PRINCIPAL INVESTIGATOR: Anish Thomas, MD

STUDY TITLE: A Phase I/II Trial of EP0057, a Nanoparticle Camptothecin with Olaparib in Patients with Relapsed/Refractory Small Cell Lung, Bladder and Prostate Cancers

STUDY SITE: NIH Clinical Center

Cohort: Affected Patient

Consent Version: 09/26/2024

WHO DO YOU CONTACT ABOUT THIS STUDY?

Anish Thomas, MD, by phone at 240-760-7343 or email anish.thomas@nih.gov

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

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

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

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

WHY IS THIS STUDY BEING DONE?

The use of EP0057 (formerly known as CRLX101) in this study is experimental. EP0057 is a sugar molecule called cyclodextrin that is linked to a chemotherapy drug called camptothecin. Linked together, the combined molecule or "nanoparticle drug conjugate" travels through the bloodstream. Once inside the cancer cells, the chemotherapy drug is released from the combined carrier molecule.

Olaparib is a drug that may stop the cancer cells from repairing the DNA damage caused by chemotherapy. Olaparib has been approved by the FDA for use in some types of breast cancers,

prostate cancers, ovarian cancers and pancreatic cancers. This drug is considered investigational in this study.

This study is divided into three parts, Phase I, Phase II and Expansion cohorts (groups). The Phase I portion of the study is being done to test the safety of the combination of EP0057 and olaparib, and to determine the highest doses of these two drugs that can be given in combination safely in participants with a variety of cancers. During Phase II and in the Expansion cohorts, this study will analyze how effective this drug combination is in treating specific cancers: small cell lung cancer (SCLC) in Phase II and urothelial carcinoma and metastatic castrate resistant prostate cancer. As of August 2021, we are no longer enrolling participants with prostate cancer as treatment being commercially available for this type of cancer has slowed down accrual to the current study. We also stopped enrolling participants with urothelial carcinoma as of August 2022 due to low past accrual and availability of other more current treatment protocols.

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

You have been asked to take part in this study because you have been diagnosed with SCLC, urothelial carcinoma or another type of cancer that does not currently have an approved treatment.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 126 people may receive study drugs at the NIH.

DESCRIPTION OF RESEARCH STUDY

What will happen if you take part in this research study?

Before you begin the study

Before you begin this study, you will have several exams and tests to make sure you are eligible for this study. If you have had these tests done recently on another NIH protocol or outside of NIH, we will collect the records instead.

The following tests may be done or records collected:

- A medical history and physical exam
- Routine blood tests to check on your health status
- As part of this study, we will do blood tests to check for infections with HIV (the virus that causes AIDS), Hepatitis B and C (viruses that infect the liver). If you are infected with any of these viruses, you will be able to take part in this study if you are getting treatment for these diseases and if the virus cannot be found through blood tests. We will tell you what the results of blood tests mean, how to find care, how to avoid infecting others, how we report these infections, and the importance of informing your partners at possible risk because of your HIV or hepatitis infection.
- A pregnancy test for individuals who can have children (by blood or urine)
- Imaging to include:

  - Computed Tomography (CT): The CT scanner is a donut-shaped machine that uses x-rays to make computer pictures of the inside of your body. During the procedure, you will need to lie still on a table inside the CT machine. An MRI makes pictures of the inside of your body using strong magnets instead of x-ray energy.
  - Technetium-99 bone scan (only for participants with metastatic castrate resistant prostate cancer): The bone scan is a test using a special camera to check for any issues in your bones. It involves the injection of a radioactive substance (Technetium-99) which is detected by the camera.
  - Echocardiogram: An echocardiogram is a painless test using sound waves to take a picture of your heart. During this test, we will put some jelly on your chest. We will then put the ultrasound probe on your chest and take the picture. We may ask you to lay on your side to get a better picture. For some pictures, we may put the probe on the upper part of your abdomen and push down firmly. This can be uncomfortable. The scan takes about 30 minutes to complete.

- Electrocardiogram (EKG): An electrocardiogram (EKG) is a test that looks at electrical activity of your heart. You will need to lie still for about 5 minutes. We will place electrodes on your chest, arms, and legs. Electrodes are small stickers that are attached to wires that go to the machine. The signals are recorded by the machine. If you have a lot of hair on your chest, it may hurt a little bit to remove the stickers.
- We will confirm your diagnosis through medical records.

