BC Cancer Agency www.bccancer.bc.ca

Headlines

Spring 10 A newsletter for brain tumour patients and their families

MEDICAL UPDATE

The Bevacizumab Clinical Trial

A **randomized, double blind, placebo controlled,** multicenter **Phase III trial** of bevacizumab, temozolomide and radiotherapy, followed by bevacizumab and temozolomide versus placebo, temozolomide and radiotherapy followed by placebo and temozolomide in patients with newly diagnosed glioblastoma

BEVACIZUMAB, ALSO KNOWN AS AVASTIN®, is an antibody treatment that targets the blood vessels supplying nutrition to aggressive tumours. Without nourishment, the tumour starves. This treatment has been used successfully to control brain tumours that become active again after they have been treated with chemotherapy and radiation, but it has not previously been used as initial therapy for newly diagnosed disease. Bevacizumab is a very promising new treatment for brain tumours, but it is not yet funded through the cancer agency, and we still have much to learn about how and when it should be administered for maximal therapeutic benefit.

The long title of this clinical trial is filled with information. It tells us that the trial will examine the effect of bevacizumab for patients with a diagnosis of glioblastoma multiforme, a grade IV brain tumour. This is a **randomized** study, meaning that a computer will randomly assign each patient enrolled in the study to one of two treatment groups. Randomization ensures that every patient who agrees to participate is equally likely to receive either treatment, and that there is no unfairness or bias in the treatment selection for any given patient.

It is also a **double-blind** study, meaning neither the patient nor the health care staff will know which treatment a patient is receiving. As a result, each patient will be monitored and evaluated using the same criteria, without the potential for subjective bias on the part of the patient or the investigator in assessing the response to treatment. Bevacizumab is administered by infusion through a vein every 2 weeks, so it would be easy to know which patients receive this drug, since treatment infusions are not a part of standard therapy for newly diagnosed brain tumour patients. In an effort to maintain the double-blind nature of the trial, the study designers have included a **placebo control**. One group of patient will get the bevacizumab infusion, and the other group will get an infusion of a harmless substance that is compatible with body fluids. There should be no effect at all for those patients receiving the placebo.

This is a **phase III** study, meaning the experimental treatment will be compared to our current standard treatment. At present, the standard treatment for glioblastoma is a combination of chemotherapy and radiotherapy. All study patients will receive the standard treatment, plus either a bevacizumab infusion or a placebo infusion every 2 weeks until their tumours become active again.

Standard therapy consists of 6 weeks of daily radiation combined with a pill-form

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This newsletter is published through the generous support of Bernie & Lee Simpson, the Hershey & Yvette Porte Neuro-oncology Endowment Fund and Schering-Plough Canada. For more information on how you can support enhanced patient care, patient information and brain tumour research, please contact Sharon Kennedy at the BC Cancer Foundation, 604 877 6160 or 1 888 906 2873 or skennedy@bccancer.bc.ca

Seizure medications

ABOUT ONE THIRD TO ONE HALF of patients first learn they have a brain tumour because they have a seizure. The presence of abnormal tissue within the brain causes seizures. This could be due to the tumour itself, swelling in the brain, bleeding due to the surgery or from the tumour, or scarring resulting from the surgery. As a result, many patients with brain tumours need to take seizure medications, also called antiepileptics, for a long period of time or even for the rest of their lives. The goal of treatment with seizure medications is to lessen the frequency and severity of seizures while keeping side effects to a minimum.

Common triggers for seizures include:

- Poor sleep
- Fever or illness
- Excessive alcohol consumption
- Stress or over-stimulation
- Menstruation
- Skipping meals

There are a number of different antiepileptic medications, but generally, they all work by reducing excessive activity of brain cells. Each medication can cause side effects, but these often lessen with time as people adapt to the medication. Sometimes more than one antiepileptic must be used to control seizures. However, when more medication is used, the potential for side effects also increases. There are some medications, called controlled release formulations, which ensure a steady level of medication in the bloodstream, thus providing more effective control of seizures. It is possible to check the bloodstream drug level of certain medications, including phenytoin (Dilantin®), carbamazepine (Tegretol®) and valproic acid (Depakote®), to be sure that the dose is within the proper range. If the dose is too high, more side effects can occur; if the dose is too low, seizures can occur.

