

PRINCIPAL INVESTIGATOR: Tim Greten, M.D.

STUDY TITLE: A Phase 2 Study of Pembrolizumab, a Monoclonal Antibody Against PD-1, in Combination with Capecitabine and Oxaliplatin (CAPOX) in Subjects with Advanced Biliary Tract Carcinoma (BTC)

STUDY SITE: National Institutes of Health Clinical Center

Cohort: Affected patient

Consent Version: 03/19/2020

WHO DO YOU CONTACT ABOUT THIS STUDY?

Tim Greten, MD, by phone at 240-760-6114 or email Tim.greten@nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to investigate whether Pembrolizumab given in combination with capecitabine and oxaliplatin (CAPOX) increases the time it takes for your disease to get worse. Pembrolizumab targets a protein on tumor cells called PD-1. PD-1 normally maintains the balance of the immune system. In cancer, PD-1 helps tumors evade detection and elimination by the immune system. Pembrolizumab may increase the immune system's ability to identify and destroy cancer cells.

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Oxaliplatin and 5FU-based Capecitabine are chemotherapy medications widely used to treat different types of gastrointestinal cancer.

Pembrolizumab, capecitabine and oxaliplatin are all approved by the Food and Drug Administration (FDA) to treat various types of cancer. However, none of the drugs has been approved for use in biliary tract cancer.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You are being asked to participate in this study because you have been diagnosed with previously treated biliary tract cancer that has spread to other parts of your body.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 19 people will take part in this study.

DESCRIPTION OF RESEARCH STUDY

Before you begin the study

Before you begin this study, you will need to have the following exams and tests to make sure you are eligible for this study. The exams and tests are part of regular cancer care. These tests will be done under a separate consent.

- A review of any past or current medical conditions, medicines you are taking and cancer history.
- Physical examination, including vital signs, height and weight
- Electrocardiogram (ECG) to evaluate your heart.
- Review of your symptoms and your ability to perform your normal activities.
- Imaging Assessments – either a computed tomographic scan (CT or PET) that produces a picture of your body using a small amount of radiation or magnetic resonance imaging (MRI) that uses a magnetic field to produce an image of your chest, abdomen and pelvis.
- You will have blood drawn (about 3 tablespoon) for:
 - routine blood tests to find out if you are anemic, have low blood counts, your blood is clotting normally and if your liver, thyroid, kidneys, and other organs are working well.
 - tests for HIV, Hepatitis B and Hepatitis C.
 - tests for tuberculosis if you have symptoms that indicate you might have the disease.
- Routine urine test.
- Pregnancy serum or urine test if you are a woman who can have children.
- You will be asked to provide a sample of your tumor from a previous surgery so that we may confirm your diagnosis. If you do not have one, you will need to have a biopsy of your tumor.

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During the study**Drug administration and schedule**

Pembrolizumab and oxaliplatin will be administered to you through an IV (intravenous catheter, a small plastic tube that is put into a vein, usually in your arm) on Day 1 of each cycle (1 cycle = 3 weeks) for 6 cycles (18 weeks). While taking oxaliplatin, you should avoid cold drinks and exposure to cold water or air, especially for the first 3 – 5 days after receiving it.

You also will start take orally Capecitabine on Day 1 of each cycle and continue for two weeks followed by one week without capecitabine treatment, for 6 cycles (18 weeks). Capecitabine should be taken with meals every 12 hours starting with the evening dose of on day 1 of each cycle and ending with the morning dose on day 14 of each cycle. If you need to take your capecitabine earlier than scheduled or you missed the dose, you can take it in the time period of +/- 4 hours of scheduled time. You will be given a Patient's Diary to complete for each cycle. In the diary, you will be asked to record date, time and missing doses. Please bring the diary with you at every study visit.

Beginning with cycle 7, you will have only Pembrolizumab infusions once every 3 weeks until your disease get worse.

