Study Title for Participants: Testing the timing of immunotherapy alone or with chemotherapy as first line treatment and maintenance in non-small cell lung cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: EA5163/S1709 INSIGNA: A Randomized, Phase III Study of Firstline Immunotherapy alone or in Combination with Chemotherapy in Induction/Maintenance or Postprogression in Advanced Nonsquamous Non-Small Cell Lung Cancer (NSCLC) with Immunobiomarker SIGNature-driven Analysis (NCT03793179)

Version Date: October 25, 2024

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. 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 non-squamous non-small cell lung cancer that has spread outside your lungs, and your cancer has been tested to be PD-L1 positive, a kind of marker in your tumor.

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 questions:

Does starting treatment with the immunotherapy drug, MK-3475 (pembrolizumab), alone, instead of a combination of immunotherapy and chemotherapy, result in a significant

improvement in overall survival (OS) (time being alive) for patients with your type of cancer? Does additional treatment with chemotherapy following immunotherapy alone also improve overall survival?

We are doing this study because we want to find out whether either of these two usual approaches to treating your type of cancer is better or worse than the other. The usual approach is defined as care most people get for PD-L1 positive non-squamous non-small cell lung cancer.

What is the usual approach to my PD-L1 positive non-squamous non-small cell lung cancer?

The usual approach for patients who are not in a research study is combination treatment with chemotherapy and immunotherapy. If the PD-L1 marker is high (greater than or equal to 50%), treatment with immunotherapy alone is considered. Patients may also receive additional chemotherapy or immunotherapy later if the disease grows. There are several chemotherapy and immunotherapy drugs approved by the Food and Drug Administration (FDA) that are commonly used. Your doctor can explain which treatment may be best for you.

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?

Rev. Add1

If you decide to take part in this study, you will be randomly assigned to a study group. Depending on your assigned study group, you will either get the immunotherapy drug, MK-3475 (pembrolizumab) alone or a combination of chemotherapy (carboplatin, pemetrexed) and MK-3475 (pembrolizumab) until your disease gets worse, the side effects become too severe, or for up to 2 years of treatment on MK-3475 (pembrolizumab). If you initially received MK-3475 (pembrolizumab) alone and your disease gets worse, you will go on to receive either chemotherapy (carboplatin, pemetrexed) alone or in addition to the immunotherapy (MK-3475/pembrolizumab) until your disease gets worse again, the side effects become too severe, or in the latter case, up to 2 additional years of treatment on MK-3475 (pembrolizumab). In each of the relevant treatment plans mentioned above, you may only receive up to 4 doses of carboplatin (1 dose per cycle/month), but pemetrexed can continue beyond 2 years if it is still working.

After you finish your study treatment, your doctor will continue to follow your condition for a total of 5 years from when you began taking part in the study and watch you for side effects. They will check your condition every 3 months after your treatment ends for first 3

years. Afterwards, they will check your condition every 6 months for the final 2 years. This means you will continue to see your doctor for a total of 5 years after you begin taking part in the study.

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 the study approach may not be as good as the usual approach for your cancer at extending your life.

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer. However, starting with immunotherapy alone may also result in fewer side effects than the combination of chemotherapy and immunotherapy.

There may be some risks that the study doctors do not yet know about.

Benefits

There is evidence that this study approach may be effective in extending the life of patients with your type of cancer and increasing survival. It is not possible to know now if the study approach will extend your life span 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: You become pregnant while on the study.
- The study is stopped by the National Cancer Institute (NCI), Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (ECOG-ACRIN). The study sponsor is the organization who 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 any good and bad effects of using only the immunotherapy drug, MK-3475 (pembrolizumab), alone first versus the combination of the immunotherapy drug, MK-3475 (pembrolizumab), and chemotherapy. This study will also compare if adding chemotherapy to immunotherapy when the disease is growing is helpful. The addition of chemotherapy regimens to the usual immunotherapy could shrink your cancer or prevent it from returning. But, it could also cause side effects, which are described in the risks section below.

This study will help the study doctors find out if this different approach is better, the same, or worse than the usual approach. The study doctors are looking to see if the study approach reduces the number of side effects compared to the usual approach without affecting your life expectancy. They also hope that it will increase the life of patients by 5 months or more compared to the usual approach.