If we find you are not eligible, we will remove you from the study.

DURING THE STUDY

You will receive EP0057 intravenously (through a small plastic tube inserted into your vein) every 2 weeks (days 1 and 15) and olaparib by mouth twice daily on days 3-13 and days 17-26 (You will be given additional instructions about the timing of the doses on Days 13 and 26 each cycle) administered in 28-day cycles. You will continue to receive treatment until your disease no longer responds or you are no longer able to tolerate the drug.

You should take the olaparib at the same time each day with a large glass of water. A light snack (biscuits/ toast) is also recommended to help reduce nausea. You should swallow the tablets whole. You will be given a pill diary at the beginning of each cycle to fill out and bring back to the study nurse at the end of the cycle.

In the Phase I part of the protocol, the EP0057 and olaparib will be tested a lower dose level in the first group of participants. If none or only one of the participants experience intolerable side effects, the next group will be enrolled at the next highest dose level. This will continue until more than one person in a group has intolerable side effects or until the highest pre-planned dose has been reached. The maximum safe dose is set at the highest dose level in which no more than one of six participants experienced an intolerable side effect.

The maximum safe dose is now determined, and in the phase II and expansion portions of the study, up to 94 participants will be enrolled at that dose to evaluate the anti-cancer activity of EP0057 and olaparib in small cell lung cancer, urothelial cancer and prostate cancer.

If you experience side effects (described later in this consent) when taking EP0057 and/or olaparib, the dosage of these drugs may be adjusted to reduce the severity of your side effects. Also, subsequent doses may be delayed until you have time to recover. If the side effects are too severe, the doctor may decide to stop all further doses of EP0057 and/or olaparib.

During treatment, the health care provider will monitor you every 2 weeks. If your doctor believes that it is necessary, based on your symptoms, the physical exam will be performed more often than indicated. You may have blood drawn to assess blood counts, liver and kidney functions (about one and a half tablespoon at each timepoint). Please see the study chart for the schedule of the tests.

ADDITIONAL RESEARCH STUDIES

An important part of the research is to determine how your body and tumor responds to the combination of drugs. This will also include the genetic analysis of the tumor cells and your normal cells. To understand this, we will collect your blood (about 10 tablespoons over the course of the study), hair samples (if you are in the phase I cohort), saliva (if you are enrolled on expansion cohort) and tumor at different time points. Hair sampling is optional. Single hairs will be plucked from the scalp with forceps. Plucked hairs from eyebrows will be collected only if we cannot get hair from your scalp.

Biopsies will be performed only in SCLC participants who enroll in phase I and all participants in phase II and expansion cohorts. All biopsies are optional. If you agree to have the biopsies, these will be performed before you start treatment, on day 4 of cycle one, and if you stop responding to the drug or your disease worsens. If your doctor determines it is safe, we will obtain a piece of your tumor (biopsy) using a needle. This process will be guided by a CT scan. You will be given local anesthesia (numbing medicine). The biopsy will be taken through a needle put through the skin into your tumor. After the procedure the nurses will watch your blood pressure and other vital signs. The biopsy to be performed is exclusively for research purposes and will not benefit you. It might help other people in the future.

You may receive conscious sedation before undergoing a biopsy, if needed. Conscious sedation is usually given to help someone relax and minimize discomfort. It can be given as a pill, a shot, an IV (intravenous catheter, a small plastic tube that is put into a vein, usually in your arm) or even inhaled. You may have to wait up to an hour to start feeling 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.

WHEN YOU ARE FINISHED TAKING THE DRUGS (TREATMENT)

In the case that you have to stop receiving treatment, you will have a clinic visit approximately 4 weeks after you discontinue taking the study drugs, in which the health care provider will perform a physical exam and blood will be drawn. You will then receive follow-up phone calls from the study team every three months.