Ongoing Procedures during each treatment cycle

While you are on the treatment, on the first day of every cycle you will have tests done:

- Physical exam and vital signs
- Review of your symptoms and your ability to perform your normal activities.
- Routine blood tests (about 3 tablespoons) to find out if you are anemic, have low blood counts, your blood is clotting normally and if your liver, thyroid, kidneys, and other organs are working well.
- Research blood tests (about 9 tablespoons).

Additional Procedures every 9 weeks:

- Imaging Assessments – either a CT scan or PET or MRI of chest, abdomen and pelvis

Research tests

In addition to the tests that we will conduct to determine whether you are having side effects or if you are responding to the study therapy, we will also collect samples from you for purposes of research only. These studies include:

- Blood samples to study the effects of therapy on your immune system will be collected during every cycle.
- Optional tumor biopsies: procedures using a needle to remove a piece of tissue or a sample of cells from your body so that it can be analyzed in a laboratory and is used to diagnose or evaluate the cancer. We may ask you to allow us to perform two biopsies: before start of the treatment and around day 1 of cycle 3, but these biopsies are optional and you will

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be asked to sign a separate consent if you agree to have them. Please see page 9 for the risks of biopsy.

- Genetic testing – Your tissue will help us study how genes might play a role in biliary tract cancer. The testing will be limited so to genes that are not known to cause diseases; therefore, we will not share the results of these research tests with you.

When you are finished taking the drugs (treatment)

You will be invited for follow up safety visit approximately 1 month after the last day you take the study drug. At these visits, you will have the following tests:

- Physical exam and vitals
- Review of your symptoms and your ability to perform your normal activities.
- Routine blood tests (about 3 tablespoons) to find out if you are anemic, have low blood counts, your blood is clotting normally and if your liver, kidneys, and other organs are working well.

After that, we will contact you by telephone or email yearly to determine your health status and to find out about any new cancer treatments that you have begun.

BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 4 months after you finish study treatment. In addition, male subjects should not donate sperm during the study and for 4 months after the last dose of study therapy. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

RISKS OR DISCOMFORTS OF PARTICIPATION

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

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss.

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

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Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.

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

- Tell the study doctor if you notice or feel anything different so they can see if you are having any symptoms.
- The study doctor may be able to treat some side effects.

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

What side effects or risks can I expect from being in this study?

Risk associated with Pembrolizumab

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.

Very Common. Out of 100 people who receive pembrolizumab, 20 or more people may have the following:

- Itching of the skin
- Loose or watery stools
- Cough

Common. Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

- Joint pain
- Rash
- Fever
- Back pain
- Pain in your belly
- Loss of skin color

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- Not enough thyroid hormone, so you may feel tired, gain weight, feel cold, or have infrequent or hard stools (hypothyroidism)
- Low levels of salt in the blood that may cause you to feel tired, feel confused, have a headache, have muscle cramps, and/or feel sick to your stomach (hyponatremia).

Uncommon. Out of 100 people who receive pembrolizumab, at least 1 but less than 5 people may have the following:

- Inflammation of the lungs, so you may feel short of breath and cough (pneumonitis).
- Too much thyroid hormone, so you may feel anxious, feel angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools (hyperthyroidism).
- Infusion reaction, where you may feel dizzy or faint, feel flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion.
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus (colitis).
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection (Severe skin reactions, including Stevens-Johnson syndrome/or toxic epidermal necrolysis).

Rare. Out of 100 people who receive pembrolizumab, less than 1 person may have the following:

- Inflammation of the nerves that may cause pain, weakness, or tingling in your hands and feet, and may spread to your legs, arms, and upper body, leading to severe muscle weakness and possible temporary paralysis (Guillain-Barré syndrome).
- Inflammation of the muscles, so you may feel weak or have pain in your muscles (myositis)
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels), so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and have vomiting that gets worse when you eat (pancreatitis).
- Inflammation of the eye, so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches (uveitis).
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, pain in the right side of your belly, yellow eyes and skin, and dark urine (hepatitis).
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness, or fainting (hypophysitis).