It is not always feasible to stop all seizures. The location of the tumour or the surgical scar may predispose a person to having more seizures. For example, people who have tumours near the cortex, or outer layer, of brain tissue are more likely to have seizures than those with tumours located deep within the brain. There are also certain triggers that can increase the risk of seizures even if seizure medications are taken properly.

Signs of toxic (too high) levels of seizure medication:

- Slurred speech
- Double vision
- Difficulty with balance
- Nausea

It is very important to take seizure medications every day exactly as prescribed. If you alter the dose, skip a dose, or stop the medication abruptly you are more likely to have side effects or seizures.

Common side effects of seizure medications include:

- Nausea and vomiting
- Diarrhea
- Blurred vision
- Dizziness
- Drowsiness
- Headache
- Fatigue

Less commonly, an itchy red rash can occur, usually within a few weeks after starting the medication. If you develop a rash, contact your healthcare team immediately, as this rash can be a sign of a serious sensitivity to the drug. People with known sensitivities to specific seizure medications are advised to wear a Medic-alert bracelet with this information. This will allow emergency room staff to treat you with the right medication should you ever be brought in with a seizure. The blood cells or liver can also be affected by seizure medications. You will be monitored through blood tests for these potential, but uncommon, side effects.

For more information about seizures and seizure medications, see the Q&A this issue, and also *Living with Seizures* in the Spring 2006 issue of Headlines at: www.bccancer.bc.ca/PPI/copingwithcancer/specificresources/Neurooncology.htm

All Headlines articles from previous issues can be found in the Headlines Index link at: www.bccancer.bc.ca/PPI/copingwithcancer/specificresources/Neurooncology.htm

What do people say about the brain tumour support groups?

"I feel normal there. I'm so used to feeling that I'm not normal, so it's a relief to come to support group."

"There is such positive energy in the group."

"I see people who are really worse off than I am there and if they can handle it, I guess I can too."

"The group is a place of healing for me."

"I always feel better after I've been to the group."

"Everyone cares about each other. I try to offer as much support and help as I can, and I receive the same in return."

Brain Tumour Support Groups, BC Cancer Agency

Kelowna
3rd Monday of each month
11:00 am to 12:30 pm
Facilitator: Brigitte Wagner
(250) 712 3929 or (250) 712 3963

Fraser Valley
Contact Maureen Parkinson for more information
(604) 877 6000 x 2194

Vancouver
1st Wednesday of each month
9:30 am to 11:00 pm
Facilitators: Maureen Parkinson, Douglas Ozier and Rosemary Cashman
(604) 877 6000 x 2194, (604) 877 6000 x 2813, or (604) 877 6072
Every other session is a split support group: one for patients, one for caregivers.

Victoria
2nd Thursday of each month
11:00 am to 12:30 pm
Facilitator: Catherine Traer-Martinez
(250) 519 5528

SPRING sprint 2010

braintumour foundation OF CANADA

For additional information,
contact Yaron Butterfield
SprintVancouver@braintumour.ca
604 707 5900 ext. 5446
or 1 800 265 5106
www.braintumour.ca

The Spring Sprint is a 3.5 km to 5 km walk/run event benefiting the Brain Tumour Foundation of Canada. The event is volunteer-based, and the funds raised provide education, information, and support to the estimated 55,000 Canadians affected by this devastating disease. Your donations also fund research into the cause and cure of brain tumours.

In 2010, the Spring Sprint campaign will make stops in 22 cities throughout eight provinces across Canada. Participants of all ages can run or walk to pay tribute to the courage of survivors and to honour loved ones they have lost. Everyone is walking with the same goal in mind: Imagine a Cure!

