PRINCIPAL INVESTIGATOR: Jeremy L. Davis, MD

STUDY TITLE: A Phase II Study of Intraperitoneal and Intravenous Paclitaxel Chemotherapy with Oral Capecitabine for Gastric Adenocarcinoma with Peritoneal Carcinomatosis

STUDY SITE: NIH Clinical Center

Cohort: Affected Patients

Consent Version: 06/01/2022

WHO DO YOU CONTACT ABOUT THIS STUDY?

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KEY INFORMATION ABOUT THIS RESEARCH

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). This section provides the information we believe is most helpful and important to you to in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

You are being asked to join this study because you have stomach cancer that has spread throughout your abdomen. Your study doctor thinks this study may be an option for you.

The purpose of this study is to find a better way to treat stomach cancer. We want to see if standard chemotherapy drugs given in a new way can help you live longer and delay the time that it takes for the cancer to get worse (progress).

Paclitaxel and capecitabine are used to treat several cancers including stomach cancer. Paclitaxel is usually given into the vein and capecitabine is given by mouth. In this study, you will receive paclitaxel through a vein and directly into your abdomen.

Paclitaxel, but not capecitabine, is approved by U.S. Food and Drug Administration (FDA) for treatment of stomach cancer. However, capecitabine is often used to treat stomach cancer because there is strong evidence that it is effective.

There are other drugs that could be used to treat your disease, and these can be given by your regular cancer doctor if you do not take part in this study. For example: cisplatin, abraxane and

docetaxel are some possible treatments that you could receive. These options are similar to the drugs being used in this study.

If you decide to join this study, here are some of the most important things you should know that will happen:

•We will perform tests (screening) to find out if you are able to take part in this study such as: complete physical examination, blood and urine tests, and imaging (such as CT, MRI, and PET scans).

•We will ask you to complete questionnaires and will collect samples (such as blood and tumor tissue) from you for research purposes, including genetic testing.

•We will review a sample of your cancer from a previous surgery to confirm your diagnosis of stomach cancer. If a sample of your cancer is not available, we will need to do a new biopsy.

•If you are a woman who can have children, you will not be able to participate in this study if you are pregnant. You will need to avoid becoming pregnant during your participation in this study.

•If you are a sexually active person with a partner capable of becoming pregnant, you and your partner will need to agree to use birth control if you want to take part in this study. It is important that your partner not become pregnant during your participation in this study.

If you are eligible to take part and decide to join this study:

•You will have an exploratory surgery procedure, called a laparoscopy. This is a surgical procedure that allows us to examine the inside of the abdomen, so we can see how much your cancer has spread. In this procedure, small cuts will be made into your abdomen and a thin tube with a light and a camera will be inserted. You will be given a medication so that you sleep through the procedure. You'll be admitted to the hospital to have this procedure and you will be discharged a day later.

You will also have a laparoscopy procedure done at the end of the first and second cycles of treatment, to find out whether or not the treatment has worked on the cancer in your abdomen.

•During the first laparoscopy, you will have an Intraperitoneal (IP) port inserted which involves placing a port under the skin on your abdomen, attaching a catheter to it and putting the catheter into your abdomen. This is what we will use to deliver the paclitaxel into your abdomen.

•You will begin treatment with paclitaxel which is given as an intravenous (IV) infusion. A small plastic tube is put into a vein in your arm and the medication is given once every three weeks. Paclitaxel will also be given through a tube directly into your abdomen, so the drug can reach your tumors directly. You will receive paclitaxel in the Oncology Outpatient Center every three weeks during the treatment portion of the study. These visits will take 4-6 hours.

•Giving paclitaxel directly into your abdomen is not an FDA approved procedure, which means the way we are giving you this medication is considered investigational.

•Capecitabine is taken by mouth. You will take capecitabine twice a day starting the evening of Day 1 and continue through the morning of Day 15 in a 21-day cycle. After 14 days you will enter a 7-day rest period.

•After you finish the first three cycles of treatment (one course), you will receive tests to see how you are doing and to see how your disease is responding. You may be able to receive up to two courses of therapy if your cancer has not worsened.

•You will be seen in the NIH Clinical Center by your study team every three weeks (Weeks 1, 4, and 7) while you are receiving treatment. After treatment, you will be seen on a less frequent basis and we would like to keep in touch with you for the rest of your life. This is described later in this consent.

As described later in more detail in this consent form, you may have side effects if you take part in this study. Some can be mild or very serious, temporary, long-lasting, or permanent, and may include death.

