Research Study Informed Consent Document

Study Title for Participants: Testing the combination of pevonedistat with chemotherapy for bile duct cancer of the liver

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
EA2187, "A Phase 2 Study of Pevonedistat in Combination with Carboplatin and Paclitaxel in Advanced Intrahepatic Cholangiocarcinoma," (NCT04175912)

Version Date: September 1, 2021

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 advanced intrahepatic cholangiocarcinoma that is no longer controlled with the first chemotherapy you tried.

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:

How well does treatment with the study drug, pevonedistat, stop your cancer from getting worse when taken alone and in combination with chemotherapy?

We are doing this study because we want to find out if this approach can control advanced intrahepatic cholangiocarcinoma (also known as bile duct cancer). For this type of cancer there is not a standard type of chemotherapy that is shown to be highly effective for this cancer once someone has already tried one type of chemotherapy. The usual approach is defined as care most people get for advanced intrahepatic cholangiocarcinoma.

What is the usual approach to my advanced intrahepatic cholangiocarcinoma?

The usual approach for patients with advanced intrahepatic cholangiocarcinoma is to first try a chemotherapy regimen containing a drug called gemcitabine (i.e. gemcitabine and cisplatin). This regimen is not FDA approved. After that therapy stops working there is no standard next line of chemotherapy for this cancer. Many patients try other types of chemotherapy, such as 5-flurouracil and oxaliplatin, but the benefit of this regimen has been quite limited. Patient with uncommon types of cholangiocarcinoma with microstallite invisibility or NTRK fushions should receive immunotherapy or targeted therapies.

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 only the study drug, pevonedistat, or you will get the study drug, pevonedistat, with carboplatin and paclitaxel. Carboplatin and paclitaxel are both FDA-approved for other cancers. Both treatments will be given until your disease gets worse, the side effects become too severe, or you decide to no longer participate.

After you finish your study treatment, your doctor will continue to follow your condition and watch you for side effects quarterly for 1 year and then every 6 months for years 2 and 3. This will be completed either through follow-up clinic visits or phone calls.

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 drugs may not be as good as the usual approach for your cancer at shrinking your cancer.

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.

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

- Anemia
- Constipation, diarrhea, nausea, and vomiting
- Tiredness, fever
- Loss of appetite
- Muscle aches
- Dizziness, headache
- Shortness of breath
- Numbness or tingling in arms and/or legs

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

Benefits

This study is not likely to help you. However, it may help the study doctors understand how this study drug works. This study may help the study doctors learn things that may help other people in the future.

There is evidence that pevonedistat treatment is effective in shrinking your type of cancer. It is not possible to know now if the study drugs will stabilize your disease faster 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 not a sudden unsafe change, risk to your health, etc. 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 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 determine whether pevonedistat alone or pevonedistat in combination with carboplatin and paclitaxel is more efficient in shrinking your cancer. The addition of pevonedistat to chemotherapy could shrink your cancer, but it could also cause side effects, which are described in the risks section below.

This study will help the study doctors find out how well pevonedistat shrinks your cancer when given alone and when in combination with chemotherapy. To determine this, the study doctors will be looking to see which of the two approaches shows better results.

Carboplatin and paclitaxel have already been approved by the FDA to treat other cancers.

There will be about 52 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 get pevonedistat through a vein in the arm over 60 minutes on days 1, 3, and 5 of the cycle. Each cycle will have 21 days. You will continue to receive treatment until your disease gets worse, the side effects become too severe, or you decide to no longer participate.

  There will be about 26 people in this group.

- **Group 2**

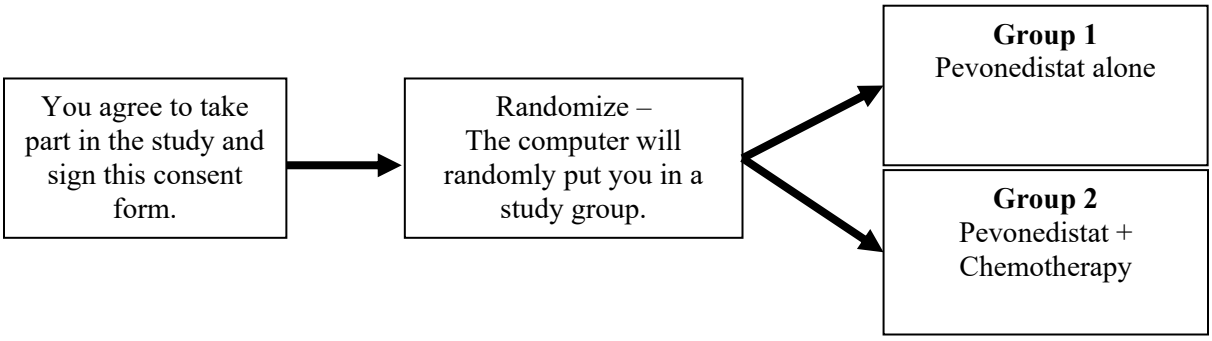
  If you are in this group, you will get pevonedistat through a vein in the arm over 60 minutes on days 1, 3, and 5 of the cycle. On day 1 you will receive carboplatin and paclitaxel through a vein in the arm. Carboplatin and paclitaxel are chemotherapy drugs that are FDA-approved for other types of cancer. Each cycle will have 21 days. After 4 cycles you and your doctor may decide to continue pevonedistat without chemotherapy.

