

## Kansas City Clinical Oncology Program

### Phase II Trial of Observation for Low-Risk Meningiomas and of Radiotherapy for Intermediate- and High-Risk Meningiomas

#### RTOG 0539

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have a meningioma. Meningiomas are tumors that usually arise from the lining of the brain or spinal cord, an area that is known as the meninges. Patients enrolled in this trial will have meningiomas that occur within the skull, around the brain. Meningiomas come in different types and grades, factors that can affect the rate of growth. Meningiomas also can occur in different locations. The location where the meningioma occurs affects how safely and completely a neurosurgeon can remove it. Patients enrolled in this trial can have meningiomas of any type and grade, and the meningioma can have been either completely or partially removed at surgery.

#### **Why is this study being done?**

For patients with a newly diagnosed, low-grade meningioma, this study will find out whether surgery alone results in a good outcome. For patients with a recurrent low-grade meningioma or a newly diagnosed higher-grade meningioma, this study will find out what effects, good and/or bad, radiation therapy has on you and on your tumor.

In addition, the researchers will try to see if they can identify through the collection of tissue and MRI scans ways to tell which meningiomas should be treated and which can be watched. Since tissue specimens from every participant will be reviewed by one central pathologist, the study will compare the pathology results of your hospital's pathologist and the study's central pathologist.

#### **How many people will take part in the study?**

About 165 people will take part in this study (number of people who participate in this study once their tumors are determined to be meningiomas by the study's central pathology reviewer).

#### **What will happen if I take part in this research study?**

#### **Before you begin the study...**

You will need to have the following exams, tests, or procedures to find out if you can be in the study. These exams, tests, or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

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- Physical and neurological exams and history
- Blood work for blood counts
- MRI scan of your brain (an image of your brain produced by magnetic rays). If this is the first time you have had surgery you will need to have had an MRI scan before and after surgery
- Pregnancy test if relevant

You will need to have the following exams, tests, or procedures done because you are in the study.

- Documentation of any steroids, antiseizure medications, or hormones (such as estrogen, progesterone replacements or contraceptives) you are taking
- Documentation of how much of your normal activities you are able to do

### **During the study...**

When you enter the study, your study doctor will need to send the block of tumor tissue obtained at the time of your brain tumor surgery to a central pathology site. There, a pathologist will confirm that the tumor is a meningioma. If the tumor is not a meningioma, you will not be able to continue to participate on this study.

If all exams, tests, and procedures show that you can be in the study, and you choose to take part, then you will need to do the following. They are part of regular cancer care:

- Documentation of any side effects you are experiencing
- Documentation of how much of your normal activities you are able to do
- Documentation of any change in your medications

### **Study Plan**

Based on the grade of your tumor and how much of the tumor was removed at surgery, you will be placed in one of three groups.

- **Group I (Low Risk):** Patients with a newly diagnosed meningioma that has been completely or partially removed by a neurosurgeon, confirmed by an MRI scan, and found to be World Health Organization (WHO) grade I\* when examined by a pathologist.
- **Group II (Intermediate Risk):** Either
  - Patients with a newly diagnosed meningioma that has been completely removed by a neurosurgeon, confirmed by an MRI scan, and found to be WHO grade II\*\* when examined by a pathologist, or
  - Patients who had a low-risk, WHO grade I\* meningioma when first diagnosed but whose tumor has now returned regardless of how much tumor was removed at their surgery.
- **Group III (High Risk):** Patients with high-risk features including a newly diagnosed or recurrent WHO grade III\*\*\* meningioma when examined by a pathologist regardless of how much tumor was removed at their surgery; a recurrent WHO grade II\*\* meningioma when examined by a pathologist regardless of how much tumor was removed at their surgery; or a newly diagnosed meningioma that has been partially removed by a neurosurgeon, confirmed by a MRI scan, and was found to be WHO grade II\*\* when examined by a pathologist.

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\*WHO grade I means that you have a benign meningioma. Meningiomas are benign if, under a microscope, they look similar to the cells that they came from and if they do not have features that suggest that they will grow quickly. This is the most common type of meningioma. It has the best prognosis of all the meningioma grades, tends to grow slowly, and is usually cured or well controlled with appropriate treatment and follow-up.

