NCI Community Oncology Research Program – Kansas City (NCORP-KC)

NRG-BN003 Consent Form

Study Title for Study Participants: Comparing Observation Versus Radiation for Newly Diagnosed Grade II Meningiomas That Have Been Completely Removed Through Surgery

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: NRG-BN003. Phase III Trial of Observation Versus Irradiation for a Gross Totally Resected Grade II Meningioma

What is the usual approach to my newly diagnosed, surgically removed grade II meningioma?

You are being asked to take part in this research study because you have a type of brain tumor called a grade II meningioma that has been completely removed through surgery. People who are not in a study and who have had a grade II meningioma completely removed may be observed without treatment; treated with radiation following surgery; or treated with radiation therapy only if their tumor comes back. For patients who receive the common approach of observation, about 50 to 75 out of 100 are free of meningioma at three to five years. The purpose of the study is to compare the approach of observation with that of treating with radiation following surgery.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have one of the usual approaches described above
- you may choose to take part in a different study, if one is available

Why is this study being done?

The purpose of this study is to compare any good and bad effects of using radiation to treat a meningioma that has been completely removed compared with the more common approach of observing the tumor and treating it with radiation if it returns. Using radiation before the tumor returns could prevent it from returning but it could also cause side effects. This study will allow the researchers to know whether this usual approach (treating you with radiation) is better, the same, or worse than the other usual approach (observation after surgery). Surgery alone has resulted in tumor control of about 50% to 75% at 3 to 5 years. We will be looking carefully at the 3-year results, and expect surgery with complete removal alone to control a WHO grade II meningioma in around 70% of patients at that interval. To be better, the use of radiation after surgery and before the tumor returns should improve the likelihood that the tumor does not grow back by at least 15% at 3 years, as compared to the surgery alone.

There will be about 148 people taking part in this study.

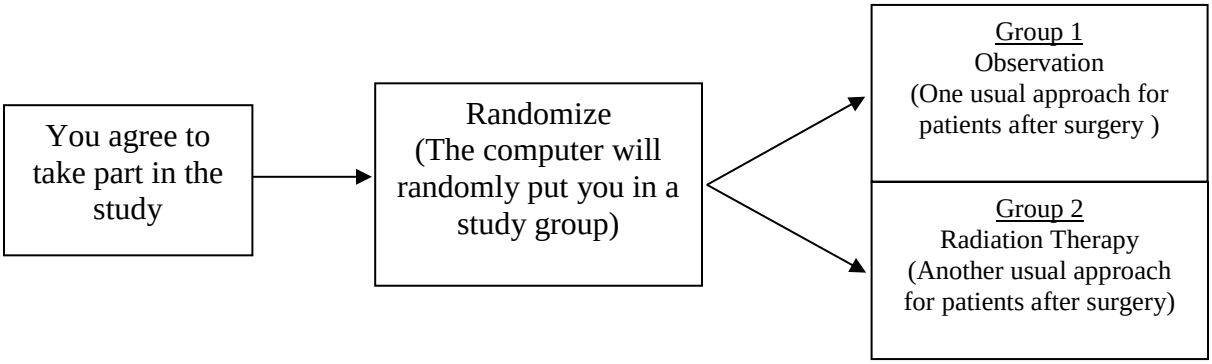
What are the study groups?

This study has two study groups.

- Group 1 will be observed following surgery, without radiation treatment (post-surgery observation).
- Group 2 will receive radiation therapy to the area of the brain where the meningioma was removed, with careful attention to minimizing the amount of radiation received by normal tissue.

A computer will by chance assign you to treatment groups in the study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the others. You will have an equal chance of being placed in either group.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



How long will I be in this study?