The most frequent side effects of paclitaxel are nausea, vomiting, diarrhea, low blood counts and difficulty swallowing. The most frequent side effects of capecitabine are swelling, blisters, redness, pain, diarrhea, sores, fever and anemia. Risks are explained in detail later in consent. Please talk to your study doctor or other members of the study team if have any questions regarding risks or alternative treatments.

Just as we do not know what side effects you might have, we cannot know if you may benefit from taking part in this study. If you do not receive any benefit, this study and the results from our research will help others in the future.

If you would rather just get standard chemotherapy for your disease, or if you do not want to undergo any laparoscopies, or to get chemotherapy in your abdomen, you should not join this trial.

You are free to stop participating in the trial at any time. If you decide to stop, the study doctor may ask you to agree to certain tests to make sure it is safe for you to stop.

The remaining document will now describe more about the research study. This information should be considered before you make your choice. 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.

The individual being asked to participate in this research study is not able to give consent to be in this study. Therefore, 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?

This is a research study. The main purpose of this study is to see if standard chemotherapy drugs given directly into your abdomen as well as by vein can help you live longer and delay the time that it takes for the cancer to get worse (progress).

WHAT WILL HAPPEN DURING THE STUDY?

Before You Begin the Study

You will have several tests performed to be certain it is safe for you to start this treatment, including:

- Medical history and physical exam
- You will provide a sample of your cancer from a previous surgery so we can confirm your diagnosis. If a sample is not available, we will need to do a new biopsy.

  You may receive conscious sedation before undergoing a biopsy, if needed, and you will be informed of the additional risks prior to undergoing the procedure. Conscious sedation is usually given to help someone relax and minimize discomfort. It can be given as a pill, a shot, an IV or even inhaled. You may have to wait up to an hour to start feel the effects depending on how it is given. Once it takes effect, you will be mostly awake, though relaxed or drowsy. You will be monitored throughout the procedure. If your biopsy will be done during laparoscopy (a minor surgery) you will be given general anesthesia instead, as indicated below in the section During the Study. The study doctor will let you know if this is the case.
- Vital signs
- Assess your ECOG performance status (ECOG measures your ability to perform your normal activities)
- EKG to check your heart
- Dietary assessment
- Routine blood (~7 tablespoons) and urine tests
- Pregnancy test (~1 teaspoon blood sample) if you are a woman who can have children.
- CT scan with or without PET scans
- Tests for Hepatitis B and C (~2 teaspoons)
- HIV testing (~1 teaspoon)

  As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. If you are infected with HIV an infectious disease specialist will decide if you can still participate in this study. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report HIV infection, and the importance of informing your partners at possible risk because of your HIV infection.

You will also be asked to co-enroll on the Surgical Oncology Program's tissue collection protocol 13C0176 ("Tumor, Normal Tissue and Specimens from Patients Undergoing Evaluation or Surgical Resection of Solid Tumors").

You will be removed from the study if you are found to be not eligible.

During the Study

Before you begin treatment, you may have the following tests and/or procedures. Some of these have already been explained at the beginning of this document:

Laparoscopy:

This is an exploratory surgical procedure that allows us to examine inside of the abdomen, so we can see how much your cancer has spread. You will be given general anesthesia (so that you sleep through the surgery) and will undergo an abdominal operation requiring an incision. General anesthesia may be given through an IV (intravenous catheter, a small plastic tube that is put into a vein, usually in your arm), a face mask, or through a tube in your nose or throat. The general anesthesia may make it difficult to think once you wake up after your surgery, but this is temporary. However, because a side effect of general anesthesia is that it may take longer to fully recover then it will feel like at the time, you should plan ahead of time not to make any important decisions for 24 hours after the operation has been completed.

The surgeon will make a small incision in your abdominal wall and insert a lighted camera into your abdominal cavity. The surgeon may also take small pieces of tissue, called biopsies, and fluid while examining the inside of your abdomen to check for tumors. If there is any leftover tissue after we have examined the biopsy sample to help us see if your cancer has spread, we may use the tissue for research purposes. You'll be admitted to the hospital to receive this procedure and you will be discharged a day later.

Intraperitoneal (IP) Port Placement:

During the laparoscopy, you will have an Intraperitoneal (IP) port inserted. This is what we will use to deliver the paclitaxel into your abdomen. We will remove the port and catheter at the end of the study or if you stop participating for any reason.

