with significant mass effect, require a low dose of steroids at least through radiation therapy.

Anti-epilepsy drugs control seizures, although special precaution must be taken to achieve optimal dosing while maintaining the effectiveness of chemotherapy. Patients who present with seizures should be treated with anti-seizure medications indefinitely. However, patients without a seizure history who are placed on antiepileptic medications prior to surgery should be tapered off, as the relatively small benefit of preventing a first-time seizure is generally outweighed by potential adverse drug effects. There are no strict guidelines that establish an antiseizure medication of choice; however, there has been a general shift away from phenytoin in favor of levetiracetam (Keppra). Both agents are effective, but levetiracetam has a favorable adverse effect profile, minimal drug-to-drug interactions (an important consideration for chemotherapy) and does not require routine drug level monitoring.

During the treatment, the degree of fatigue that patients experience ranges from minimal (e.g., not affecting the ability to perform full-time work) to profound (e.g., spending the majority of the day in bed), though generally is tolerable. Brain stimulating agents such as modafinil, Provigil and methylphenidate (Ritalin) can occasionally reduce fatigue. Most patients adjust their lifestyles to accommodate for fatigue. Regular exercise has been shown to decrease fatigue. Anti-emetic drugs prevent vomiting and help control nausea. Anti-depressant, anti-anxiety medications or sleeping medications may be also considered to improve quality of life during the treatment.

BIOLOGIC, TARGETED, AND IMMUNO THERAPIES

Purposeful altering of the natural behavior of tumor cells is a newer area of medicine called “biologic” or “targeted therapy” or “immunotherapy”. Some of the substances used in this type of therapy are found in nature, others in chemicals with side effects that may alter tumor cells. These new molecular targeted therapies, which are still under investigation, are designed to stop signals going into the tumor cell, which halts growth. Several pathways in the brain encourage cell growth. In GBM, several growth factor receptors (e.g. EGFR, VEGF, PDGFR) are overexpressed or mutated, which causes cells to grow out of control, increased survival of abnormal cells and increased blood supply to the tumor. Specific drugs that inhibit these growth receptors have been developed in clinical trials. Cellular signaling pathways – pathways where one reaction causes another reaction in the cells – are very important in cell growth, not stopping abnormal cells from dying, causing tumor invasion into normal tissue and stimulating a new blood supply to tumors.

Immunotherapy is a new promising and exciting area of treatment designed to trigger the body’s own immune system to fight and halt tumor growth. Recent breakthroughs in understanding of the mechanisms, leading to full T-cell activation and recognition of the importance of overcoming tumor-induced immunosuppressive mechanisms, have shed a new light on how to generate effective anti-tumor response and sparked a renewed and enthusiastic effort to apply this method as a treatment for malignant brain tumors. These treatments include checkpoint inhibitors and cancer vaccines that utilize a tumor’s antigens. Antigens have signals that alert the system there are abnormalities in cells. The vaccine attacks the cells by using genetically engineered dendritic cells to stimulate the immune system and cause a response. Dendritic cells are potent immunostimulatory cells that continuously look for

antigens, and then activate a strong immune response. Immune checkpoints inhibitors are drug–antibodies which unleash T-cells attack on cancer cells.

Checkpoint proteins tell the immune system that a cell is healthy. There may be other molecules signaling that the cell is cancerous, but if there are enough checkpoint proteins on the cell surface, the immune system may overlook the “bad” signals. The best known example of a checkpoint protein is PD-L1 (for Programmed Death Ligand 1; its receptor is PD-1). The body needs PD-L1 to keep the immune system T-cells from attacking healthy cells. Cancer cells may upregulate (speed up the production of) PD-L1 as a protective mechanism. When PD-L1 activates the PD-1 receptor on the surface of a T-cell, the T-cell is signaled to destroy itself. With recent FDA-approval of checkpoint inhibitors: Optivo (Nivolumab), Keytruda (Pembrolizumab) and Tecentriq (Atezolizumab) for metastatic melanoma, lung cancer, Hodgkins’ lymphoma, kidney and bladder cancer, these new drugs are being studied in newly diagnosed and recurrent glioblastoma. Immunotherapy may represent the next frontier of the most promising personalized therapies in this new decade.