STUDY CHART

Day	What to do and what will happen to you
Before starting	Medical history and physical exam. Blood samples Echocardiogram and CT scan Pregnancy test if you can become pregnant. Tumor biopsy if you agree

Cycle 1

Day 1	Physical exam Blood samples Pregnancy test if you can become pregnant (may be obtained up to 3 days prior to Day 1). Hair samples (Phase I cohort only) First dose of EP0057 intravenously. EKG if your first study EKG was abnormal. *
Day 2	Blood samples (Phase I cohort only)
Day 3	Blood (Phase I cohort) Hair samples (Phase I cohort only) First dose of olaparib orally, starting today until day 13 (You will be given additional instructions about the timing of the doses on Day 13).
Day 4	Tumor biopsy if you agree. Blood samples (Phase I cohort only) Hair samples (Phase I cohort only)
Day 7	Blood samples for assessing blood counts (can be performed at local health care provider)

Day 15	Recording of any health problems, including side effects from the study drugs; Physical exam. Blood samples for assessing blood counts, liver and kidney functions Blood samples (Phase II SCLC cohort only) Second dose of EP0057 intravenously. EKG if your first study EKG was abnormal.
Day 17	Start olaparib orally, starting today until day 26 (You will be given additional instructions about the timing of the doses on Day 26).
Day 21	Blood samples for assessing blood counts (can be performed at local health care provider)
Day 28	Recording of any health problems, including side effects from the study drugs; Physical exam. Hair samples (Phase I cohort only) *

Cycle 2 and beyond

Day 1	Recording of any health problems, including side effects from the study drugs; Physical exam. Blood samples. Pregnancy test if can become pregnant (may be obtained up to 3 days prior to Day 1). EP0057 intravenously. EKG if your first study EKG was abnormal.
Day 3	You will receive a dose of olaparib orally, starting today until day 13 (You will be given additional instructions about the timing of the doses on Day 13).
Day 15	Recording of any health problems, including side effects from the study drugs. Blood samples will be collected for assessing blood counts, liver and kidney functions EP0057 intravenously. EKG if your first study EKG was abnormal.

Day 17	Olaparib orally, starting today until day 26 (You will be given additional instructions about the timing of the doses on Day 26).
Day 28	A CT scan will be performed after every 2 cycles
Day 28	Recording of any health problems, including side effects from the study drugs; Physical exam. Hair samples (Phase I cohort only) **

End of Treatment/ Follow up	
	Recording of any health problems, including side effects from the study drugs.; Physical exam. Blood samples Tumor biopsy if you agree. Follow-up phone calls every 3 months

* The EKG will be done 1-3 hours after the EP0057. It will only be required for the first 2 cycles.

** Hair samples may be collected any time after the last dose of olaparib but before the next dose of EP0057 between days 26-28.

BIRTH CONTROL

If you can bear children: If you are breast feeding or pregnant, you may not take part in the study because we do not know how these medicines would affect your baby or your unborn child. If you can become pregnant, you will need to use a highly effective form of birth control and your partner must use a condom before starting study treatment, during study treatment, and for 6 months after you finish study treatment.

You must have a negative pregnancy test prior to enrolling in the study.

Highly effective forms of birth control include:

- Total abstinence (when this is the preferred and usual lifestyle of the participant). Withdrawal and periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) are not acceptable methods of contraception.
- Sterilization:
    - defined as having had surgical bilateral oophorectomy with or without hysterectomy, total hysterectomy, or tubal ligation at least six weeks before taking study treatment. In case of oophorectomy alone, only when the

reproductive status of the participant has been confirmed by follow up hormone level assessment.
    - Vasectomy for at least 6 months prior to screening. The vasectomized partner should be the sole partner for that participant.
- Use of oral, injected or implanted hormonal methods of contraception or placement of an intrauterine device (IUD) or intrauterine system (IUS), or other forms of hormonal contraception that have comparable efficacy (failure rate <1%), for example hormone vaginal ring or transdermal hormone contraception. In case of use of oral contraception individual should have been stable on the same pill for a minimum of 3 months before taking study treatment

If you can father children: We do not know if using EP0057 or olaparib will affect sperm, but reproductive organ effects were observed in animal studies. Therefore, due to this potential risk, you should not get your partner pregnant during the study drug period and for 3 months following the last dose of study drug. Even if you are surgically sterilized (i.e. have had a vasectomy) you must use condoms and avoid sperm donation from the time of signing the informed consent form, and throughout the entire study drug treatment period, and for 3 months following the last dose of study drug.

