PRINCIPAL INVESTIGATOR:	Andrew M. Blakely, M.D.
STUDY TITLE:	Phase II Study of Intravenous and Intraperitoneal Paclitaxel and Oral Nilotinib for Peritoneal Carcinomatosis from Colorectal, Appendiceal, Small Bowel, Gastric, Cholangiocarcinoma, Breast, Ovarian, or Other Gynecologic Primary Cancer
STUDY SITE:	NIH Clinical Center
Cohort:	Affected Patient
Consent Version:	07/08/2024

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 in making your decision about participating in this study. Additional information that may help you decide can be found in other sections of the document. Taking part in research at the NIH is your choice.

You are being asked to take part in this study because you have peritoneal carcinomatosis, a term used to describe tumors that have spread to the lining of your abdomen from other cancers such as cancer of the appendix, colon (commonly referred to as the large intestine), small bowel (the small intestine), stomach, bile duct (specifically cholangiocarcinoma), breast, ovary, or other organs. Your peritoneal carcinomatosis is too widespread to be treated with surgery.

Standard chemotherapy drugs used in this study are paclitaxel, which is usually given through your vein (intravenous or IV) and nilotinib, which is given by mouth. The main purpose of this study is to see if this combination with paclitaxel given directly into your abdomen (i.e., intraperitoneal or IP) as well as by vein (i.e., intravenous or IV) can help reduce the size or number of tumors enough to make you a candidate for surgery. Intraperitoneal paclitaxel is often used clinically for the treatment of peritoneal carcinomatosis.

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: standard chemotherapy or targeted therapies are some possible treatments that you could receive. These options are somewhat similar to the drugs being used in this study but are not given directly into the abdomen.

If you would prefer other drugs or treatments, you should consider not joining this study.

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

- To find if you are a fit for the study, we will review your health history, including any previous scans (e.g., CT) of your chest, abdomen, and pelvis. We may need to repeat some of the scans if necessary. We will do physical exams, routine blood and urine tests, HIV testing, pregnancy test if applicable, a test of your heart (electrocardiogram/ECG), and review results from tissue samples biopsied before. We may have to collect a new sample of your tissue, biopsy sample that you might have given before or take a fresh biopsy. A diagnostic laparoscopy (the first laparoscopy on this study) will be performed to find out if we can treat your disease with surgery.

  A laparoscopy 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. 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 we find that you are a fit, and you choose to participate, you will begin study therapy.
- You will have another laparoscopy (the second laparoscopy on this study), like the one done at screening. During this second 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 be admitted to the hospital to have this procedure and you will be discharged a few days later.
- You will also have a laparoscopy procedure done at the end of the third and sixth cycles of treatment (the third and fourth laparoscopy procedures on this study), to find out whether or not the treatment has worked on the cancer in your abdomen.
- Study therapy will be given in cycles of 3 weeks (21 days) for 3 cycles (9 weeks, Cycles 1-3). After you complete 3 cycles (9 weeks), we will perform CT scans and a 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. A description of the research is found later in the consent in the Section titled “Additional Research Testing”. Some abdominal fluid will also be collected for research purposes. If your cancer has shrunk or has stayed the same, we will give you another 3 cycles (i.e., Cycles 4-6) of treatment. If your cancer has shrunk to the point of being able to be removed with surgery, we may discuss coming off treatment to undergo that surgery. If your cancer has worsened, we will **not** give you any more treatment. After you complete Cycles 4-6, we will perform CT scans and another laparoscopy to see how you are doing and how the cancer has responded to the treatment. If your disease is stable, or your disease is getting better, but your tumors still cannot be safely and completely removed with surgery, you can continue to receive treatment of oral nilotinib and only IV paclitaxel, until the disease

progresses or you experience adverse effects that necessitate stopping the therapy, or for up to one year.