Other researchers are using gene or oncolytic virus (polio or adeno or herpes virus) therapies as a way of controlling tumor growth. In one method, specially-engineered genes make tumor cells more susceptible to drug therapy. In another method, gene therapy is used to stimulate the body’s natural production of immune substances. Or, gene therapy may be used to restore the normal function of tumor suppressing genes within tumor cells.

OPTUNE (NOVOTTF-100A SYSTEM) THERAPY

Optune is a wearable and portable, FDA-approved device that has been shown in clinical trials to safely deliver continuous therapy to the area of the brain where the GBM tumor is located. Optune delivers therapy through adhesive patches, called transducer arrays.

These transducer arrays are applied to the scalp and are connected to the device and battery. It is recommended that the Optune device is used for at least 18 hours a day.

This should be discussed with your doctor as a treatment option.

CLINICAL TRIALS

Several of the treatments discussed in this publication are available to patients through clinical trials. Trials are open for both patients with newly-diagnosed tumors and those with recurrent tumors.

Clinical trials test the safety and effectiveness of treatments that have already shown significant promise in laboratory studies. For patients, they provide access to therapies that would otherwise be unavailable. All clinical trials, conducted in phases – 0, I, II and III – are overseen by government (FDA) and local hospital boards (IRB), and are subject to rigorous regulation and oversight.

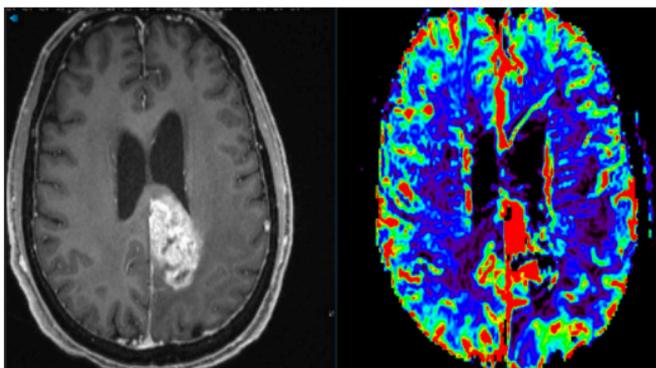
The American Brain Tumor Association's TrialConnect® service matches patients with appropriate clinical trials based on tumor type and treatment history. Patients or families can contact a TrialConnect® specialist at 877-769-4833, Monday through Friday, from 8:30 a.m. to 6:30 p.m. EST, or create a patient profile at: www.abtatrialconnect.org.

EVALUATING A TREATMENT

When evaluating a treatment, ask your doctor how the recommended treatment will affect your prognosis. What are the expected benefits of this treatment? What are the risks? What quality of life can you expect during and

Contrast-enhanced MRI scan and perfusion MRI with increased cerebral blood volume (cbv) of active tumor (not radiation necrosis or pseudo tumor progression), glioblastoma Photo courtesy of S. Phuphanich, MD

after
the



treatment? If this is an investigational treatment, how many patients with your tumor type have received this treatment, and what were their results? Is there a placebo control arm as part of the study? Is this covered by insurance and a research fund?

Before evaluating any treatment in clinical trials, ask your doctor the same questions about prognosis, benefits and risks that you would ask when evaluating another treatment.

Also understand in which phase (0, I, II or III) of this investigation you would be participating.

RECURRENCE

To measure effectiveness of treatment and to monitor for possible tumor recurrence, an initial follow-up scan will be done about two to six weeks following completion of radiation therapy. The scan will be repeated every two to three months for about a year, then on a schedule set by your doctor.

During this time, some patients may continue to receive ongoing temozolomide chemotherapy treatment, which is typically administered each month as a monthly maintenance, five-day schedule for 6–12 months.