You will continue to receive treatment until your disease gets worse, the side effects become too severe, or you decide to no longer participate.

There will be about 26 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.

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:

- Physical exams done more frequently during the first cycle of treatment,
- A blood or urine pregnancy test if you are a woman of child-bearing potential,

Your study doctor will need to use some of the tissue left over from your biopsy when you were diagnosed with cancer. This sample is a required part of the study. The study team will assess this tissue to evaluate how effective treatment is in relation to the presence of certain proteins in your tumor. You and your study doctor will not get the results of this testing.

Any residual material from this analysis will be requested for banking for future unknown research. To permit the use of your leftover material, please refer to the consent questions below under the "Optional Studies" section of this document.The study team will also request any results of genetic testing done on your tumor before going on the clinical trial. These tests are considered standard of care. These tests look for genetic mutations that occur

in tumors that help us learn about the biology about your cancer. We will use these results to help us identify other genetic markers that may predict benefit from the study drug, pevonedistat. You and your study doctor will not get the results of this testing.

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 drugs may not be as good as the usual approach for your cancer at shrinking 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 study 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 4 months after you have completed the study.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Side Effect Risks

The drugs 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 drugs.

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 and Group 2 – Possible side effects of pevonedistat are listed in the tables below.

Possible Side Effects of Pevonedistat

(Table Version Date: July 10, 2020)

COMMON, SOME MAY BE SERIOUS In 100 people receiving MLN4924 (Pevonedistat HCl), more than 20 and up to 100 may have:
• Diarrhea, nausea, vomiting • Tiredness, fever • Loss of appetite • Pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving MLN4924 (Pevonedistat HCl), from 4 to 20 may have:
• Anemia which may require blood transfusion • Infection, especially when white blood cell count is low which may cause painful and frequent urination • Bloating, constipation • Sores in the mouth which may cause difficulty swallowing • Chills • Swelling of arms, legs • Cold symptoms such as stuffy nose, sneezing, sore throat • Bruising, bleeding • Dehydration • Dizziness, headache • Muscle weakness • Numbness, tingling or pain of the arms and legs • Feeling of "pins and needles" in arms and legs • Worry, confusion • Difficulty sleeping • Cough, shortness of breath, wheezing • Nose bleed • Fluid around lungs

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving MLN4924 (Pevonedistat HCl), from 4 to 20 may have:
• Increased sweating • Itching • Low blood pressure which may cause feeling faint

RARE, AND SERIOUS In 100 people receiving MLN4924 (Pevonedistat HCl), 3 or fewer may have:
• Abnormal heartbeat • Kidney damage which may cause swelling, may require dialysis

Study Group 2 – Possible side effects of Carboplatin and Paclitaxel are listed in the tables below. These drugs are part of the usual approach for treating this type of cancer:

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

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 • 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

Additional Drug Risks

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

The study drugs, pevonedistat, paclitaxel, and carboplatin could interact with other drugs. Certain other drugs can change how your body processes pevonedistat. This could decrease the effect of pevonedistat, or it could increase the side effects from pevonedistat. Your study doctor will give you a drug information handout and wallet card that lists these possible

interactions. Share this information with your family members, caregivers, other health care providers, and pharmacists.

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 6 months 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.
- the costs of getting the 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 pevonedistat while you take part in this study. However, you and/or your insurance plan will need to pay for the costs of preparing this study agent and giving it to you.

There are no costs to you or your insurance for the submission of the mandatory tissue specimen collected prior to study treatment.

There are no costs to you or your insurance for the baseline ECG that you will have prior to randomization.

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 sponsor and any company supporting the study now or in the future. This would include any organization helping the company with the study.
- 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 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.
- 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. This optional study will not benefit your health. The researchers leading this optional study 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 this optional study 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 this optional study. If you sign up for, but cannot complete this study for any reason, you can still take part in the main study.

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

Optional sample collections for known laboratory studies and/or 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, the leftover material that was sent by your doctor as part of the mandatory pre-trial tissue submission will be retained and banked for future unknown research. Storing samples for future studies is called "biobanking." 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 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. Any material leftover from the mandatory tissue specimen submitted for the planned research study (collected prior to treatment), described in the first part of this document, will be stored for future research. No additional tissue submission is requested.
2. Your sample 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?

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 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, (*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 sample that remains in the biobank will be destroyed or returned to your study 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 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 keep any leftover material from the tissue submitted for the mandatory lab research study described above?

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 _____