\*\*WHO grade II means that you have an atypical meningioma. Meningiomas are atypical if, under a microscope, they have features that suggest that they will grow at an intermediate rate. This is the second most common meningioma grade, but atypical meningiomas are more likely to come back than grade I tumors are. These meningiomas therefore require more aggressive treatment.

\*\*\*WHO grade III means that you have the highest grade of meningioma. These tumors are called either anaplastic or malignant meningiomas, which means that they look the least like the cells that they came from and that they usually grow more quickly than meningiomas of other grades. These meningiomas have the highest risk of coming back and therefore require the most aggressive treatment.

A total of 55 patients will have low-risk meningiomas (Group I), 55 will have intermediate-risk meningiomas (Group II), and 55 will have high-risk meningiomas (Group III).

**If you are in Group I:** You will follow the common practice of being observed without further treatment. You will be observed closely by your study doctor at least every 6 months for at least 3 years, so your study doctor can see if and when your tumor comes back

**If you are in Group II:** You will receive radiation therapy daily, Monday through Friday, for 30 treatments. The dose will be 54 Gy. You will be seen in follow-up at least every 3 months for at least 3 years.

**If you are in Group III:** You will receive radiation therapy daily, Monday through Friday, for 30 treatments. The dose will be 60 Gy. You will be seen in follow-up at least every 3 months for at least 3 years.

**When I am finished receiving radiation therapy (Groups II and III) .... OR**  
**When I have reached the follow-up stage (Group I) ....**

The following tests and procedures will be repeated regularly when you are seen in follow-up as part of your normal care:

- Physical and neurological exams
  - Group I: At least every 6 months for 3 years, then at least yearly for 10 years
  - Groups II and III: At least every 3 months for 3 years, then at least yearly for 10 years
- MRI scan of your brain
  - Group I: Every 6 months for 3 years, then yearly for 10 years
  - Groups II and III: 3 months after you stop receiving radiation therapy, then at least every 6 months for 3 years, then at least yearly for 10 years

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As a result of your being in the study, the following tests and procedures will be repeated regularly when you are seen in follow-up:

- You will be asked about any side effects of treatment you are experiencing.
- You will be asked to document your ability to perform your normal activities.
- You will be asked about any steroids, antiseizure medications or hormones (such as estrogen, progesterone replacements or contraceptives) you are taking.

### **How long will I be in the study?**

If you are in Groups II or III, you will receive radiation therapy for about 6 weeks. Patients in all groups will be followed closely for 3 years and will be seen at least yearly for 10 years from then on.

### **Can I stop being in the study?**

Yes. You can decide to stop at any time. Tell your study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell your study doctor if you are thinking about stopping, so he or she can evaluate any risks from the radiation therapy (Groups II and III). Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

Your study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

### **What side effects or risks can I expect from being in the study?**

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop receiving treatment. In some cases, side effects can be serious, long lasting, or may never go away. In rare situations, a severe side effect may be life threatening.

You should talk to your study doctor about any side effects that you have while taking part in the study.

### **Risks and side effects related to the radiation therapy include those that are:**

#### **MRI Risks:**

During the study, you may be asked to have 1 MRI scan. MRI scans release radio waves, which can be very noisy, and therefore you will be given earplugs to block out the noise. You may briefly experience claustrophobia during the MRI procedure. Gadolinium is a liquid given by injection into a vein during your MRI scan. It helps the doctor better see the brain tissue. It may cause headache, discomfort at the injection area, nausea, vomiting, dizziness, rash, numbness or tingling in the hands or feet. In severe cases, an allergic reaction may also occur. You must inform your treating physician during the screening visit if you are aware of any allergy to a dye given as part of a test you have had in the past. Gadolinium-containing contrast liquids have

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been associated with a rare disease called nephrogenic systemic fibrosis (NSF,) but only in patients whose kidney function is abnormal. In this rare disease, a scar-like tissue appears in the lungs, liver, muscles and heart. To date, there have been no reports of NSF after gadolinium injection in patients with normal kidney function. You will not be allowed to take part in this study if your kidney function is abnormal.