This immunotherapy drug, MK-3475 (pembrolizumab), is already approved by the FDA for use in metastatic lung cancer whose tumors express high levels of PD-L1 or when chemotherapy has stopped working. There is also data to support the use of MK-3475 (pembrolizumab) in patients with tumors that have lower levels of expression (such as greater than 1%). The use of MK-3475 (pembrolizumab) itself is not experimental, but the study intends to help determine which of the usual treatment plans involving this drug for patients with your type of cancer is better. There will be about 846 people taking part in this study.

What are the study groups?

This study has 3 study groups.

- **Group 1**

  If you are in this group, you will get the immunotherapy drug, MK-3475 (pembrolizumab), for up to 2 years, unless your disease gets worse sooner than 2 years or the side effects become too severe. If your disease gets worse, you will then get the chemotherapy drugs, carboplatin and pemetrexed. You will get up to 4 doses of carboplatin, but you will get pemetrexed until your disease gets worse or the side effects become too severe.

  You will get these drugs through a vein in the arm on the first day of each cycle. Each cycle lasts 21 days.

There will be about 200 people in this group.

- **Group 2**

  If you are in this group, you will get the immunotherapy drug, MK-3475 (pembrolizumab), for up to 2 years, unless your disease gets worse sooner than 2 years or the side effects become too severe. If your disease gets worse, you will then receive the chemotherapy drugs, carboplatin and pemetrexed, in addition to MK-3475 (pembrolizumab). You will get up to 4 doses of carboplatin, but you will get both MK-3475 (pembrolizumab) and pemetrexed for up to 2 years, until your disease gets worse or the side effects become too severe. After two years, you will get pemetrexed alone until your disease gets worse or the side effects become too severe.

  You will get these drugs through a vein in the arm on the first day of each cycle. Each cycle lasts 21 days.

  There will be about 200 people in this group.

- **Group 3**

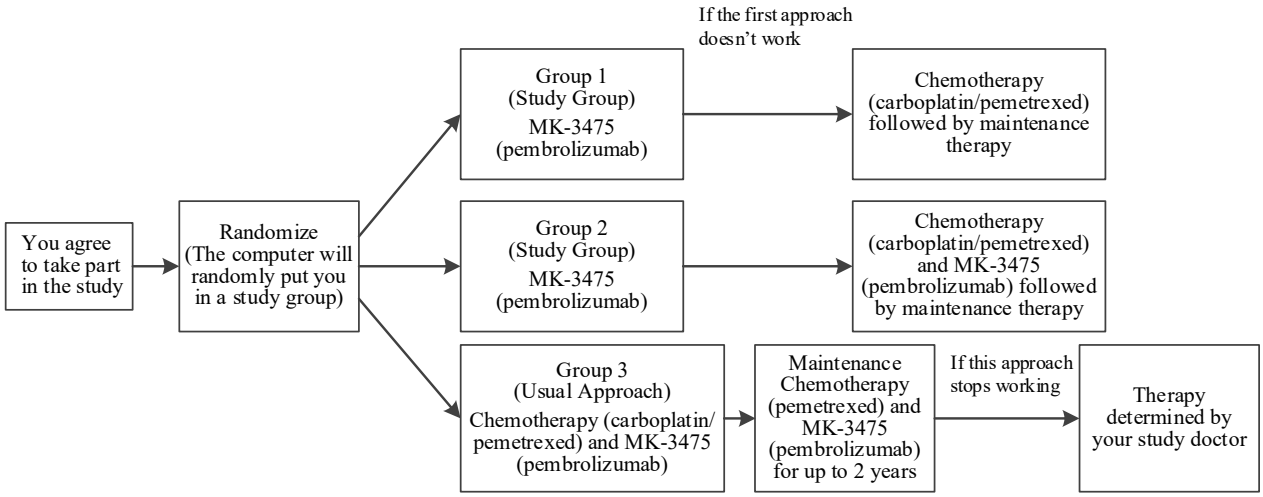
  If you are in this group, you will get the immunotherapy drug, MK-3475 (pembrolizumab), and the chemotherapy drugs, pemetrexed and carboplatin until your disease gets worse or the side effects become too severe. You will stop getting carboplatin after 4 doses, while pemetrexed and MK-3475 (pembrolizumab) will be continue to be given together for up to 2 years total. If your disease gets worse sooner than 2 years, you will proceed to another therapy determined by your study doctor. If not, after 2 years, you will continue to get pemetrexed alone until your disease gets worse or the side effects become too severe. If all of the study drugs stop working, you will proceed to another therapy determined by your study doctor.

  You will get these drugs through a vein in the arm on the first day of each cycle. Each cycle lasts 21 days.