If you or your partner become pregnant while you are receiving study drug or within 3 months (for participants who can father children) or 6 months (for participants who can bear children) after your last dose of study drug, you should notify the study doctor right away. The study doctor will ask to follow your pregnancy, or your partner's pregnancy to its outcome.

RISKS OR DISCOMFORTS OF PARTICIPATION

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

During the study you may have risks and/or discomforts from the study drugs and procedures as described below. You may experience some, none, or all of these risks and/or discomforts, and they may be mild, moderate, or severe. There is always the chance of a very rare or previously unknown risks and/or discomfort occurring. There is also the risk of death.

If you experience any risks and/or discomforts, whether they are listed below or not, you must tell your study doctor who may be able to give you medicine to ease the discomfort. In addition, if a severe reaction to a study drug occurs, your doctor may decide to reduce the amount of study drug you take, or maybe even withdraw you from the study. You will be monitored closely for all risks and/or discomforts.

RISKS FROM EP0057

One risk is that you may get a drug that does not help treat your disease or that makes your condition or disease worse. The investigational study drug, EP0057, contains a cancer chemotherapy drug known as camptothecin. The very common, severe risk from camptothecin alone is inflammation and bleeding in the bladder. This risk has occurred with EP0057, but has been reported as mild to moderate and has resolved within a few weeks. EP0057 may cause other risks or discomforts similar to other cancer chemotherapy because the drug affects rapidly dividing cells in your body, which can include both cancer cells and other normal cells.

The risks or discomforts from EP0057 can range from mild and reversible to severe, long lasting and possibly life-threatening. EP0057 is an investigational drug, so not all of the risks or discomforts are known at this time. You need to tell your doctor or a member of the study team immediately about any symptoms that you experience while taking part in the study.

The following risks and discomforts have been reported from previous and ongoing studies of EP0057.

VERY COMMON (>10% OF PATIENTS REPORTED):

- Low number of red blood cells that can cause tiredness and shortness of breath (anemia) If this becomes severe, you may need to come into the clinic or hospital to have a transfusion of red blood cells.
- Feeling tired or lacking energy (fatigue)
- Nausea
- Inflammation of the bladder (cystitis)
- Blood in the urine (hematuria)

COMMON (3-10% OF PATIENTS REPORTED):

- A decrease in white blood cells (specific type called neutrophils), which can lead to infection requiring antibiotic treatment and possibly hospitalization (neutropenia)
- Diarrhea
- Vomiting
- Dysuria (painful or uncomfortable urination, typically a sharp, burning sensation)
- Difficulty passing stool (constipation)
- Fever or chills
- A decrease in white blood cells (not specified by type) in blood (leukopenia)
- A reduction in platelets (blood cells that help the blood to clot), which can lead to bleeding requiring one or more platelet transfusions (thrombocytopenia)
- Numbness, tingling or weakness in hands or feet (peripheral neuropathy)
- Loss of hair (alopecia)
- Decreased appetite
- Presence of white blood cells in the urine (leukocyturia)
- Presence of protein in the urine, which may cause fluid retention (proteinuria)

UNCOMMON (1-2% OF PATIENTS REPORTED):

- Swelling or build-up of fluids in the extremities (peripheral edema)
- Muscle discomfort or pain (myalgia), joint pain (arthralgia)
- Altered taste
- Bladder spasm
- Blood in the urine and painful voiding (hemorrhagic cystitis)
- Increased need to urinate at night (nocturia)

