Research Study Informed Consent Document

Study Title for Participants: Testing the addition of nivolumab to chemotherapy for patients with metastatic anal cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: EA2176 "A Randomized Phase III Study of Immune Checkpoint Inhibition with Chemotherapy in Treatment-Naïve Metastatic Anal Cancer Patients" (NCT04444921)

Version Date: October 22, 2024

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 anal canal cancer that has spread to limited number of places in your body; this is called metastatic disease.

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: Will adding an immune checkpoint inhibitor to the usual combination of chemotherapy drugs help prevent your

cancer from getting worse?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your anal canal cancer. The usual approach is defined as care most people get for naïve metastatic anal cancer. These treatments may reduce symptoms and may stop the tumor from growing for a few months or longer.

What is the usual approach to my metastatic anal cancer?

The usual approach for patients who are not in a study is treatment with Food and Drug Administration (FDA)-approved chemotherapy treatments.

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 get chemotherapy for up to 6 months or you will get chemotherapy plus a drug called nivolumab for 6 months. After the 6 months of chemotherapy, you will continue to receive nivolumab until your cancer gets worse or up to 2 years. You may continue to take nivolumab after 2 years, but it would no longer be supplied by this study. You and your doctor will discuss which option is best for you. All of these treatments have been approved by the Food and Drug Administration (FDA), but the use of nivolumab to treat your cancer with chemotherapy is considered investigational.

After you finish treatment, your doctor will continue to follow your condition for 3 years. After you stop receiving the study treatment, you will visit the clinic once every 3 months for 3 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 the study treatment may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

There is also a risk that you could have additional side effects, which is added to the standard treatments. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- Fatigue.
- Low white blood cell count
- Shortness of breath.
- Musculoskeletal pain.
- Decreased appetite.

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

Benefits

There is evidence that nivolumab is effective in stabilizing your type of cancer and other type of cancers that have spread to limited number of places. However, it is not possible to know now if the nivolumab treatment will benefit you 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. This may mean slowly stopping the study drugs so that there is no sudden unsafe change, risk to your health. 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 (NCI). 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 the usual treatment (chemotherapy) alone to using nivolumab plus the usual treatment. The addition of nivolumab to the usual treatment could shrink your cancer, keep it from growing, or not give additional benefit. Additionally 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 treatment (chemotherapy plus nivolumab) is better, the same, or worse than the usual approach of chemotherapy alone. To decide if it is better, the study doctors will be looking to see if nivolumab when given with the usual treatment will slow the progression of your cancer.

The study drug nivolumab, is already approved by the FDA for use in different types of cancer, including lung, skin (melanoma), kidney, bladder, colorectal, and some types of liver cancers.

But, most of the time it is not used until the usual treatment stops working. This study is looking to enroll approximately 200 patients.

What are the study groups?

There are two study groups.

- **Group 1**

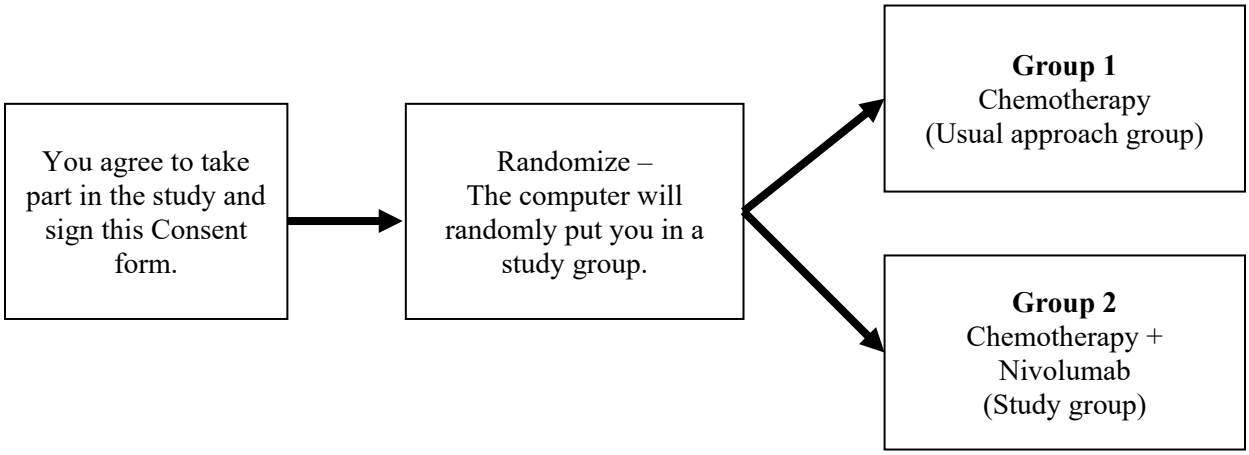
  If you are in this group, you will get the usual drugs used to treat this type of cancer called carboplatin and paclitaxel. You will get these drugs intravenously. You will receive doses of carboplatin based on your weight every 28 days, and you will receive 80 mg/m^2 of paclitaxel on days 1, 8, and 15 of a 28-day schedule. Treatment is repeated for up to 6 months. There will be about 65 people in this group.

- **Group 2**

  If you are in this group, you will get a study drug called nivolumab plus the usual drug used to treat this type of cancer, carboplatin and paclitaxel. You will get these drugs in different doses during different times. Nivolumab 240 mg will be administered intravenously on days 1 and 15 of the first 4 weeks then nivolumab 480 mg will be given on day 1 every 4 weeks until your cancer gets worse. You will also receive doses of carboplatin based on your weight every 28 days, and you will receive 80 mg/m^2 of paclitaxel on days 1, 8, and 15 of a 28-day schedule. Chemotherapy treatment is repeated for up to 6 months. There will be about 130 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 twice the chance of being in Group 2 as opposed to Group 1.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the top and read going down left then 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:

- Blood counts done weekly during the first cycle of treatment.
- Physical exams done on day 1 of each cycle.
- Tumor measurements will be taken every 2 cycles.