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- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, having joint, muscle, and belly aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan (adrenal insufficiency).
- Type 1 diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination, and weight loss. You are likely to need regular insulin shots.
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain (nephritis).
- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath, and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting (myocarditis).
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis).
- A condition that may make you feel weak and tired and may cause drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing (myasthenic syndrome/myasthenia gravis including exacerbation).
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs (sarcoidosis).
- Inflammation of the brain with confusion and fever. This may also include disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness (encephalitis).
- Inflammation of the spinal cord with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, and constipation (myelitis).

Additionally, since pembrolizumab was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of this side effect:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling (arthritis)
- Severe responses of the immune system that cause the body to attack its own blood cells, spleen, liver, lymph nodes, skin and brain. This may include fever, rash, inflammation of the liver, yellowing of the skin, an enlarged liver and spleen, low blood counts, and enlarged lymph nodes. The nervous system may also be affected and cause confusion, seizures, and even coma (hemophagocytic lymphohistiocytosis).

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- Changes in eyesight, eye pain, whitish patches on the skin and hearing loss (Vogt-Koyanagi-Harada syndrome).
- If you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GVHD), which may include diarrhea, skin rashes, and liver damage, after receiving pembrolizumab. Sometimes this condition can lead to death.
- If you have had a solid organ transplant (for example, if you have received a kidney or heart transplant), you may experience rejection of the transplanted organ. Your doctor will monitor you and should tell you what signs and symptoms you should report depending on the type of organ transplant that you have had.

Risk associated with Capecitabine**Very Common:**

- Swelling of the body
- Blisters on the skin
- Redness, pain or peeling of palms and soles
- Pain
- Diarrhea, loss of appetite, nausea, vomiting
- Sores in mouth which may cause difficulty swallowing
- Fever
- Anemia which may require blood transfusions
- Infection, especially when white blood cell count is low
- Bruising, bleeding
- Feeling of "pins and needles" in arms and legs
- Tiredness

Less Common:

- Blurred vision, dry or itchy eyes
- Muscle spasms, body aches
- Abnormal heartbeat
- Restlessness, irritability
- Swelling of face, fingers and lower legs
- Constipation
- Difficulty with balancing

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Rare:

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Difficulty speaking, walking or seeing
- Internal bleeding which may cause blood in vomit or black tarry stools
- Damage to the heart

Risk associated with Oxaliplatin**Very Common:**

- Anemia which may require blood transfusion
- Diarrhea, nausea, vomiting, constipation, loss of appetite
- Tiredness
- Bruising, bleeding
- Infection, especially when white blood cell count is low
- Numbness and tingling of the arms and legs
- Feeling of "pins and needles" in arms and legs
- Pain
- Fever, cough

Less Common:

- Blood clot which may cause swelling, pain, or shortness of breath
- Abnormal heartbeat which may cause fainting
- Hearing loss
- Dry eye, mouth, skin
- Swelling and redness of the eye
- Blurred vision with chance of blindness
- Visual loss
- Problem with eyelid
- Fluid in the belly
- Heartburn, passing gas
- Difficulty walking, opening mouth, talking, with balance and hearing, smelling, eating, sleeping, emptying the bladder

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- Swelling of the body which may cause shortness of breath
- Blockage of the airway which may cause shortness of breath, cough, wheezing
- Bleeding from multiple sites including vaginal bleeding, bleeding of the testis, or bleeding of the brain
- Internal bleeding which may cause black tarry stool, blood in vomit or urine, or coughing up blood
- Damage to organs which may cause shortness of breath
- Sores in throat or mouth which may cause difficulty swallowing
- Chills
- Swelling and redness at the site of the medication injection
- Liver damage which may cause yellowing of eyes and skin
- Kidney damage which may require dialysis
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Weight gain, weight loss, dehydration
- Dizziness, headache
- Changes in taste, voice
- Abnormal body movement including the eye and eyelid
- Stroke which may cause paralysis, weakness
- Inability to move shoulder or turn head
- Muscle weakness
- Seizure
- Worry, confusion, depression
- Increased urination
- Stuffy nose, shortness of breath, hiccups, sinus problems
- Scarring of the lungs
- Hair loss, itching, rash, hives
- Increased sweating, flushing, hot flashes
- High blood pressure
- Low blood pressure which may cause feeling faint