- Decreased urine flow or incomplete emptying of bladder (urinary retention)
- Infusion related reaction (symptoms, such as skin rash or red areas on the skin (hives) that are intensely itchy (urticarial), fast heart rate, low blood pressure, coughing or breathing difficulties, are related to the drug administration and may range from symptomatic discomfort to fatal events)
- Shortness of breath (dyspnea)
- Urinary tract infection
- Increased ALT (a liver enzyme) in the blood
- Dehydration
- Hemoglobin Decreased
- Pain in the extremities (arms and legs)
- Abdominal pain
- Increased AST (a liver enzyme) in the blood
- Weakness (asthenia)
- Blood creatinine increased
- Chills
- Dizziness
- Increased need to urinate (micturition urgency)
- Abdominal distension
- Increased blood alkaline phosphate increased
- Bone pain
- Cough
- Indigestion (Dyspepsia)
- Flatulence
- High levels of sugar in the blood, if sugar in the blood is too high, it may require hospitalization or treatment (hyperglycemia)
- Abnormally susceptible or sensitive physiologically to a specific agent (as a drug or antigen) (hypersensitivity)
- Low potassium level in the blood (hypokalemia)
- Difficulty sleeping or falling asleep (insomnia)
- Lymphocyte count decreased
- Muscle discomfort or pain (myalgia)
- Urinary frequency (pollakiuria)
- Rash
- Puncture or hole in the last part of the small bowel (ileal perforation)
- Pinpoint, round spots that appear on the skin as a result of bleeding (petechiae)
- Infection in one or both of the lungs, symptoms vary from mild to severe, such as high fever, shaking chills, a cough with phlegm that does not improve or get worse, shortness

of breath, chest pain when breathing or coughing (pneumonia)

RISKS FROM OLAPARIB

VERY COMMON, MAY BE SERIOUS (In 100 people receiving olaparib, 10 or more people may be affected)

- Low red blood cell count (anemia) which may cause you to feel tired, weak, or have shortness of breath. In some instance, this decrease in red blood cell count may be serious and require blood transfusions (when you are given new blood or blood products from a donor).
- A decrease in white blood cells (specific type called neutrophils) with or without fever. In some cases, this decrease can be serious and lead to infection requiring antibiotic treatment and possibly hospitalization (neutropenia)
- A decrease in white blood cells in blood (leukopenia) which may be serious in rare cases
- Loss of appetite
- Dizziness
- Headache
- Altered taste (dysgeusia)
- Cough
- Shortness of breath
- Nausea or vomiting which may be serious in some cases (feeling sick or actually being sick). If required, you will be offered medication to control these symptoms.
- Diarrhea, which is frequent, loose water stools, which can cause dehydration and may require hospitalization and treatment with intravenous fluids. Although rare, severe and prolonged diarrhea can be life-threatening.
- Constipation
- Heartburn (dyspepsia)
- Fatigue (including feeling weak)

COMMON, MAY BE SERIOUS (In 100 people receiving olaparib, more than 1 but less than 10 people may be affected)

- A reduction in platelets (blood cells that help the blood to clot), which can lead to bleeding requiring platelet transfusions (thrombocytopenia)
- Lymphocyte (type of white blood cell that is part of the immune system) count decrease which may lead to an infection
- Inflamed and sore mouth (stomatitis)
- Upper abdominal pain
- Rash
- Blood creatinine increase (creatinine is a measure that tells us how well your kidneys are working). This may mean that your kidneys are not working well.

- A blood clot that starts in a vein (venous thromboembolism). These clots can also develop in deep veins in the arm, lower leg, thigh or pelvis and can in serious cases travel to the lungs.

UNCOMMON, MAY BE SERIOUS (In 1,000 people receiving olaparib, more than 1 but less than 10 people may be affected)

- Irreversible abnormal blood counts and bone marrow damage, which may lead to leukemia (myelodysplasia).
- Undesirable reactions produced by the normal immune system (hypersensitivity)
- Swelling that occurs just beneath the surface of the skin (angioedema)
- Skin irritation or inflammation (dermatitis)
- Increased red blood cell size and volume (mean cell volume increased)
- Cancer of the blood and bone marrow (the soft inner part of certain bones, where new blood cells are made), also called acute myeloid leukemia
- Embolism (blockage of an artery, typically by a clot of blood)
- Pulmonary embolism (blockage in one of the arteries in your lungs)
- Inflammation of the lung tissue (pneumonitis), which may cause new or worsening symptoms of shortness of breath. This may be serious or life threatening.