Local events in:

Vancouver
When: Saturday, May 29th
Where: Burnaby Lakes (Rowing Pavilion)
Distance: 5 km
Registration Opens at 10:00 am
Event Begins at 11:00 am

Victoria
When: Sunday, May 30th
Where: Cedar Hill Recreation Centre
Distance: 3.5 km
Registration Opens at 9:30 am
Event Begins at 11:00 am

To register, go to **www.springsprint.ca**

The Bevacizumab Clinical Trial
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of chemotherapy called temozolomide, to be taken daily before radiation and on the weekends. Following this combination treatment, patients on standard therapy receive 6 cycles of temozolomide chemotherapy (for 5 consecutive days of each 28 day cycle for a total of 6 months) at a higher dose than during the combination treatment with radiation. In the study, all patients will receive the infusions of bevacizumab or placebo every 2 weeks throughout the combined chemo and radiation, and also during the 6 cycles of chemo alone, and will continue to receive these infusions after all treatment is completed, until the tumour shows signs of renewed activity.

This study will include regularly scheduled assessments of patients, including patients' subjective assessments of how they are feeling, both physically and psychologically. It will also determine the MGMT status of all participants. MGMT, or methylguanine methyltransferase, is a DNA repair protein. When this protein is inactivated in the tumours of patients with glioblastoma, the tumour cannot repair the damage done to it by chemotherapy. As a result, those patients with inactivated or "silenced" MGMT respond better to treatment and survive longer. The investigators will examine the relationship between patients' MGMT status and their response to the standard and experimental treatments in this trial.

For more information about clinical trials, see previous issues of Headlines at: www.www.bccancer.bc.ca/PPI/copingwithcancer/specificresources/Neurooncology.htm

Concurrent chemoradiation: Spring 2006

Guide to clinical trials: Spring 2007

For information about MGMT: Fall 2007, Fall 2008 and Summer 2009

Question + answer

Q I was diagnosed with a brain tumour in late January after having a seizure at work. The surgeon said he got all the tumour out, and it's fortunately low grade. For some reason I still have seizures or sometimes just the feeling that I'll have a seizure, but then the seizure doesn't come. I'm taking Dilantin, but it makes me feel groggy and affects my thinking. When can I stop this medicine, or should I be on a different medicine? And when will the seizures stop happening?

A The brain is a large bioelectric organ. This electrical activity needs to be tightly regulated by maintaining an appropriate and consistent microenvironment around the electrical cells, called neurons. Epileptic seizures occur when that microenvironment is disrupted, allowing neurons to discharge haphazardly and spontaneously. There are many events that can injure the brain and disrupt the neurons' environment. Examples include brain tumours, infection, stroke, and scar tissue from surgery or trauma.

Many brain tumour patients remain at risk for seizures, even after a successful surgery, because the brain tissue never heals back to its original state, and thus that delicate balance of electrical activity remains disrupted.

If seizures are completely controlled, patients can sometimes eventually wean off their anti-seizure medication. Studies have shown that successful discontinuation of medication varies with the length of time a patient has remained seizure-free. Basically, the longer you have gone without seizures, the better your chances are of remaining seizure-free off the medication. This typically means 3-5 years of treatment.

For those who continue to be at high risk for seizures or who are incompletely controlled with their medication, there are many options available for treatment. You are not confined to one drug, and under the guidance of a neurologist, you can usually find a medication regimen that can give you the right combination of seizure control and favourable side effect profile.

By Dr. Brian Thiessen, Neuro-oncologist, BCCA, Vancouver centre

Editions of *Headlines* are also available as a pdf download at:
www.bccancer.bc.ca/PPI/copingwithcancer/specificresources/Neurooncology.htm
If you would like to submit an article, ask a question, or serve on our patient and family advisory board, please contact Rosemary Cashman at rcashman@bccancer.bc.ca or 604 877 6072 (phone) 604 877 6215 (fax).

All content by Rosemary Cashman unless otherwise specified.