If you are randomized to Group 2, you will receive the radiation therapy 5 days per week for 6 1/2 to 7 weeks (33 treatments). After you finish radiation therapy, your doctor will continue to watch you for side effects and follow your condition through office visits at months 3, 6 and 12 for the first year from randomization, every 6 months for year 2 and 3, then yearly for 10 years. If you are randomized to Group 1 (post-surgery observation), your doctor will follow you through office visits at the same intervals. Patients in both Groups will have MRIs at least every 6 months from randomization for 5 years, then at least yearly for 10 years.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual treatment approaches for your meningioma. However, before you are randomized to a study group, you will need to have the following extra tests:

Tissue Sample

Small pieces of meningioma tissue removed at the time of your surgery will be taken for the study before you begin treatment on this study. This sample is required in order for you to take part in this study because the research on the sample is an important part of the study. Your study doctor will need to send this tissue to a central pathology site. There, a pathologist will confirm that the tumor is a grade II meningioma. If the tumor is not a grade II meningioma, you will not be able to continue on the study. There is no cost to you for the central review. If there is any tissue leftover, you have the option to say ‘yes or ‘no’ on whether it can be stored in a biobank for future research. Biobanking will be discussed in the section on optional studies.

Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information.

Neither you nor your health care plan/insurance carrier will be billed for the collection of the tissue that will be used for this study.

Quality of Life/Neurocognitive Function Study

Patients in both groups will be asked to fill out a form with questions about your symptoms, such as fatigue, and your physical and emotional well-being. You will also be asked to complete three thinking measures to evaluate your thinking abilities such as memory; this will be administered by a trained test administrator in the clinic. Researchers will use this information to better understand how patients feel during treatments and what effects the treatments are having. If you do not speak English, French, or Spanish you will not be asked to complete the form about your symptoms or the three thinking measures.

If you speak English

You will be asked to fill out the form about your symptoms and complete the three thinking measures at different times during your regular office visits for this study:

- Before you are randomized to a study group,
- At 6, 12, 24, 36, and 60 months after you are randomized;
- If your tumor comes back.

If you speak French or Spanish

You will be asked to fill out the form about your symptoms at different times during your regular office visits for this study:

- Before you are randomized to a study group,
- At 6, 12, 24, 36, and 60 months after you are randomized;
- If your tumor comes back.

The form and thinking measures will take about 20 to 30 minutes to complete. They will ask about things like fatigue, quality of life, and memory. You may feel uncomfortable answering some of the questions, and you can skip any you do not want to answer.

Neither you nor your health care plan/insurance carrier will be billed for your participation in the quality of life/neurocognitive function study.

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss
- The radiation therapy may not be better, and could possibly be worse, than other usual approaches for meningiomas.

The radiation therapy used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. Your study doctor will be following your condition and will watch for side effects.

There is also a risk that you could have side effects from the radiation therapy.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.

- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 2- Possible Side Effects of Radiation Therapy

COMMON, SOME MAY BE SERIOUS In 100 people receiving brain radiation, more than 20 and up to 100 may have:
• Scalp redness or soreness • Hair loss, which may be temporary or permanent • Temporary hearing decrease or loss • Tiredness • Temporary increase of brain tumor symptoms such as headaches, seizures, or weakness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving brain radiation, from 4 to 20 may have:
• Changes in thinking patterns, decrease ability to concentrate, behavior changes, difficulty walking, difficulty talking • Permanent hearing decrease or loss • Cataracts • Nausea, Vomiting • Dry mouth, changes in taste • Loss of appetite • Abnormal hormone levels related to changes to the pituitary gland may cause symptoms such as low blood sugar, low blood pressure, and fatigue which may require hormone replacement.

RARE, AND SERIOUS In 100 people receiving brain radiation, 3 or fewer may have:
• Damage to the brain • Swelling of the brain • Blurred vision with chance of blindness • A cancer resulting from treatment of your meningioma

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks: If you are randomized to Group 2, you should not get pregnant while receiving radiation therapy in this study. The radiation therapy used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use if you are randomized to Group 2.

What possible benefits can I expect from taking part in this study?

It is not possible to know at this time if observing you after surgery, or treating you with radiation only if the meningioma returns, is better than treating you with radiation immediately after surgery, so this study may or may not help you. This study will help researchers learn things that will help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

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

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the Central Institutional Review Board at 888-657-3711.