  There will be about 200 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 a 33% chance of being in Group 1 (study group), Group 2 (study group), or Group 3 (usual approach).

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.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- Complete blood count and blood chemistry tests to check the liver and kidney functions before you begin the study and before the initiation of each treatment course. This may be conducted at more frequent intervals if your physician finds them to be necessary.
- Imaging (CT, MRI, and/or PET scan) will be performed before you begin the study and every 6 weeks, 9 weeks, or 12 weeks of therapy to see if your cancer is responding to therapy. The timing of the imaging will depend on how long you have been on the study and which part of the study you are on.
- Electrocardiogram, if you have any risk factors for heart disease, before you begin the study.

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

General Risks

Rev. Add3
Rev. Add5

If you choose to take part in this study, there is no guarantee that the study approach is better than the usual approach for your cancer or condition at extending your life, and could be worse. 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 immunotherapy and chemotherapy drugs 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 for 120 days after you have completed the study.

Side Effect Risks

Rev. Add3

The MK-3475 (pembrolizumab) 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 will let you know if changes occur that may affect your health. There is also a risk that you could have side effects from the study drug(s)/study approach. 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.
- Your study doctor may adjust the study drugs to try to reduce side effects.

Drug Risks

The tables below show the most common and most serious side effects 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, Group 2, and Group 3 – Possible side effects of MK-3475 (pembrolizumab), carboplatin, and pemetrexed are listed in the tables below:

Possible Side Effects of MK-3475 (pembrolizumab)

Risk Profile for Pembrolizumab (MK-3475) (CAEPR Version 2.8, August 14, 2024)

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Pembrolizumab (MK-3475), more than 20 and up to 100 may have:

- Tiredness

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving Pembrolizumab (MK-3475), from 4 to 20 may have:

- Nausea
- Loss of appetite
- Pain in back
- Joint stiffness
- Swelling and redness of the skin

Pembrolizumab (MK-3475) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Anemia which may require blood transfusion
- Pain in lymph nodes
- Blood clot which may cause bleeding, confusion, paralysis, seizures and blindness
- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness
- Diarrhea
- Sores in the mouth which may cause difficulty swallowing
- Pain in belly
- Sores in the bowels
- Chills, fever
- Reaction during or following a drug infusion which may cause fever, chills, rash, low blood pressure
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly
- Pain or swelling of the joints
- Problem of the muscle, including swelling, which can cause muscle pain and severe

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving Pembrolizumab (MK-3475), from 4 to 20 may have:

muscle weakness sometimes with dark urine

- Skin: itching; acne; rash (can be severe); blisters and peeling on the skin, mouth; skin changes; hives

RARE, AND SERIOUS

In 100 people receiving Pembrolizumab (MK-3475), 3 or fewer may have:

- A syndrome starting with flu-like symptoms and followed by swelling, tenderness which may cause flu-like symptoms, blurred vision, ringing in the ears, changes in hair or hair loss
- Inability to digest food which may cause bloating
- Swelling of the gall bladder
- Swelling of the spinal cord
- Feeling of "pins and needles" in arms and legs
- Redness, pain or peeling of palms and soles

Pembrolizumab (MK-3475) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Heart problems including swelling and heart failure. Symptoms and signs of heart problems may include: Shortness of breath, swelling of the ankles and body.
- Swelling and redness of the eye which may cause blurred vision with a chance of blindness
- Swelling of the bowels
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Damage to organs in the body when donor cells attack host organs which may cause yellowing of eyes and skin, itchy dry skin
- Damage to organs in the body when the body produces too many white cells
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in a coma
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs.
- Swelling of the brain (encephalitis/meningitis) which may cause headache, confusion, sleepiness, seizures and stiff neck
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling
- Lung problems (pneumonitis and other conditions). Symptoms may include: new or

RARE, AND SERIOUS In 100 people receiving Pembrolizumab (MK-3475), 3 or fewer may have:
worsening cough, chest pain, shortness of breath. • Skin rash developing 1-8 weeks after a drug is given which may be accompanied by fever, lymph node swelling and organ failure • Swelling or tenderness of blood vessels

Pembrolizumab works by helping your immune system to fight your cancer. However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e., causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

Rev. Add1 **Possible Side Effects of Carboplatin**

(Table Version Date: October 23, 2018**)**

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Vomiting, nausea • Pain • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, from 4 to 20 may have:
• Visual loss • Diarrhea, Constipation, belly pain • Changes in taste • Numbness and tingling in fingers and toes