- You will begin treatment with nilotinib, which is taken by mouth, 4 days before the laparoscopy and IP port placement (i.e., nilotinib on Days -4 to -1 with the surgery on Day 0) and every day after that for the rest of the cycles of treatment without a break. This medication should be taken by mouth twice a day and swallowed whole with water, on an empty stomach (at least 2 hours after or 1 hour before a meal). You will be given a pill diary to take notes of your nilotinib intake. You will not take nilotinib on the morning of your laparoscopy to minimize any risks with the medication used to help you sleep through the procedure. Your study doctor will remind you not to take nilotinib on the morning of your laparoscopy at a time closer to your procedure date.
- You will receive the paclitaxel both through the IP port into your abdomen and through a regular IV or IV port into a vein.
- IP paclitaxel will be given on the first day (Day 1) of each 3-week cycle. The infusion will be given for about 1 hour, but may be given over a total of 3 hours if your study doctor needs to slow the rate of the infusion drug if you experience side effects. You will receive the first infusion at the inpatient unit. All of the other infusions will be given in the outpatient center and will last for about 3-4 hours.
- IV paclitaxel will be given on Day 1 of the first 2 weeks of each cycle, except during the first week of Cycle 1 when it will be given on Day 2. The infusion will be given for about 1 hour.
- Before getting IV paclitaxel doses in Cycle 1, you will be given pre-medications to help lessen or prevent some side effects. If you do not have any side effects during Cycle 1, these medications may be stopped for other cycles.
- You may experience side effects from taking part in this study. Some can be mild or very serious, temporary, long-lasting, or permanent, and may include death. Examples of some of the side effects that you may have include: changes in blood counts (such as low white cells), gastrointestinal issues (such diarrhea, nausea, vomiting), rashes, infections, fatigue, and bleeding.
- You will be seen regularly during the study. You will have clinical, laboratory, and imaging tests to see how you are doing and to assess your disease. We will also collect required samples from you (including blood, tumor tissue, fluid from your abdomen) for both clinical and research purposes.
- After the study treatment has ended, you will need to be seen either at the NIH Clinical Center or by a local physician to assess your health about 6 weeks after stopping treatment, and then about every 3 months for the next 3 years.

If you join this study, you may have up to a total of 5 laparoscopy with biopsy procedures. It is important for you to understand that some of these procedures are for research only. You would not have these research procedures done if you were not part of this study. If you don't want these extra laparoscopy procedures, you should consider not joining this study.

We cannot know if you may benefit from taking part in this study. If you do not benefit, this study and the results from our research will help others in the future.

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 the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

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?

We are asking you to join this research study because you have peritoneal carcinomatosis, a term used to describe tumors that have spread to the lining of your abdomen from other cancers such as cancer of the appendix, colon, small bowel, stomach, bile duct, breast, ovary, or other organs. The tumors in your abdomen cannot be safely and completely removed with surgery (a procedure called cytoreductive surgery).

Standard chemotherapy drugs used in this study are paclitaxel, which is usually given through your vein (i.e., intravenous or IV) and nilotinib, which is given by mouth. The main purpose of this study is to see if this combination with paclitaxel given directly into your abdomen (i.e., intraperitoneal or IP) as well as by vein (i.e., intravenous or IV) can help reduce the size or number of tumors enough to make you a candidate for surgery. Intraperitoneal paclitaxel is often used clinically for the treatment of peritoneal carcinomatosis.

WHAT WILL HAPPEN DURING THE STUDY?

Before you begin the study

We will do the following tests or procedures to find out if you are a fit for the study. This is called screening. All of these tests or procedures are part of your regular care and may be done even if you are not being considered to join the study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- Medical history: A complete review of your medical history, including obtaining information about your diagnosis and previous treatments, and reviewing information about your other conditions. If you have medical records from another clinic or hospital, you will be asked to get copies of these records, or your study doctor may be able to request them on your behalf.
- Physical examination: This will include taking your vital signs (temperature, blood pressure,

heart rate, breathing rate), seeing how you function in your daily activities, any current symptoms of your condition and a review of all medications that you take.

- Routine blood tests (about 2 tablespoons) to check:
    - blood counts
    - blood chemistries
    - how well your blood clots
    - for HIV: 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 you may still be able to participate in this study. (If you are HIV-positive but are on antiretroviral therapy and have an undetectable viral load, you may be considered for this study after the study doctor's consultation with a NIAID physician.) 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.
- Routine urine analysis
- If you are capable of becoming pregnant, a pregnancy test (urine or about 1 teaspoon blood sample) will be done. You will not be able to participate if you are pregnant.
- A sample of tissue from any previous tissue biopsy will be tested at NCI to confirm your diagnosis, stage, and status of your disease. We may need to take a new sample if a previous sample is unavailable.
- We will measure the electrical activity and the function of your heart using an electrocardiogram (ECG).
- Laparoscopy: This is a surgical diagnostic procedure to examine the organs inside the abdomen. In this procedure, small incisions will be made and a thin tube with a light and a camera will be inserted into your abdomen. Some fluid may be collected to check on the status of your disease and immune system (abdominal fluid and about 3 tablespoons of blood). You will be given general anesthesia to help you sleep through the procedure.
    - 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.
- CT scan to evaluate your disease.
- You will also be asked to co-enroll on one other study so that any remaining tumor samples can be used for future research purposes: the Surgical Oncology Program's tissue collection protocol 13C0176 ("Tumor, Normal Tissue and Specimens from Patients Undergoing Evaluation or Surgical Resection of Solid Tumors").