High-grade astrocytomas can be aggressive tumors. Over time they usually recur, and when they do, it may be as a

higher grade tumor. Sometimes the tumor cells move, or migrate, into the surrounding tissue and give rise to another tumor. Most high-grade astrocytomas recur at, or near, the original site. While tumor recurrence on the opposite side of the brain and outside of the central nervous system is rare, it is occurring more often as patients live longer.

Recurrent tumors can be treated. Depending on the patient's overall medical condition and the growth characteristics of the tumor, a second surgery may be considered. Although a course of conventional radiation can be given only once, a form of stereotactic radiation may be given after conventional radiation for small tumor (<4 cm³). Therapy with a second line drug such as lomustine (CCNU) or gleostine (generic CCNU alone or in combination with bevacizumab or bevacizumab alone) low-dose daily temodar may be considered even if prior drug treatment was not effective. In addition, implanted biodegradable wafers (Gliadel) containing the chemotherapy drug BCNU may be considered for glioblastoma patients undergoing surgery for removal of a recurrent tumor. Most biological, targeted drug and vaccine or immuno therapies are available to those with recurrent tumors as part of clinical trials.

PROGNOSIS

“Prognosis” means a prediction of outcome. This information is usually based on information gathered from *groups* of people with the same disease. It is important to remember these statistics are not individualized. How well a person responds to treatment is affected by the grading of malignancy of the tumor cells, the amount of tumor removed and their general health. Age also plays a key role in outcome. Younger adults and children tend to have a better prognosis.

Because these tumors are apt to grow into surrounding tissue, anaplastic astrocytomas and glioblastomas can be very difficult to treat. Without treatment, these aggressive tumor cells multiply rapidly. The goal of treatment is to slow tumor growth and improve quality of life.

Prognosis is usually reported in years of “median survival.” Median survival is the time at which *an equal number of patients do better and an equal number of patients do worse*. With standard treatment, median survival for adults with an anaplastic astrocytoma is about two to three years. For adults with the more aggressive glioblastoma, treated with concurrent temozolomide and radiation therapy, median survival is about 14.6 months with a two-year median survival rate of 27%; five-year survival is 10%. However, there are case reports of patients surviving for 10-20 years.

Children with high-grade tumors (grade III and IV) tend to do better than adults; five-year survival for children is about 25%.

In addition, glioblastoma patients who have had their MGMT gene shut off by a process called methylation have prolonged survival rates. The MGMT gene is thought to be a significant predictor of response.

However, not all glioblastomas have the same biologic abnormalities. This may be the reason different patients respond differently to the same treatments and why different patients with the same tumor have different outcomes. Researchers continue to study the common characteristics of long-term brain tumor survivors, and how individual personalized therapy may be more optimally used to treat brain tumor patients.

NOTES/QUESTIONS

AMERICAN BRAIN TUMOR ASSOCIATION PUBLICATIONS AND SERVICES

CARE & SUPPORT

CareLine: 800-886-ABTA (2282)

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PUBLICATIONS

About Brain Tumors: A Primer for Patients and Caregivers

Brain Tumors – A Handbook for the Newly Diagnosed*

Brain Tumor Dictionary*

Caregiver Handbook*

Returning to Work: Accessing Reasonable Accommodations*

Quick Guide to the Family and Medical Leave Act*

Tumor Types:

Ependymoma

Glioblastoma and Malignant Astrocytoma

Medulloblastoma

Meningioma

Metastatic Brain Tumors

Oligodendroglioma and Oligoastrocytoma

Pituitary Tumors

Treatments:

Chemotherapy

Clinical Trials

Conventional Radiation Therapy

Proton Therapy

Stereotactic Radiosurgery*

Steroids

Surgery

Most publications are available for download in Spanish.

*(exceptions are marked *)*

CLINICAL TRIALS

TrialConnect®: www.abtatrialconnect.org or 877-769-4833

*More brain tumor resources and information
are available at www.abta.org.*

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