RARE, AND SERIOUS In 100 people receiving Carboplatin, 3 or fewer may have:
• Changes in vision • Changes in taste • Damage to organs which may cause hearing and balance problems • Numbness and tingling of the arms and legs

Possible Side Effects of Pemetrexed

Rev. Add1

(Table Version Date: December 14, 2018**)**

COMMON, SOME MAY BE SERIOUS In 100 people receiving Pemetrexed, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Constipation, nausea, vomiting, loss of appetite • Sores in mouth which may cause difficulty swallowing • Tiredness • Peeling of skin

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Pemetrexed, from 4 to 20 may have:
• Damage to the lungs which may cause shortness of breath • Scarring of the lungs • Liver damage which may cause yellowing of eyes and skin • Kidney damage which may cause swelling, may require dialysis • Diarrhea • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body • Swelling and redness of the area of radiation • Itching

RARE, AND SERIOUS In 100 people receiving Pemetrexed, 3 or fewer may have:
• Blood clot which may cause swelling, pain • Blockage of the bowels • Numbness and tingling of the arms and legs • Hair loss

Additional Drug Risks

The study drug could interact with other drugs. Please talk to your study doctor about the possible interactions.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

Imaging Risks

The CT, PET, and MRI scans that you may get in this study will expose you to low amounts of radiation. Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer.

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 or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 120 days after your last dose of study drug.

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 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. This includes any blood tests, all imaging scans, and the electrocardiogram.
- The costs of getting the MK-3475 (pembrolizumab) and standard chemotherapy drugs, carboplatin and pemetrexed, ready and giving it to you.
- 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 or your insurance provider will not have to pay for the MK-3475 (pembrolizumab) while you take part in this study.

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. 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.

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.

The ECOG-ACRIN Cancer Research Group and the SWOG Cancer Research Group are conducting this study. ECOG-ACRIN and SWOG are cancer research groups that conducts studies for the National Cancer Institute. Your doctor is a member of ECOG-ACRIN, SWOG, or another group that is participating in this study. To help protect your privacy, ECOG-ACRIN has obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS). With this Certificate, ECOG-ACRIN cannot be forced (for example, by court subpoena) to disclose information that may identify you in any federal, state or local civil, criminal, administrative, legislative or other proceeding. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

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:

- The study sponsor, ECOG-ACRIN, and Merck & Co., Inc., or any drug company supporting the study, or the study drug, now or in the future.
- The 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 the groups it works with to conduct research.
- Alliance for Clinical Trials in Oncology
- NRG Oncology
- Southwestern Oncology Group (SWOG)
- The biobank and researchers approved to study your samples or health data.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, 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.

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

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 the study doctor *(*insert name of study doctor[s]*)*

at *(*insert telephone number, and email address if appropriate*)*.

For questions about your rights while in this study, call the *(*insert name of organization or center*)* Institutional Review Board at *(*insert telephone number*)*.

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 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 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 the following studies.

Optional sample collections for bio-banking 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, a sample of tissue from your previous biopsy as well as tissue from the biopsy performed as part of your routine care if your cancer worsens and blood will be collected and stored. Storing samples for future studies is called "bio-banking." The biobank is being run by ECOG-ACRIN 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 blood and tissue 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 just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and 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.

If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample collection?

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

1. About four (4) teaspoons of blood will be collected from a vein in your arm before you start therapy, on cycle three day one (6 weeks), and if your cancer worsens. The blood will usually be collected at the same time as the blood collected for your clinical tests to monitor your health.
2. A sample of your archived tumor tissue collected at the time of your diagnostic biopsy, as well as tumor tissue from the routine care biopsy performed if your cancer worsens, will be sent to the biobank for research. Only tumor tissue from procedures performed as part of your standard of care will be sent.
3. 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.
4. 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.
5. 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. Rarely, an infection can happen where the needle was placed. Feeling dizzy or fainting can also happen, but this should only last a few minutes after blood is drawn.

Rev. Add5

Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.

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 samples 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 samples 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, *(*insert name of study doctor for main trial*)*, at *(*insert telephone number of study doctor for main trial*)*, who will let the biobank know. Then, any samples that remain 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, *(*insert name of study doctor for main trial*)*, at *(*insert telephone number of study doctor for main trial*)*.

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

Samples for unknown future studies:

May we have samples of your tissue and blood for future research?

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's signature _____

Date of signature _____

Signature of person(s) conducting the informed consent discussion _____

Date of signature _____