PRINCIPAL INVESTIGATOR: Anish Thomas, M.D.

STUDY TITLE: Phase I/II trial of PLX038 (PEGylated SN38) and Rucaparib in Solid tumors and Small Cell Cancers.

STUDY SITE: NIH Clinical Center

Cohort: Affected patient

Consent Version: 02/02/2023

WHO DO YOU CONTACT ABOUT THIS STUDY?

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

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 make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

You are being asked to take part in this study because you have small cell lung cancer or small cell cancer outside your lungs. You may also be asked to participate in the first part of the study only (see description below), if you have a solid tumor.

The purpose of this study is to find safe combination of PLX038 and rucaparib and see if this combination will cause your tumors to shrink.

The use of PLX038 in this study is considered investigational which means it has not been approved by the U.S. Food and Drug Administration (FDA) to treat cancer. However, the FDA has given us permission to use PLX038 in this study. PLX038 works by blocking a protein, called topoisomerase I. Cells need this protein to divide and grow. PLX038 blocks this protein so the cancer cells can't divide and grow.

Rucaparib has been approved by the U.S. Food and Drug Administration (FDA) for use in some cancers found primarily in women; however, it is not approved for small cell cancers. Rucaparib belongs to group of drugs called PARP inhibitors that target and block several pathways needed for cancer cells to grow and cause cancer cell to die.

There are other standard of care drugs and/or procedures that may be used to treat your disease, and these can be given to you by your regular cancer doctor if you are not in this study. For example: there is chemotherapy and radiation therapy. You may also participate in another clinical trial either at the Clinical Center (CC) or another institution. The treatment given in this study and the known possible side effects may or may not be significantly different than if you were to receive standard care or being in another clinical trial. For example: chemotherapy and

radiation therapy cause fatigue, hair loss, bruising and bleeding, infection, low blood cell counts. Immune checkpoint inhibitors may cause inflammation of the lung, intestines or liver, and kidney, heart, or problems of the nervous system. Any of these treatments can cause nausea, vomiting, diarrhea and rash.

PLX038 and rucaparib have similar side effects to those listed above: low blood cell counts, fatigue, nausea, vomiting, diarrhea, rash, changes in kidney and liver function blood tests.

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. If you are capable of becoming pregnant, you will need to use appropriate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry, for the duration of study treatment and up to 6 months after the last dose of the study drug (s). You must tell the study doctor if your birth control method fails while you are in the study. If you think or know you have become pregnant during the restricted period, please contact the research team member as soon as possible.

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

- First, we will perform tests to find out if you fit the study requirements. We will do standard blood tests and scans to test your health and see the status of your disease.
- In the first part of the study, called phase I, we want to find out what combination of PLX038 and rucaparib is safe to use. This safe combination will be used in the second part of the study (phase II) to determine if PLX038 and rucaparib will cause tumors to shrink. You cannot choose which part of the study to enroll in; enrollment will occur in sequential fashion, meaning that participants will enroll as they are screened and determined to be eligible.
- If you fit the study requirements and decide to take part, you will start your treatment with PLX038 and rucaparib. We will then send you home with a supply of rucaparib that you will need to take. We will need to see you at the Clinical Center every 3 weeks while you are receiving treatment. You will not generally need to stay in the hospital for this study. The only exception is possible admission for collection of blood every few hours at the beginning of treatment – on days 1, 4 and 6. Each visit should last no more than 8 hours.
- As described above and later in more detail in this consent form, you may have side effects if you take part in this study. Some can be mild or very serious, temporary, long-lasting, or permanent, and may include death. You will be seen regularly during the study. You will have clinical, laboratory, and imaging tests to see how you are doing and see how your disease is responding. We will also collect required samples from you (such as: blood, tumor tissues and hair) for both clinical and research purposes.
- After the study treatment has ended we would like to see you in the Clinical Center approximately one month later to check on your health. After that we are planning to contact you by phone or e-mail to learn about your health status, and to see how you are doing, for the rest of your life or until the study is stopped. If you stop treatment for

reasons other than worsening of your disease, we will continue to invite you for imaging studies approximately every 9 weeks until worsening of your disease. You can have these studies at home institution and send us the results.

This study may benefit you by shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Even if you do not benefit from this study, the results from our research will help others in the future.

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

The remaining document will now describe more about the research study. This information should be considered before you make your choice. Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

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

WHY IS THIS STUDY BEING DONE?

This is a research study. The purpose of this study is to find safe combination of PLX038 and rucaparib and see if this combination will cause your tumors to shrink.

We are asking you to join this research study because you have:

- A solid tumor (Phase I only)
  OR
- Small cell lung cancer or small cell cancer outside your lungs (Phase I or Phase II).