RARE, MAY BE SERIOUS (In 10,000 people receiving olaparib, more than 1 but less than 10 may be affected)

- Flat, firm, hot, red, and painful lumps that usually appear on the shins (erythema nodosum)
- Red blood cells that are larger than normal (anemia macrocytic)
- Decrease in the amount of red blood cells (hematocrit decrease)

RISKS YOU MIGHT EXPERIENCE OTHER THAN THE DRUG SIDE EFFECTS

Biopsy Risks

Risks associated with the biopsies, which are pain and bleeding at the biopsy site. Sometimes a CT scan may be needed to identify the right tumor to biopsy.

Radiation Risks

During your participation in this research study, you will be exposed to radiation from up to 3 CT guided biopsies and 9 CT scans. The amount of radiation exposure you will receive from these procedures is equal to approximately up to 12.3 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 CTs that you get in this study will expose you to roughly the same amount of radiation as up to 41 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 1.2 out of 100 (1.2%) and of getting a fatal cancer is 0.6 out of 100 (0.6%).

You may not participate in this study if you are pregnant. If you are able to become 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.

Risks from CT scans

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 you to receive the contrast.

You may also 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.

Blood Draw Risks

Risks associated with blood draw, which include pain and bruising, lightheadedness, and rarely, fainting. Up to 15 tablespoons of blood may be drawn at any visit, with no more than 55 tablespoons in an 8-week period.

Hair Collection Risks

Pain associated with hair collection.

Echocardiogram Risks

Other than mild discomfort during the test, there are no known risks to an echocardiogram.

Electrocardiogram Risks

Other than having some minor skin irritation from the electrodes, there are no known risks related to the EKG.

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 condition or disease that has a genetic component.

Conscious Sedation Risks

The common side effects of conscious sedation include drowsiness, delayed reflexes, hypotension, headache, and nausea. These are generally mild and last no more than a few hours.

INCIDENTAL FINDINGS

Your tissue (tumor and normal tissue) and blood that is collected will 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) are the molecules inside cells that carry genetic information and pass 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.

In order 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 all of the results from similar tumors to see if there are any changes in the DNA that are common to a particular type of tumor. In order 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), growing your tissue for a short time in culture in the laboratory and growing your tumor tissue in mouse models and looking in great detail at the parts of the genes that produce specific proteins. When we are examining these pieces of 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.

Some of your samples may be tested in a laboratory that is certified to perform genetic testing. If this happens, we will offer to share the results for these tests.

Some of the analyses will be performed in our laboratory and will be 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. Changes that we observe unrelated to our research may or may not be valid. Therefore, we do not plan to inform you of the 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 that could be clinically relevant, we will contact you to ask if you would like to provide another sample to be tested at a certified lab and meet with a credentialed genetics healthcare provider for genetics education and counseling (either in clinic or via phone conference). The genetics healthcare provider will explain to you the nature of the result, implications for you and your family members, the need to confirm the results with an outside certified laboratory, the time frame for analysis, and implications of results including risks, benefits, and limitations.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to see if this experimental combination treatment will cause your tumors to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. The knowledge gained from this study may help others in the future who have cancer.

ALTERNATIVE APPROACHES OR TREATMENTS

What other choices do I have if I do not take part in this study?

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

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

Please talk to your doctor about these and other options.

STOPPING THERAPY

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

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if you become pregnant
- if new information shows that another treatment would be better for you
- if you are permanently no longer able to provide consent

In this case, you will be informed of the reason therapy is being stopped.
You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to the pharmaceutical companies providing the drug or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the

NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases can**not** be recalled and destroyed.

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 but they do not need to report their personal finances to the NIH.

The National Institutes of Health and the research team for this study are using EP0057 provided by Ellipses and Olaparib developed by AstraZeneca through a joint study with your researchers and the company. The company also provides financial support for this study.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that it may be used for future research on any topic and shared

broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

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

Genomic Data Sharing

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

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

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

You will not receive compensation for participation in this study.

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

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

Will taking part in this research study cost you anything?

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

- If some tests and procedures 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 will not be provided or paid for by the NIH Clinical Center.

- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

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

- The 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, NCI) or their agent(s) or their agent(s)
- Qualified representatives from Ellipses, the pharmaceutical company who produces EP0057 and Astra Zeneca, the pharmaceutical company who produces olaparib.

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 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.

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, about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Anish Thomas, anish.thomas@nih.gov, 240-760-7343. 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: _____.