If the tests show that you are not a fit, we will remove you from the study.

During the study

If the screening process showed that you are fit to participate in the study, and if you decide to take part, you will be asked to undergo:

Laparoscopy

As part of this study, you may have up to 4 more laparoscopy procedures in addition to the 1st laparoscopy procedure that you had as part of the screening for this study (a total of up to 5 laparoscopy with biopsy procedures overall). The total number will depend on how long you are in the study.

- The 2nd laparoscopy procedure on this study will be done to place a catheter in your abdomen (this is discussed more below in the section titled "Intraperitoneal (IP) Port Placement").
- The 3rd and 4th laparoscopy procedures will be done after the first 3 cycles of medication (9 weeks) and the next 3 cycles of medication (18 weeks).
- If you have more than 6 cycles of chemotherapy medication, we may ask if we can do another laparoscopy procedure (the 5th laparoscopy procedure) to see how your disease has responded to the chemotherapy medication.

As described above, each laparoscopy procedure will be done under anesthesia.

During the laparoscopy procedure the surgeon may take small pieces of tissue, called biopsies, and fluid while examining the inside of your abdomen to check for tumors. Normal tissue is obtained when cancer tissue is removed. 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 will be admitted to the hospital to receive this procedure and you will be discharged a 1-2 days later, or 3-4 days later when the intraperitoneal port is placed (see below).

Intraperitoneal (IP) Port Placement

During the second (2nd) laparoscopy of the study, 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, unless you prefer to leave it in place for other treatments on a different clinical study that might require the use of the catheter.

Study Medications

You will receive 2 medications: **nilotinib**- given as an oral medication, and **paclitaxel**- given both through the IP port in your abdomen and through a regular IV or port in your vein.

You will be given the medications in cycles of 3 weeks (21 days) for 3 cycles (9 weeks, Cycles 1-3). After you complete 3 cycles (9 weeks), we will perform CT scans and a laparoscopy to see how you are doing and if your cancer has responded. 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 will also be collected for research purposes.

If your cancer has shrunk or has stayed the same, we will give you another 3 cycles (i.e., Cycles 4-6) of treatment. If your cancer has shrunk to the point of being able to be removed with surgery, we may discuss coming off these medications to undergo that surgery.

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

The second set of 3 cycles (9 weeks, Cycles 4-6) of paclitaxel and nilotinib will be 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 Cycles 4-6, we will perform CT scans and another laparoscopy to see how you are doing and how the cancer has responded to the treatment.

After 6 cycles, if your disease is stable, or your disease is getting better, but your tumors still cannot be safely and completely removed with surgery, you can continue to oral nilotinib and only IV paclitaxel until your disease worsens or you experience intolerable side effects, for up to one year. You will continue to have research samples taken and CT scans performed for as long as your study therapy continues. A repeat laparoscopy may be performed to confirm a response or to confirm progression of disease.

Nilotinib: Please take this drug for 4 days before your first laparoscopy on this study and port placement (Days -4 to -1 with surgery on Day 0) and every day after that for the rest of the cycles of medication without a break. This medication should be taken by mouth twice a day and swallowed whole with water, on an empty stomach (at least 2 hours after or 1 hour before a meal). You will be given a pill diary to take notes of your nilotinib intake.

You will not take nilotinib on the morning of your laparoscopy to minimize any risks with the medication used to help you sleep through the procedure. Your study doctor will remind you not to take nilotinib on the morning of your laparoscopy at a time closer to your procedure date.

Paclitaxel: You will receive the paclitaxel both through the IP port into your abdomen and through a regular IV or port in your vein.

