Study Title for Participants: Testing whether the use of brain scans alone instead of brain scans plus preventive brain radiation affects lifespan in patients with small cell lung cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: S1827, "MRI Brain Surveillance Alone Versus MRI Surveillance and Prophylactic Cranial Irradiation (PCI): A Randomized Phase III Trial in Small-Cell Lung Cancer (MAVERICK)"

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have small cell lung cancer.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

Does the use of brain scans alone instead of brain scans plus preventive brain radiation affect the lifespan of patients with small cell lung cancer?

We are doing this study because we want to find out if this approach is better or worse than the usual approach. The usual approach is defined as care that most people get for small cell lung cancer.

What is the usual approach to preventing brain metastases in patients with small cell lung cancer?

The usual approach for patients who are not in a study is prophylactic cranial irradiation (PCI). PCI is defined as radiation therapy that is delivered to the brain in hopes of preventing spread of cancer into the brain. Some doctors choose to use a type of PCI that avoids the hippocampus. The hippocampus is part of your brain involved in memory and learning.

In addition, MRI scans are used to monitor the possible spread of the cancer with an MRI machine over time.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will either receive PCI for two weeks and brain MRIs for two years, or you will just receive brain MRIs for two years.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that monitoring with MRIs alone may not be as good as PCI.

There is also a risk that you could have side effects from the PCI. However, PCI is the usual approach and being in this study does not increase the risk of side effects from PCI.

Benefits

There is evidence that monitoring with brain MRIs is effective in identifying brain metastases in patients with small cell lung cancer. It is not possible to know now if this approach will extend your life compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your 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.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women in the PCI group: You become pregnant before completing PCI.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or the study sponsor (the National Cancer Institute [NCI]). The study sponsor is the organization that oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to compare the effects of using brain MRIs alone versus brain MRIs plus PCI on the lifespan of patients with small cell lung cancer. The use of brain MRIs alone could reduce side effects of receiving PCI, which are described in the risks section below.

This study is hoping to show that monitoring with MRI scans alone (delaying radiation until the actual spread of the cancer) is at least as good as the combination of PCI with MRI scans.

There will be about 668 people taking part in this study.

What are the study groups?

This study has 2 study groups.

- Group 1

  If you are in this group, you will receive the usual approach of PCI. This requires that you go to a radiation treatment center five days per week for two weeks. Each treatment will last about 20 minutes. Your doctor will decide whether to use the type of PCI that avoids your hippocampus.

  You will also have an MRI 3, 6, 9, 12, 18, and 24 months after you start the study.

  You and your doctor will decide if you will also receive the medicine memantine. Memantine is not being studied in this trial. Memantine is a pill commonly given during radiation to the brain that may decrease the risk of side effects on memory and thinking. Memantine is FDA-approved for use in patients with dementia.

  There will be about 334 people in this group.

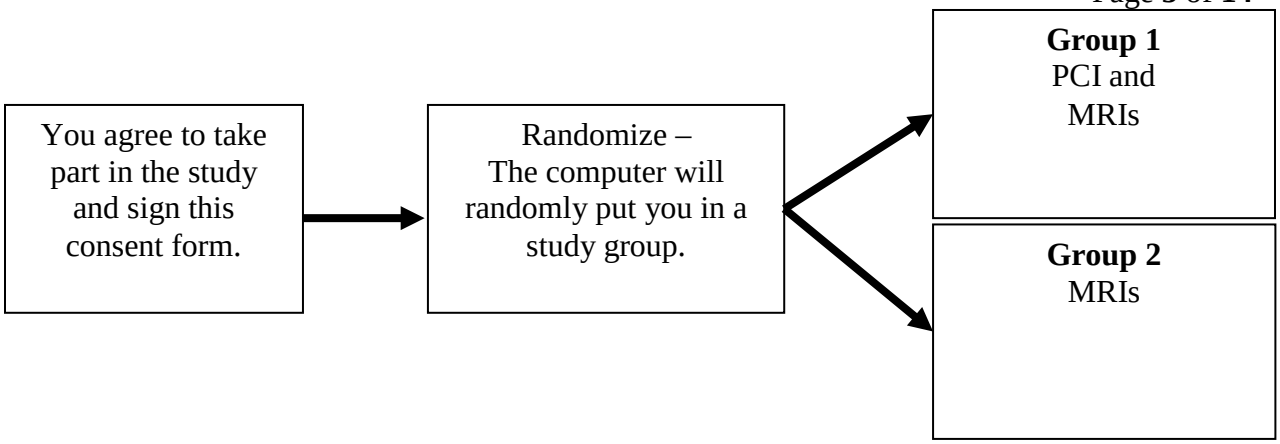
- Group 2

  If you are in this group, you will not receive PCI. You will have an MRI 3, 6, 9, 12, 18, and 24 months after you start the study.