Esophagogastroduodenoscopy (EGD):

This is a test to examine the lining of your esophagus, stomach and the first part of your small intestine. You will receive this procedure only if your doctor decides that you need this test. A long, flexible tube with a camera on the end will be inserted through your mouth and into your stomach. This tube will be used to collect tissue samples from the lining of your stomach. We will apply a numbing agent to the back of your throat to reduce your discomfort and give you a medication to make you drowsy. Most people sleep through this procedure.

First Course of Study Treatment

Paclitaxel

You will receive the paclitaxel both through the IP port into your abdomen and through a regular IV into a vein on the first day of Week 1, Week 4 and Week 7. The treatment will be given in the outpatient center or on an inpatient unit and will last for about 4-6 hours. During this time, routine care such as vital signs, blood tests, and scans will be done if your study doctor thinks you need

them. For 2 hours after the paclitaxel is infused into your abdomen, you will be instructed to change your position every 15 minutes.

Capecitabine

Please take this drug for the first 14 days of the 21-day cycle by mouth twice a day and swallow it whole with water. You will not take this drug during the last 7 days of the 21-day cycle. You will be given a pill diary to take notes of your capecitabine intake.

After One Course (Three Cycles) of Treatment are Complete

After you complete one course of treatment (i.e., 3 cycles for a total of 9 weeks), we will perform CT/PET Scans and laparoscopy to see how you are doing and if your cancer has responded to treatment. During your laparoscopy we will also perform another biopsy from inside of your abdomen. We may use any leftover biopsy tissue for research purposes. Some abdominal fluid may also be collected for research purposes.

If your cancer has shrunk or has stayed the same, we will give you another course of treatment.

If your cancer has worsened, we will **not** give you any more treatment.

Second Course of Study Treatment

The second course consists of three more cycles (9 weeks) of paclitaxel and capecitabine given in the same manner as in the first course. During this time, routine care such as vital signs, blood tests, and scans will be done if your doctor thinks you need them.

After you complete the second course of treatment, we will perform CT/PET scans and laparoscopy again to see how you are doing and how the cancer has responded to the treatment.

Additional Research Testing

Quality of Life Questionnaire

You will be asked to complete Quality of Life questionnaires assessing your general well-being and function for research purposes throughout the study at the following times: once prior to your first course of study treatment, at the end of each treatment course you complete, and at each post-treatment clinical visit. It will take about 30 minutes to complete the questionnaire and will only be done if you can complete the survey in English.

If at any time you no longer want to complete the questionnaire you may do so. Your decision to participate or not to participate in completing the questionnaire will not have an effect on your treatment in the study.

Research Samples

We will collect samples (blood, abdominal fluid and tissue) from you for research purposes only on this study. Blood samples may be collected from you for research purposes prior to your first course of study treatment (~2 teaspoons), once during Week 3 (~1.5 teaspoons) and again during Week 6 (~1.5 teaspoons), and at the end of each treatment course you complete (~1.5 teaspoons). On the day you receive paclitaxel, we will take multiple samples over the course of 24 hours (~2.5 tablespoons total) starting from just before you receive the study drug.

Blood samples collected from you for research purposes will be used to study:

- The impact of the study treatment on your cancer and how it changes your tumors and your immune response.
- How the genes in your DNA help the treatment drugs to transport, target and attack your tumors.
- How your body processes the paclitaxel you are given.

Tumor tissue and abdominal fluid collected from you during your procedures will be used for research in order to:

- Determine how much of the study treatment has reached and accumulated in your tumors and what genetic changes the treatment has made in your tumor tissue and immune response.
- Identify the biomarkers associated with cancer cell progression to understand the molecular mechanisms of tumor development, growth, and response to treatment.
- Identify if the study treatment is effectively destroying your cancer.

All of your samples collected for research purposes on this study may be used to look for specific changes in the DNA in tumors that could be used to develop new ways of diagnosing and treating cancer. DNA (also called deoxyribonucleic acid) in the cells carries genetic information and passes it from one generation of cells to the next – like an instruction manual. Normal tissue contains the DNA (instructions) that you were born with, DNA in tumor cells has changed – or mutated – and we think that change in the DNA is what causes tumors to form and to grow. RNA (also called ribonucleic acid) carries the instructions from the DNA to the parts of your cells that make proteins.

To look at your DNA, we may do what is called "DNA sequencing." This is where we will do special tests in the lab to look at the sequence, or order, of how your DNA is put together. This is what makes you unique.