**Likely**

- Scalp redness or soreness
- Hair loss, which may be temporary or permanent
- Ear/ear canal reactions (irritation or other skin reaction, fluid buildup), possibly resulting in short-term hearing loss
- Fatigue
- Tiredness/sluggishness
- Temporary worsening of symptoms such as headaches, seizures, or weakness

**Less Likely**

- Mental slowing
- Decreased memory
- Permanent hearing loss
- Cataract(s)
- Dry eye(s)
- Decreased sense of smell
- Decreased sense of taste
- Dry mouth
- Behavioral change
- Decreased vision

**Rare but Serious**

- Severe local damage to normal brain tissue, a condition called necrosis (tissue deterioration) which can cause swelling. Radiation necrosis can mimic recurrent brain tumor and may require surgery for diagnosis and treatment. Short- or long-term steroid use may be needed.
- Injury to the eyes with the possibility of loss of part of your vision or blindness
- Worsening of neurologic problems such as muscle weakness, loss of sensation, decreased balance, trouble walking, decrease in motor function, difficulty speaking, and seizures.
- Development of other tumors (either benign or malignant)
- Edema (swelling of the brain), possibly requiring short- or long-term steroid use and surgery, and very rarely leading to death
- Brainstem or spinal cord damage

**Reproductive risks:**

You should not become pregnant while receiving radiation on this study because the radiation can affect an unborn baby. If you are a woman of childbearing potential, it is important you understand that you need to use birth control while receiving radiation on this study. Check with your study doctor about what kind of birth control methods to use

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and how long to use them. Some methods might not be approved for use in this study. If you are a woman of childbearing age and have not been surgically sterilized (tubal ligation or hysterectomy), you must have a pregnancy test before receiving radiation on this study.

For more information about risks and side effects, ask your study doctor.

### **Are there benefits to taking part in the study?**

Taking part in this study may or may not make your health better. If you are in Group I, you may benefit from surgery alone, without radiation therapy. If you are in Groups II or III, you may benefit from the addition of radiation therapy through improved control of your meningioma. We do know that the information from this study will help doctors learn more about meningiomas. This information could help future patients.

### **What other choices do I have if I do not take part in this study?**

Your other choices may include:

- Receiving treatment or care for your meningioma without being in a study
- Participating in another study
- Receiving no treatment other than close observation and follow-up
- Having surgery alone or surgery in combination with radiation treatment

Talk to your study doctor about your choices before you decide if you will take part in this study.

### **Will my medical information be kept private?**

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The Radiation Therapy Oncology Group (RTOG)
- Local institutional research boards
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people

### **What are the costs of taking part in this study?**

You and/or your health plan/insurance company will pay for the costs of your treatment in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting other treatment for your meningioma.

You will not receive payment for taking part in this study.

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For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://cancer.gov/clinicaltrials/understanding/insurance-coverage>. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

**What happens if I am injured because I took part in this study?**

It is important that you tell your study doctor \_\_\_\_\_ [investigators/ name(s)], if you feel that you have been injured because of taking part in this study. You can tell your study doctor in person or call him/her at \_\_\_\_\_ [telephone number].

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

**What are my rights if I take part in this study?**

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

**Who can answer my questions about the study?**

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor \_\_\_\_\_ [name(s)] at \_\_\_\_\_ [telephone number].

For questions about your rights while taking part in this study, call the Kansas City Clinical Oncology Program Institutional Review Board (a group of people who review the research to protect your rights) at 816-823-0560.

**Please note:** This section of the informed consent form is about additional research that is being done with people who are taking part in the main study. You may take part in this additional research if you want to. You can still be a part of the main study even if you say 'no' to taking part in this additional research.

Consent Form for Use of Samples for Research

**About Using Tissue/Blood/Urine for Research**

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Tissue: You have had surgery to see if you have a meningioma. During surgery, your doctor removed some or all of your meningioma. A portion of this tissue will be sent to a central study pathologist who will review tissue from all patients enrolled in the study. The pathologist will examine the tumor tissue to confirm that the tumor is a meningioma and to confirm the tumor grade. This review is an essential part of the clinical trial; therefore, permission to let the pathologist review the tissue is mandatory to your participation in the main part of this study.