  There will be about 334 people in this group.

We will use a computer to assign you to one of the study groups. This process is called "randomization". It means that your doctor will not choose and you cannot choose which study group you are in. You will be put into a group by chance. You will have an equal chance of being in Group 1 or Group 2.

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.



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

- Before you begin the study, and again 3, 6, 12, 18, and 24 months after you start the study, you will complete three tests to see how the study is affecting your thinking abilities, such as memory. These will be administered by a trained test administrator in the clinic and will take about 30 minutes each time.
- Images from the MRIs you have during the study will be sent to a research lab. Researchers will use them to learn more about the effects of PCI on the brain. You will not need to have any extra MRIs for this purpose.

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

General Risks

If you choose to take part in this study, there is a risk that the study approach may not be as good as the usual approach at preventing brain metastases..

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The PCI used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and after you have completed the study.

Side Effect Risks

The radiation used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

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

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.
4. Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- If you decide to take memantine, your study doctor may adjust the dose of memantine to try to reduce side effects.

The tables below show the most common and most serious side effects of PCI that doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 1: Possible Side Effects of PCI

NOTE: The below are possible side effects of whole brain radiation. Standard prophylactic cranial irradiation (PCI) doses for Small-Cell Lung Cancer, however, are usually lower and therefore, some of these risks may have a lower incidence than described in the table.

COMMON, SOME MAY BE SERIOUS In 100 people receiving whole-brain radiation therapy, more than 20 and up to 100 may have:
• Hair loss, which may be permanent • Dry mouth and/or change in taste • Scalp reddening or tanning and irritation (Your skin will be examined once a week during radiation therapy) • Memory loss, problems thinking clearly, or difficulty managing multiple tasks, which can occur in the first few months after whole-brain radiotherapy and may be permanent • Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving whole-brain radiation therapy, from 4 to 20 may have:
• Temporary worsening of tumor-like symptoms such as seizures or weakness • Drainage of clear fluid from the ears or plugging of the ears with decreased hearing • Behavioral change and/or increased sleepiness (occurring four to ten weeks after radiotherapy is complete and lasting for several days up to two weeks) • Cataracts and eye damage with the possibility of impaired vision • Nausea and/or vomiting • Headaches

RARE, AND SERIOUS In 100 people receiving whole-brain radiation therapy, 3 or fewer may have:
• Severe local damage to or death of normal brain tissue, which may require surgery to remove • Hardening of the arteries in the brain, which may lead to strokes • A second new cancer caused by radiation, in the brain or nearby organs • Eye damage with the possibility of permanent blindness

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.

For women: Do not get pregnant while receiving PCI. Tell your study doctor right away if you think you have become pregnant before completing PCI.
For men receiving PCI: Do not father a baby while receiving PCI or for 6 months after your last PCI treatment. Tell your study doctor right away if you think that your partner has become pregnant within 6 months after your last PCI treatment on this study.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your small cell lung cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of PCI.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The tests that will see how the study is affecting your thinking ability and memory

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. Contact information for your study doctor is listed on the consent cover page. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related

injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

No funds have been set aside to compensate you in the event of injury.

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 or receive copies of some of the information in 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:

- Montana Cancer Consortium
- The study sponsor, SWOG Cancer Research Network
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study
- The FDA and the groups it works with to review research
- The NCI and the groups it works with to review research
- The NCI's National Clinical Trials Network and groups it works with to conduct research

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

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.

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 information for your study doctor is listed on the consent cover page.

For questions about your rights while in this study, call the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

Optional studies that 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. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with small cell lung cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these 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. Contact for Future Research

Occasionally, researchers working with SWOG may have another research idea that relates to people who were on a SWOG study. In some cases, to carry out the new research, we would need to contact participants in a particular study. You can agree or not agree to future contact.

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

2. Optional sample collections for storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Unknown future studies

If you choose to take part in this optional study, samples of your blood will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by the SWOG Cancer Research Network and is supported by the NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may be passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

What is involved in this optional sample collection?

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

1. About 2 teaspoons of blood will be collected from a vein in your arm before you begin the study and then every three months for two years. If your disease gets worse, blood will also be collected at that time.
2. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

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

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

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 to this optional sample collection?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, who will let the biobank know. Contact information for your study doctor is listed on the consent cover page. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor. Contact information for your study doctor is listed on the consent cover page.

Please circle your answer below to show if you would or would not like to take part in this optional study:

Samples for unknown future studies:

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the 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 and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)

(Required for initial consent only)