IP paclitaxel will be given on the first day (Day 1) of each 3 week cycle. The infusion will be given for about 1 hour but may be given over a total of 3 hours if your study doctor needs to slow the rate of the infusion drug if you experience side effects. You will receive the first infusion at the inpatient unit immediately after the catheter placement. All other infusions will be given in the outpatient center and will last for about 3-4 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 body position every 15 minutes.

IV paclitaxel will be given on Day 1 of the first 2 weeks of each cycle, except during the first week of Cycle 1 when it will be given on Day 2. The IV infusion will be given over about 1 hour. The IV infusion will be given in the inpatient unit immediately after the catheter placement, and all other times will be given in an outpatient center.

Before getting paclitaxel doses in Cycle 1, you will be given pre-medications to help lessen or prevent some side effects. If you do not have any side effects during Cycle 1, you will not receive these medications before future cycles.

Starting in Cycle 2, you will be given the IP and IV paclitaxel treatment doses one at a time on Day 1, so that we may be able to better determine the cause of any side effects that may occur during a specific treatment dose.

Certain medications that effect your heart rhythm or clearance of drugs from your body will need to be used with caution or avoided all together while you are participating on this study. If any physician other than the study team prescribes a medication for another condition, or you take any new over-the-counter medications, vitamins, or herbal supplements, you must tell us and check with us prior to starting. This is important because the interaction of some medications may cause serious side effects and/or may still be unknown.

You should also avoid grapefruit products as these may affect how your body processes the study medications. Your study team will discuss in more detail which medications to avoid during your study participation.

Assessments

The results from tests performed at screening will be shared with the study team. You might need to repeat some of those tests before you start on the medications. During the study, the following assessments will be done:

- Your medical history, including previous cancer treatments, any current or previous medications (prescription, supplement, and over-the-counter medicines), will be reviewed.
- A complete physical examination will be performed that will include your vital signs (blood pressure, pulse, body temperature, level of oxygen in your blood and respiratory rate) and evaluation of your ability to carry out daily activities.
- Routine blood (approximately 18 tablespoons) and urine samples will be collected. These samples will allow us to measure your liver and kidney function, red and white blood cells, platelets, electrolytes, and more.
- If you are capable of becoming pregnant, a pregnancy test (urine or about 1 teaspoon blood sample) will be done before you receive study therapy and before each scan. You will not be able to participate if you are pregnant or if you are nursing (including breast feeding) or have plans to nurse (including breastfeed) during treatment because we do not know how these medicines would affect your baby or your unborn child.
- Consultation with surgical oncology and medical oncology and other doctors as needed.
- Electrocardiogram (ECG) to measure the electrical activity of your heart.
- Questionnaires you will complete on a computer to assess your physical and mental health and quality of life. It will take about 20-30 minutes to complete and will only be done if you can complete the questionnaires in English. These will be completed 4 or 5 (if you continue treatment after 6 cycles) times during the study: before starting treatment, after 3 and 6 cycles of treatment, and at the end of treatment.
- Tumor imaging with CT scan (a series of x-ray images taken of parts of your body) of your chest, abdomen, and pelvis will be done to assess sites of your disease. These are performed

before you begin study therapy and every 9 weeks while you are on study therapy. After 6 cycles of therapy, these will be done every 12 weeks.

Additional Research Testing

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 (blood, abdominal fluid and tissue) from you for purposes of research only.

The samples collected for these studies include:

- Tumor biopsies will be taken during the time of each laparoscopy. Normal tissue is obtained when cancer tissue is removed.
- Blood samples (about 8 teaspoons each time) to learn more about how the study drugs affect your body, the cancer, and your immune system: to be collected before starting treatment, and at your laparoscopy after Cycle 3 and after Cycle 6.
- Fluid from your abdomen to learn more about how the study drugs affect your body, the cancer, and your immune system: to be collected before starting treatment, and at your laparoscopy after Cycle 3 and after Cycle 6.
- Blood (about 8 teaspoons overall), abdominal fluid, and tumor samples to see how much of the chemotherapy drugs are in your blood and tissue (pharmacokinetics studies): when starting treatment, and several times during the first 3 days of Cycle 1.