To determine which parts of the DNA have mutated, we will compare the DNA in your tumor cells to DNA from your normal cells. We will then analyze the results from similar tumors to see if there are any changes in the DNA that are common to a particular type of tumor.

However, you should know that the analyses that we perform in our laboratory are for research purposes only; they are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing or testing for routine clinical care. For these reasons, we will not give you the results of the research tests done on your research samples in most cases. There may be exceptions to what we share with you and this is described later in this consent form in the section for "**Return of Research Results**".

HOW LONG WILL THE STUDY TAKE?

End of Treatment Visit

After therapy is stopped, we would like to see you for a safety visit 30 days after your last dose of study drug. This visit will take about 8 hours.

Long-Term Follow-Up

After you finish the end of treatment visit described above, you will return to the NIH 3 months after the last dose of drug; then every 3 months for the first 2 years. After that, you will return every 6 months for the Years 3-5, and then every 6 months or yearly after 5 years (detailed below). Follow up visits may vary +/- 2 weeks for the first 2 years, and +/- 4 weeks thereafter.

Your follow-up visit will include physical exam, dietary assessment, labs, scans and Quality of Life questionnaire (for 5 years only) and each visit will take about 8 hours. It will take about 30 minutes to complete the questionnaire and will only be done if you can complete the survey in English.

If you are unable to come to NIH for your follow-up visit, you may visit your local physician for follow-up every 3 months for the first 2 years, every 6 months for Years 3-5 and then yearly, if felt to be appropriate by your study doctor. We may arrange for you to have certain needed tests done at outside labs for your follow-up, which may include scans to assess your disease and an electronic version of the questionnaire for our research. We may ask that you send the test results completed for your follow-up to us for our records. After your visit we would like to continue to touch base with you to check on how you are doing, either here at the Clinical Center or by phone or secure videocall/other NIH approved remote platform.

After 5 years, if you are not able to come to NIH (and no longer want to complete follow-up visits with your local physician for this study) we may contact you, for the rest of your life, to see how you are doing and if you started new cancer treatment. If your cancer did not respond to the therapy, or if at any time you let us know that you no longer want to return to the NIH or see your local physician for study visits, you will not need to return. Instead we will contact you by phone or videocall/other NIH approved remote platform to see how you are doing and if you started new cancer treatment.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

Approximately 74 people will participate in this study at the NIH.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the study doctor if you have any questions.

It is probable that you will experience some of the side effects listed below, but it is unlikely that you will experience all of them. You will be watched closely, and we will give you medicines to try and prevent or reverse the side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. In some cases, side effects can be serious, long lasting, or may never go away. We will tell you if we learn any new information that may affect your health, welfare, or decision to stay in this study. You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks Associated with Paclitaxel

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 • Decrease in white blood cells which increases risk of infection • 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

Risks Associated with Capecitabine

COMMON, SOME MAY BE SERIOUS In 100 people receiving Capecitabine, more than 20 and up to 100 may have:
• 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 • Anemia which may require blood transfusions • Infection, especially when white blood cell count is low • Bruising, bleeding

COMMON, SOME MAY BE SERIOUS In 100 people receiving Capecitabine, more than 20 and up to 100 may have:
• Feeling of "pins and needles" in arms and legs • Tiredness • Fever

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Capecitabine, from 4 to 20 may have:
• Blurred vision, dry or itchy eyes • Muscle spasms, body aches • Abnormal heartbeat • Restlessness, irritability • Swelling of face, fingers and lower legs • Dehydration, that when severe may lead to kidney damage • Constipation • Difficulty with balancing

RARE, AND SERIOUS In 100 people receiving Capecitabine, 3 or fewer may have:
• 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

Risks of Study Procedures

Blood Draws

Risks include temporary discomfort, pain, redness, bleeding, bruising, and swelling at the site where the needle is inserted, and/or very rarely inflammation/infection of the vein, which could require antibiotics. You may also experience dizziness, nausea, or rarely, fainting during blood taking. Please tell the study doctor if you do not feel well after having your blood 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. If received, the most common risks of conscious sedation last up to a few hours after being given and can include drowsiness, feeling slow or sluggish, low blood pressure, headache, and nausea. Tumor biopsy will be done by a specialist using the CT scanner or ultrasound to guide the biopsy needle into the tumor to ensure accuracy. We will give you more information about the risks of radiation during the CT guided biopsies on this study in this consent form below.