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- Blood will be collected for additional research studies prior to starting treatment, Day 1 of cycle 2, 4, and 8 and Day 1 of cycle 12 or at the end of your therapy whichever occurs first.

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 nivolumab plus chemotherapy may not be as good as chemotherapy alone at shrinking or stabilizing your cancer.

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 nivolumab 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 7 months after you have completed the study.

Side Effect Risks

The nivolumab 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 drug.

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.

Since this study is looking at a combination of the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new 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 Groups 1 and 2

Possible side effects of Paclitaxel and Carboplatin are listed in the tables below. These drugs are part of the usual approach for treatment this type of cancer.

Possible Side Effects of Paclitaxel (Table Version Date: September 26, 2017)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, more than 20 and up to 100 may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

COMMON, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, 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 • Pain • Sores in mouth which may cause difficulty swallowing • Diarrhea, nausea, vomiting • Muscle weakness • Numbness, tingling or pain of the arms and legs • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, from 4 to 20 may have:
• Abnormal heartbeat • Blood clot which may cause swelling, pain, shortness of breath • Damage to the lungs which may cause shortness of breath

RARE, AND SERIOUS In 100 people receiving Paclitaxel, 3 or fewer may have:
• Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness • A tear or a hole in the bowels which may cause pain or that may require surgery • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body

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:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Study Group 2

In addition to side effects listed above, people who are in Group 2 may also have some side effects from nivolumab. These side effects are listed below.

Possible Side Effects of Nivolumab

(CAEPR Version 2.5, June 10, 2023)

Special precautions Side effects of Nivolumab may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when Nivolumab is used in combination with ipilimumab. **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse.**

COMMON, SOME MAY BE SERIOUS In 100 people receiving nivolumab, more than 20 and up to 100 may have:
• Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving nivolumab, from 4 to 20 may have:
• Anemia which may require blood transfusion • Swelling and redness of the eye • Pain • Diarrhea, nausea • Dry mouth • Fever

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving nivolumab, from 4 to 20 may have:

- Swelling and redness at the site of the medication injection
- Bruising, bleeding
- Pain or swelling of the joints
- Loss of appetite
- Reaction during or following a drug infusion which may cause fever, chills, rash

Nivolumab 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:

- Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- 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.
- Skin: itching; rash, blisters including inside the mouth; loss of skin pigment
- 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.
- 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.

RARE, AND SERIOUS

In 100 people receiving nivolumab, 3 or fewer may have:

- Swelling of arms and legs which may cause a feeling of heaviness and tightness
- Dry eyes
- Sores in the mouth which may cause difficulty swallowing
- 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
- Swelling of the bowels

Nivolumab 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:

- Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma

RARE, AND SERIOUS In 100 people receiving nivolumab, 3 or fewer may have:
• 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. • Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body. • Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine • Swelling of the brain (meningitis/encephalitis) which may cause: headache, stiff neck confusion, sleepiness, seizures or injury to the brain which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome) • Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut damage), and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received Nivolumab therapy, since the risk and severity of transplant-associated complications may be increased.

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.

Patients of childbearing potential must continue contraception until 5 months past the last dose of nivolumab.

What are my responsibilities in this study?

If you chose 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 doctor's visits or hospital stays outside of this study

- If you have been or are currently in another research study

Do not get pregnant or breastfeed while taking part in this study.

Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 5 months after the last dose of study treatment.

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.
- the costs of getting the nivolumab, carboplatin, and paclitaxel 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 nivolumab while you take part in this study.

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You and/or your insurance will not need to cover the cost of your blood collected for research-only studies.

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 is conducting this study. ECOG-ACRIN is a cancer research group that conducts studies for the National Cancer Institute. Your doctor is a member of ECOG-ACRIN 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 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:

- The study sponsors, NCI and ECOG-ACRIN, and the drug company supporting the study, Bristol-Myers Squibb or any drug company supporting the study now or in the future. This would include any organization helping the company with the study now or in the future.
- 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 laboratory, Sysmex Inostics, which will be performing research testing if you agree to participate.
- 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.

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 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 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 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.

Optional sample collections for known laboratory studies and storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood 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.

Known future studies

If you choose to take part in this optional study, we would like to collect blood samples for research studies. The samples will be used by researchers to learn about how the study treatment affects your cancer.

If you choose to take part in this optional study, researchers are also requesting that you allow the storage of leftover blood samples for banking for future research projects. 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. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use.

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.

What is involved in this optional sample collection?

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

1. An additional four (4) teaspoons of blood will be collected from a vein at the following timepoints: Prior to Start of Treatment, Cycle 2, Day 1, Cycle 4, Day 1, Cycle 8, Day 1, and either Cycle 12, Day 1 or Discontinuation of Treatment. The blood will be collected at the same time as the blood collected for your clinical tests to monitor your health.
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.

Generally, hospitals will keep some of your tissue. This tissue may be used to help treat you 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 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 doctor, (*insert name of doctor for main trial*), at (*insert telephone number of doctor for main trial*), who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your doctor. This will not apply to 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 doctor, (*insert name of doctor for main trial*), at (*insert telephone number of 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 known future studies:

May we have samples of your blood for laboratory research studies?

- I agree that my samples and related health information may be used for the laboratory research studies described above.

YES NO

Samples for unknown future studies:

May we keep any blood samples leftover after the laboratory research studies for future research?

- My samples and related 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.

Participant's signature _____

Date of signature _____

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

Date of signature _____