Cell cultures

Cell cultures may be created from samples of the tumor and normal tissue removed during your surgery for research purposes. These cell cultures may be used to:

- Grow cell groups (called organoid cell cultures) outside of the human body from your tumor and normal tissue in dishes. These grown cell groups can "live" for long periods of time and can act like small organs, which will help us better understand details of tumor cells nature, functions, and how tumors grow.
- Study detailed changes to cancer cells when exposed to commercially available cancer drugs using a precision analysis machine and pieces of the tissue removed during surgery or biopsy.

Genetics

All of your samples collected for research purposes on this study (such as the tumor and normal tissue) 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.

To look at your DNA, we may use do what is called "whole genome sequencing." This is where we will do special tests in the lab to look at the entire 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. To examine the tumor and normal tissue we may use several different techniques depending on the type of tissue we collect. These could include growing cell lines (cells which keep dividing and growing in the laboratory, sometimes for years allowing us to continually study those cells), xenograft studies (placing or growing cells in another animal, such as mice), and looking in detail at the parts of the genes that produce specific proteins.

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."

When you are finished with study treatment

When you finish the study treatment, we will ask you to come to the clinic for a safety follow-up visit about 6 weeks (between 4-8 weeks) after you finish treatment, and then about every 3 months for up to 3 years. If you are unable or unwilling to return to the Clinical Center for this visit, a request will be made to collect required labs from a local physician or laboratory. If this is not possible, we may call you to review any symptoms you may be experiencing. These visits will include:

- Reviewing your medical history, physical exam with vitals, having routine blood samples collected for analysis (which will total about 3 teaspoons), and review of any side effects or symptoms you may be experiencing.
- Completing questionnaires to assess your physical and mental health and quality of life.
- Tumor imaging with a CT scan of your chest, abdomen, and pelvis to assess sites of your disease for the 3 years of follow-up, or until your disease comes back or gets worse, whichever comes first.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for around 3.5 years.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have about 48 people start the study drugs at the NIH.

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

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.

- May not be able to take part in future studies.

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important things to know about side effects:

- 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, and some may never go away.
- Some side effects may make it hard for you to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. Your study doctor can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

Risks and side effects related to the treatment and the procedures on this study are identified below:

Risk 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 • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Sores in mouth which may cause difficulty swallowing • Diarrhea, nausea, vomiting • Pain • 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

Risk Associated with Nilotinib

COMMON, SOME MAY BE SERIOUS In 100 people receiving Nilotinib, more than 20 and up to 100 may have:
• Change in heart rhythm • Cough • Infection, especially when white blood count is low • Anemia, which may require blood transfusions • Bruising, bleeding • Diarrhea, constipation, nausea, vomiting • Pain • Swelling and redness of the throat and sinuses (might not be caused by infection), which may cause difficulty breathing and swallowing • Headache, fever, tiredness • Itching, rash • Increased sweating, especially at night

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Nilotinib, from 4 to 20 may have:
• Heart attack, which may cause chest pain, shortness of breath • Swelling of arms or legs • Bleeding from multiple sites, including the brain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Nilotinib, from 4 to 20 may have:
• Internal bleeding, which may cause black tarry stool or blood in vomit • Prior liver infection that returns, which may cause yellow eyes and skin • Muscle weakness, spasm • Hair loss

RARE, AND SERIOUS In 100 people receiving Nilotinib, 3 or fewer may have:
• Stroke, which may cause paralysis • Numbness and pain of arms and legs • Tumor lysis syndrome, which may cause kidney damage which may require dialysis

General Risk

Due to of the risk of arrhythmia (problem with the rate of rhythm of your heartbeat), please contact your study team of healthcare provider if you develop significant vomiting, nausea, or diarrhea, and be seen if you develop diarrhea with nausea or vomiting due to the risk of loss of important fluid and electrolytes.

Other Study Risks

Blood Collection

The possible side effects of drawing blood include pain, bleeding, bruising, dizziness, light-headedness, fainting and, on rare occasions, local blood clot formation or infection with redness and irritation of the vein. The amount of blood collected on this study will be a maximum of about 6 tablespoons at once, or about 17 tablespoons over 8 weeks.

Urine Collection

There are no physical risks associated with urine collection.

Electrocardiogram (ECG)

An electrocardiogram is a test that is performed while you lie still for about 5 minutes. It involves placing electrodes (small stickers that are attached to wires that go to the machine) on the chest and arms/legs and recording the electrical activity of your heart.