General Anesthesia

Risks of general anesthesia include temporary confusion and memory loss, although this is more common in the elderly, dizziness, difficulty passing urine, bruising or soreness from the IV drip, nausea and vomiting, shivering and feeling cold, sore throat due to the breathing tube.

Electrocardiogram (EKG)

This test evaluates your heart rate and rhythm by measuring electrical impulses from the heart through electrodes that are placed on the skin. You must lie down and be still without talking during the 5 minutes the EKG is being recorded. This procedure is associated with minimal discomfort.

Questionnaire

The questionnaire may contain questions that are sensitive in nature. You are asked to only answer questions that you are comfortable with.

Scans and Contrast

CT and PET scans are common standard imaging tests used in the diagnosis of cancer. The most common discomfort is the length of time a patient must lay still during a scan. Occasionally, a patient may become uncomfortable with the closed space of the machines. If this occurs, your doctor can order a medicine to help you relax during this scan. If a contrast agent (the special dye) is given with the scan there is a small risk of having a reaction to the contrast. In that small group of patients who have a reaction, the most common symptoms are nausea, pain in the vein where the contrast was given, a metallic or bitter taste in the mouth, and a warm or flushing feeling that lasts from 1-3 minutes. Rarely do these symptoms require any treatment. In very rare cases, people have had severe reactions that affect their breathing and heart rhythm. If you have had a reaction in the past, be sure to tell you doctor or nurse about it.

An IV catheter may need to be inserted for administration of the contrast agent or anesthetic. This can cause pain at the site where the IV is placed and carries a small risk of bruising or infection, or inflammation of the skin and vein with pain and swelling.

For oral contrast: You may experience vomiting, nausea, cramping, bloating, constipation or diarrhea after drinking the contrast.

What are the risks of radiation from being in the study?

During your participation in this research study, you will be exposed to radiation from 6 PET/CT scans as well as 3 CT-guided biopsies over the course of the first year. The amount of radiation exposure you will receive from these procedures is equal to approximately 9.6 rem. A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called “background radiation.” No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans, PET/CT scans and CT-guided biopsies that you get in this study will expose you to the roughly the same amount of radiation as 32.0 years' worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 1.0 out of 100 (1.0%) and of getting a fatal cancer is 0.5 out of 100 (0.5%).

You may not participate in this study if you are pregnant. If you are capable of becoming pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

Esophagogastroduodenoscopy (EGD)

- Slowing of breathing and abnormal heart rhythms from the medications used to make you drowsy.
- A tear in your digestive track – these are rare (3 in every 10,000 procedures) and are treated with antibiotics.
- Fever, ulcers, serious infection and scarring and narrowing of the esophagus.
- Bleeding from the GI tract.
- The contents of your stomach may be breathed into your lungs.
- Allergic reaction to the drugs given during the procedure.

Risks of Intraperitoneal Port Insertion

Intraperitoneal Port Insertion is a minimally-invasive procedure. The risks from this procedure and general anesthesia include:

- Pain
- Infection at the area of insertion or inside the abdomen.
- Rarely, the port may become blocked, displaced, or stop working and require a procedure to fix or replace it.

Risks of Laparoscopy

Laparoscopy is minor surgery. The risks from these operations, in addition to the risks of general anesthesia include:

- Pain
- Temporary slowing or stopping of bowel function, known as an ileus. This could take several days to resolve and may require that the tube in your nose that drains your stomach stay in place longer.
- This surgery may also cause changes in your bowel pattern, either constipation or diarrhea. Fluid may develop in your abdomen, known as ascites. This may go away on its own or may need to be drained if it becomes too uncomfortable.

- Rarely, this surgery may cause injury to organs in the abdomen such as the intestines, stomach, bladder and blood vessels. If this occurs you may require prolonged hospitalization or additional surgery.
- There may be an increased risk of wound healing or infection after this surgery because of the use of paclitaxel and capecitabine.

What are the Risks Related to Pregnancy?

If you are capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 3 months after you finish study treatment (the restricted period). If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus. You must tell the study doctor if your birth control method fails during the restricted period. If you think or know you have become pregnant during the restricted period, please contact the research team member identified at the top of this document as soon as possible.

If you are a sexually active person with a partner capable of becoming pregnant, it is important that your partner not become pregnant during the restricted period. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you think your partner has become pregnant during the restricted period, please contact the research team member identified at the top of this document as soon as possible. If you and your partner plan for your partner to become pregnant after the restricted period, please discuss this with the study team.

Privacy Risks Associated with Genetic Testing

It may be possible that genetic information from you could be used by law enforcement agencies or other entities to identify you or your blood relatives.