What are the costs of taking part in this study?

You and/or your health plan/insurance company will need to pay for all of the costs of treating and monitoring your meningioma while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in this study.

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

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group. Some of these organizations are:

- NRG Oncology
- Other organizations in the National Clinical Trials Network (NCTN): Alliance for Clinical Trials in Oncology (ALLIANCE), ECOG-ACRIN Cancer Research Group (ECOG-ACRIN), SWOG, and Imaging and Radiation Oncology Core (IROC)
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

ADDITIONAL STUDIES SECTION: *(Indicate clearly to participants that this is a separate section)*

This section is about optional studies you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with meningioma in the future.

The results will not be added to your medical records and the results will not be provided to you or your study doctor unless you specifically request it.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

1. Optional Sample Collections for Laboratory Studies and/or Biobanking for Possible Future Studies

Researchers are trying to learn more about meningiomas, cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

pHH3 Laboratory Study
If you choose to take part in this study, the study doctor for the main study would like to collect a sample of tissue that is left over from your surgery. The tissue will be used to see if a tumor marker called the phospho histone H3 mitotic index (pHH3) can be used to find out which meningiomas are more likely to grow back after surgery.

Biobanking for Possible Future Studies
If you choose to take part, a sample of tissue left over from your surgery will be collected.

In addition, a sample (about 2-3 teaspoons or 1 tube) of your blood will be collected at three timepoints: (1) before you are randomized to a Study Group; (2) when you visit the office at 6 months after you are randomized; and (3) when you visit the office at 12 months after you are randomized.

The researchers ask your permission to store and use your samples and related health information (for example, your response to treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking". The Biobank is being run by NRG Oncology and supported by the National Cancer Institute.

Blood DNA Laboratory Study
(***for patients who chose to take part in the biobanking study described above***)
If you choose to take part in this study, researchers may take DNA from your blood samples provided above. Researchers may compare this DNA to the DNA in your meningioma tumor, to try to find genes that have changed in your tumor. Finding genes that are connected to meningioma tumor growth may help researchers find new treatments for patients with this tumor.

WHAT IS INVOLVED?

If you agree to take part, here is what will happen next:

1) About 2-3 teaspoons or 1 tube of blood will be collected from a vein in your arm before you are randomized to a study group and at 6 and 12 months after you are randomized.
2) Tissue remaining from the sample sent for central pathology review as part of your participation on the main part of this study will be sent to the Biobank. Your sample and some related health information will be sent to a researcher for use in the study described above. Remaining samples may be stored in the Biobank, along with samples from other people who take part. The samples will be kept until they are used up. Information from your medical record will be updated from time to time.
3) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer Institute, will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
4) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
5) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
4) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. *(For non-US participants, please verify existence of such laws before including the following text.)* There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biobank and NRG Oncology staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom NRG Oncology sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

ARE THERE ANY COSTS OR PAYMENTS?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?

If you decide you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the use of your samples for research, contact the study doctor, _____, *(insert name of study doctor for main trial),* at _____ *(insert telephone number of study doctor for main trial).*

Please circle your answer to show whether or not you would like to take part in each option :

SAMPLES FOR THE LABORATORY STUDIES:

pHH3 Laboratory Study

I agree to have my left-over tumor tissue from my study entry biopsy submission collected and I agree that my left-over tumor tissue and related information may be used for the pHH3 laboratory study described above.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to learn about results from this study.

YES NO

SAMPLES FOR FUTURE RESEARCH STUDIES:

My left-over tumor tissue from my study entry biopsy submission, blood samples, and related information may be kept in a Biobank for use in future health research.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

YES NO

Blood DNA Laboratory Study
(for patients who *chose to take part in the biobanking study described above)*
I agree to let researchers take DNA from my blood samples.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to learn about results from this study.

YES NO

This is the end of the section about optional studies.

Release

By signing this form you authorize NCORP-KC 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.

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

My Signature Agreeing to Take Part in the Main Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled 'yes'.

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____