In addition, we would like to keep some of the tissue that is left over for future research. If you agree, this tissue will be kept and may be used in research to learn more about meningiomas and other diseases. You will not be charged for the processing of your tissue for any of this research. Please read the information sheet called "How is Tissue Used for Research" to learn more about tissue research. This information sheet is available to all at the following web site: [http://www.rtog.org/tissue%20for%20research\\_patient.pdf](http://www.rtog.org/tissue%20for%20research_patient.pdf)

Blood: As a result of your participation in the trial, you also will have a blood test performed before you enter the study. We would like to collect for future research about three tablespoons of blood during this time (all Groups). We would also like to collect for future research about three tablespoons of blood taken at the following additional times: 1 month after you have finished receiving radiation (Groups II and III) and if your disease gets worse while you are on the study (all Groups). If you agree, this blood will be kept and may be used in research to learn more about meningiomas and other diseases. You will not be charged for the processing of your blood for any of this research.

Urine: In addition, we would like to keep some of your urine for future research. We would collect your urine at the following times: at the beginning of the study (all Groups), on the day you finish receiving radiation therapy (Groups II and III), and 1 month after you have finished receiving radiation (Groups II and III). If you agree, the urine will be kept and may be used in research to learn more about meningiomas and other diseases. You will not be charged for the processing of your urine for any of this research.

The research that may be done with your tissue, blood, and urine is not designed specifically to help you. It might help people who have meningiomas and other diseases in the future.

Reports about research done with your tissue, blood, and urine will not be given to you or your study doctor. These reports will not be put in your health record. This research will not have an effect on your care.

### **Things to Think About**

The choice to let us keep the left over tissue, blood, and urine for future research is up to you. No matter what you decide to do, it will not affect your care or your participation in the main part of the study.

If you decide now that your tissue, blood, and urine can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your tissue, blood, and urine. Then any tissue that remains will be returned to the institution that submitted it, and any blood or urine that remains will be destroyed.

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In the future, people who do research may need to know more about your health. While the Radiation Therapy Oncology Group may give them reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes tissue, blood, and urine are used for genetic research (about diseases that are passed on in families). Even if your tissue, blood, and urine are used for this kind of research, the results will not be put in your health records.

Your tissue, blood, and urine will be used only for research and will not be sold. The research done with your tissue, blood, and urine may help to develop new products in the future.

### Benefits

The benefits of research using tissue, blood, and urine include learning more about what causes meningiomas and other diseases, how to prevent them, and how to treat them.

### Risks

The greatest risk to you is the release of information from your health record. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

### Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence circle "Yes" or "No". If you have any questions, please talk to your study doctor or nurse, or call our research review board at IRB's phone number.

No matter what you decide to do, it will not affect your care.

1. My specimens may be kept for use in research to learn about, prevent, or treat cancer as follows:

- Tissue  Yes  No
- Blood  Yes  No
- Urine  Yes  No

2. My specimens may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease) as follows:

- Tissue  Yes  No
- Blood  Yes  No
- Urine  Yes  No

3. Someone may contact me in the future to ask me to take part in more research.  
 Yes  No

### Where can I get more information?

You may call the National Cancer Institute's Cancer Information Service at:

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**1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615**

You may also visit the NCI Web site at <http://cancer.gov/>

- For NCI's clinical trials information, go to: <http://cancer.gov/clinicaltrials/>
- For NCI's general information about cancer, go to <http://cancer.gov/cancerinfo/>

You will get a copy of this form. If you want more information about this study, ask your study doctor.

**Release**

By signing this form you authorize KCCOP to access and obtain information that is required for the study. This may include your medical records, labs, radiologic films and reports and pathology specimens. This authorization to disclose your medical records shall not expire, even upon death, unless specifically revoked in writing by you.

**Signature**

I have been given a copy of all 10 pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

\_\_\_\_\_  
**Participant**

\_\_\_\_\_  
**Date**

\_\_\_\_\_  
**Printed name of Person Obtaining Consent**

\_\_\_\_\_  
**Signature of Person Obtaining Consent**

\_\_\_\_\_  
**Date**

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