Other than possibly experiencing some minor skin irritation from the electrodes there are no anticipated risks related to complete the electrocardiogram. If you have a lot of hair on your chest, it may hurt a little bit when the stickers are removed.

CT Scans and Contrast

The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures showing the inside of your body. During the procedure, you will need to lie still on a table inside the CT machine. The table will move you in and out of the machine during the scan and you will

be instructed to hold your breath. The scan itself will only take a few minutes to complete, the entire visit will take about 30 minutes.

There is a chance of developing an allergic reaction from the contrast material, which may cause symptoms ranging from mild itching or a rash to severe difficulty breathing, shock or rarely, death. The contrast material may also cause kidney problems. The study doctors will do a blood test prior to the test to confirm that it is safe for you to receive the contrast.

For IV contrast: You may feel discomfort when the contrast material is injected. You may feel warm, flushed, get a metallic taste in your mouth or, rarely, may make you vomit or feel sick to your stomach.

The risks of an IV catheter include bleeding, 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.

Laparoscopy

Laparoscopy is a minor surgery. The most common risk are bleeding, infection, and damage to organs in the abdomen. Less common risks include complications from general anesthesia, inflammation of the abdominal wall, and blood clots. During the laparoscopy, peritoneal tissue will be biopsied. The likely side effects of peritoneal tissue harvest include discomfort or pain, redness, swelling, and/or bruising at the site.

Risks from 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.

Port Insertion

Intraperitoneal port insertion is performed at the time of laparoscopy. The most common risks are local discomfort from the port reservoir and infection of the skin around the port. Less common risks are scar tissue formation associated with the port catheter and/or chemotherapy administration via the port, bowel irritation, or abdominal pain associated with chemotherapy administration. Rarely, bowel obstruction or perforation can occur, which would likely require surgery to correct. Over time, the port may not work as well, which would preclude using it for additional therapy, and may need to be removed or replaced.

Questionnaires

We will ask you to complete questionnaires that will take approximately 20-30 minutes to complete. The questionnaires will ask you about your physical and mental health and overall quality of life. Some of the questions in the questionnaire may be upsetting or make you feel uncomfortable. You can skip any of the questions you do not want to answer, and you can stop at any time.

What are the risks related to pregnancy?

If you are able to become pregnant, we will ask you to have a pregnancy test before starting this study. You will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 90 days 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 study team as soon as possible.

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 up to 6 CT scans of your chest, abdomen and pelvis each year during this treatment. The amount of radiation exposure you will receive from these procedures is equal to approximately 6.6 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." This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans that you get in this study will expose you to roughly the same amount of radiation as 22 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 0.7 out of 100 (0.7%) and of getting a fatal cancer is 0.3 out of 100 (0.3%).

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 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 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 lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the treatment'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 of the knowledge gained from the results of the research studies.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could:

- Choose to be treated with surgery, radiation, or drugs already approved by the FDA for your disease.
- Choose to take part in a different study, if one is available.
- Choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

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 provide another sample to verify the findings we have seen in our lab. If the results are verified, you will be re-contacted and offered a referral to a genetic healthcare provider to discuss the results.

EARLY WITHDRAWAL FROM THE STUDY

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

- if your study doctor 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 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 therapy is being stopped.

If you are withdrawn from the study we would like to see you for a safety visit around 6 weeks after the last dose of medications you receive.

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. 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 can**not** be recalled and destroyed.

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 store and use these specimens and data for studies other than the ones described in this consent form that are 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 peritoneal carcinomatosis or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the 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 that are similar to this study 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 specimens and 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 specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

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.

How long will your specimens and data be stored by the NIH?

Your specimens and data may be stored by the NIH. When this study is closed, we will keep the data and samples for future research 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 specimens and 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.

PAYMENT

Will you receive any type of payment for taking part in this study?

You will not receive any payment for taking part in this study.

REIMBURSEMENT

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

On this study, the NCI will reimburse the cost for some of your expenses such as those for hotel, travel, meals. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

COSTS

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 are performed outside the NIH Clinical Center, you may have to pay for these costs.

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 specimen, 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 sample 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 NIH 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
- The study Sponsor, Center for Cancer Research, or their agent(s)

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

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 information that 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 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.

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. Andrew M. Blakely, M.D., 240-760-7647, andrew.blakely@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

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 subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

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: _____.