Rare:**PATIENT IDENTIFICATION****Consent to Participate in a Clinical Research Study**

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- Redness, pain or peeling of palms and soles
- Brain damage, Reversible Posterior Leukoencephalopathy Syndrome, which may cause headache, seizure, blindness

Risks from Blood collection:

Local pain, bruising, bleeding, blood clot formation, and, in rare instances, an infection might occur at the site where blood is drawn. There is also the possibility of dizziness or fainting while your blood is being drawn.

Risks from Biopsy:

This procedure usually causes only brief discomfort at the site from which the biopsy is taken. Rarely, infection or bleeding may occur at the needle site.

The tumor biopsy will be done by a specialist using a CT scanner to guide the biopsy needle into the tumor to ensure accuracy. To collect the research biopsies, you will be exposed to two CT scans. This radiation exposure is not required for your medical care and is for research purposes only. The amount of radiation you will receive in this procedure is 1.5 rem which is below the guideline of 5 rem per year allowed for research subjects by the NIH Radiation Safety Committee. The average person in the United States receives a radiation exposure of 0.3 rem per year from natural sources, such as the sun, outer space, and the earth's air and soil. If you would like more information about radiation, please ask the investigator for a copy of the pamphlet, An Introduction to Radiation for NIH Research Subjects.

POTENTIAL BENEFITS OF PARTICIPATION**Are there benefits to taking part in this study?**

The aim of this study is to find out whether the experimental treatment increases the time it takes biliary tract cancer to worsen. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

ALTERNATIVE APPROACHES OR TREATMENTS**What other choices do I have if I do not take part in this study?**

Instead of being in this study, you have these options:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

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Please talk to your doctor about these and other options.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you become pregnant
- if you have side effects from the treatment that your doctor thinks are too severe
- if your treatment is delayed for more than 28 days
- if new information shows that another treatment would be better for you
- if he/she decided to close the study

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Pine Pharmaceuticals, the Center for Cancer Research, NCI or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases **cannot** be recalled and destroyed.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to \$15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

The National Institutes of Health and the research team for this study are using therapies developed by Merck through a joint study with your researchers and the company. The company also provide financial support for this study.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along

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with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

We may put your research data in a large database for broad sharing with the research community. These databases are commonly called data repositories. These data repositories might or might not be located at the NIH. The information in this database could include but is not limited to genetic information, ethnicity and sex. If your individual research data is placed in one of these repositories, it will not be labeled with your name or other information that could be used to easily identify you, and only qualified researchers will be able to look at your data. These researchers must receive prior approval from individuals or committees to access the data.

In addition to the use and sharing of your specimens and data described above, we might remove any information from your specimens and data that can identify you such as name, address, or medical record number, and then use the specimens and data for additional research studies at the NIH or other places. If we do this, we might not contact you to ask your permission or otherwise inform you.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

Genomic Data Sharing

As part of this research study, we will put your genomic data in a large database for broad sharing with the research community. These databases are commonly called data repositories. The information in this database will include but is not limited to genetic information, race and ethnicity, and sex. If your individual data are placed in one of these repositories, they will be labeled with a code and not with your name or other information that could be used to easily identify you, and only qualified researchers will be able to access them. These researchers must receive prior approval from individuals or committees with authority to determine whether these researchers can access the data.

Summary information about all of the participants included in this study (including you) is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.

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NIH policies require that genomic data be placed in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. Someone will work with you to provide more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board

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When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain

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federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Tim Greten, M.D., gretentf@mail.nih.gov, 240-760-6114. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

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Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant

Print Name of Research Participant

Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR

Print Name of LAR

Date

Investigator:

Signature of Investigator

Print Name of Investigator

Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*

Print Name of Witness

Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.

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