Psychological or Social Risks Associated with Return of Incidental or Secondary Findings

As part of the research study, it is possible that you could learn that you have genetic risks for another disease or disability. This may be upsetting and, depending on what you learn, might create a need to make challenging decisions about how to respond.

Although your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, learning your research results could mean something about your family members and might cause you or your family distress. Before joining the study, it may be beneficial to talk with your family members about whether and how they want you to share your results with them.

Protections Against Misuse of Genetic Information

This study involves genetic testing on samples. Some genetic information can help predict future health problems of you and your family and this information might be of interest to your employers or insurers. The Genetic Information Nondiscrimination Act (GINA) is a federal law that prohibits plans and health insurers from requesting genetic information or using genetic information. It also prohibits employment discrimination based on your health information. However, GINA does not

address discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease that has a genetic component.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

However, the potential benefit to you might be shrinking of your tumor or decrease in 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.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because what we learn in this study may eventually be used to treat others with your disease.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

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

- Choose to be treated with surgery, radiation or with other chemotherapy drugs.
- Choose to take part in a different study, if one is available.
- Choose not to be treated for cancer and instead receive comfort care to relieve symptoms.

You should discuss with your doctor your other choices and their risks and benefits.

DISCUSSION OF FINDINGS

New Information About the Study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of Research Results

When we are examining your DNA, it is possible that we could identify possible changes in other parts of your DNA that are not related to this research. These are known as "incidental medical findings".

These include:

- Changes in genes that are related to diseases other than cancer
- Changes in genes that are not known to cause any disease. These are known as normal variations.
- Changes in genes that are new and of uncertain clinical importance. This means that we do not know if they could cause or contribute to a disease or if they are normal variations.

Since the analyses that we perform in our laboratory are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing, the genetic changes that

we find may or may not be valid. Therefore, we do not plan to inform you of all of the genetic results of testing on your tissue and blood that is performed in our research lab. However, in the unlikely event that we discover a finding believed to be clinically important based on medical standards at the time we first analyze your results, we will contact you. This could be many years in the future. We will ask you to have an additional tube of blood drawn to verify the findings we have seen in our lab.

Once the results are available, we will offer to have you come to NIH (at our expense) to have genetic education and counseling to explain this result.

If you do not want to come to NIH, we will help you find a local genetic healthcare provider who can explain it to you (at your expense).

If you are not contacted, you should not assume that that you do not have any gene variants that might be related to a disease.

EARLY WITHDRAWAL FROM THE STUDY

Your doctor may decide to stop your participation in the study for the following reasons:

- if he/she believes that it is in your best interest
- if your disease worsens or comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- if you become pregnant
- if you do not follow the study rules
- if the study is stopped for any reason

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

After therapy is stopped we would like to see you for a safety visit 30 days after your last dose.

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.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will Your Specimens or Data Be Saved for Use in Other Research Studies?

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to use these specimens and data for studies other than the ones described in this consent form that going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding stomach cancer or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may

lead to development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

Will Your Specimens or Data Be Shared for Use in Other Research Studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your data. For example, if some research with your data has already been completed, the information from that research may still be used. Also, for example, if the data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the use and sharing of your data described above, we might remove any information from your data that can identify you such as name, address, or medical record number, and then use the 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.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. These researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

Will Your Genomic Data Be Shared Outside of This Study?

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.

As part of this study, we will put your genomic data in a large database which will be freely available to the public. These databases are commonly called data repositories. These data are intended for other researchers to use and learn from but anyone can gain access to them, including law enforcement. The information in this database will include but is not limited to genetic information, race, 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. This information when combined with information from other public sources could be used to identify you, though we believe it is unlikely that this will happen.

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.

How Long Will Your Data be Stored by the NIH?

Your specimens and data will be stored at NIH indefinitely.

Risks of Storage and Sharing of Specimens and Data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will I 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 I receive reimbursement or direct payment by NIH as part of my 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.

The NCI generally does not cover expenses during screening. If you are scheduled for and begin treatment 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 me 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 are 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 may 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.

CONFLICT OF INTEREST(COI)

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

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

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

Some of your health information, and/or information about your data, from this study will be kept in a central database for research. Your name or contact information will not be put in the database. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your data and health information. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you.

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 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

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 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, Dr. Jeremy L. Davis at 240-858-3731 or jeremy.davis@nih.gov. 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.

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 should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking participant or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate participant**

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: _____.