PLX038 is considered investigational which means it has not been approved by the U.S. Food and Drug Administration (FDA) to treat your cancer. PLX038 is designed to block a protein, called topoisomerase I. Cells need this protein to divide and grow. PLX038 blocks this protein so the cancer cells can't divide and grow.

Rucaparib has been approved by the U.S. Food and Drug Administration (FDA) for use in some cancers found primarily in women; however, it is not approved for small cell cancers. Rucaparib belongs to group of drugs called PARP inhibitors that target and block several pathways needed for cancer cells to grow and cause cancer cell to die.

WHAT WILL HAPPEN DURING THE STUDY?

For both phase I and Phase II, PLX038 will be administered to you by IV (through an intravenous catheter, a small plastic tube that is put into a vein, usually in your arm) on Day 1 of each cycle (1 Cycle = 21 days).

You will take rucaparib by mouth on Day 6 of Cycle 1 and continue for 14 days with the last doses on Day 19 followed by seven days without rucaparib treatment. You will continue this schedule of rucaparib dosing on days 6-19 of every 21 days cycle. If we have to shorten or lengthen the cycle for any reason, we will instruct you further on when to stop taking rucaparib.

Rucaparib should be taken 2 times a day. Try to space your doses out evenly throughout the day, so ideally, take a dose at 8 am and 8 pm. You may take the tablets with or without food. If you need to take your rucaparib earlier than scheduled or you missed a dose, you can take it in the time period of +/- 2 hours of the scheduled time. If you vomit after taking rucaparib, please, do not immediately take another tablet. You should simply proceed with next dose as scheduled.

If you have nausea or vomiting caused by rucaparib, we will give you ondansetron to prevent it. You will need to take ondansetron by mouth with small meal or snack approximately 30 minutes prior to each dose of rucaparib.

During each cycle, you will be given growth colony stimulating factor (G-CSF) at least 72 hours after PLX038 administration. G-CSF is a medication that stimulates the production of blood cells. This will help prevent and/or treat low white blood cells which is usually a risk associated with cancer treatment.

You will be given a Medication Diary to complete for each cycle. In the diary, you will be asked to record the date and time of each dose of rucaparib. You will also be asked to record missed doses. Please bring the diary with you at every study visit.

At each visit, please also bring empty bottles and any unused medication you may have.

Rucaparib may increase your sensitivity to sunlight. You should take all of the usual sun protection precautions when going outside. It is advised that you avoid excessive sun exposure, wear protective clothing (including wearing a hat and sunglasses), and use sunscreens regularly (sun protection factor 50 or greater).

If your doctor is convinced that you have unacceptable side effects caused by one of treatment drugs, this drug will be stopped, and you may continue treatment with the other drug if your study doctor finds that it is in your interest. Treatment will continue until you have unacceptable side effects (both drugs) or you are no longer benefiting from the study therapy.

Treatment and all study related procedures will be done during outpatient visits without planned hospitalization. However, we might still choose to keep your overnight if needed for blood collection and other situations that arise.

Before you begin the study

Before you begin this study, you will need to have standard clinical exams and tests to make sure you are eligible for this study. The exams and tests are part of regular cancer care. Most of these tests will be done under a separate protocol.

You will be asked to provide documentation to confirm your diagnosis. If documentation is not available, we will perform a biopsy (collect a sample of your tumor) to confirm your diagnosis.

We may also perform an additional blood test telling us about the status of a certain gene that affects how safe the study therapy might be for you. We may also perform an electrocardiogram (EKG – a record of your heartbeat) to evaluate your heart.

If treatment does not start within 28 days after enrollment to this study, some tests may need to be repeated.

During the study

Ongoing procedures before treatment and with every cycle:

- Physical examination, including weight and vital signs.
- Review of your symptoms, medications and your ability to perform your normal activities.
- Discussion of any symptoms you might be having
- Routine blood tests to find out if you are anemic, have low blood counts, and if your liver, kidneys, thyroid, clotting system and other organs are working well. About a tablespoon and a half may be collected at each timepoint.
- Pregnancy test if you are a woman who can have children.

Ongoing procedures before treatment and every 3 cycles:

- Imaging assessments/scans – either a CT (a series of x-ray images taken of parts of your body) or MRI (magnetic testing, which does not involve any radiation) of chest, abdomen and pelvis.

A computer tomography (CT) scan produces a series of x ray images taken of parts of your body.

Magnetic resonance imaging (MRI) uses a strong magnetic field and radio waves to take pictures of your body. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the cylinder. We will place soft padding or a coil around your head. You will be in the scanner about 30 minutes. You may be asked to lie still for up to 30 minutes at a time. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at any time.

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 from you for purposes of research only. The samples are being done to look at the effects of therapy on your immune system and markers of tumor activity, including collecting and testing tumor cells.

The samples included for these studies include:

- Blood samples to study:
  - drugs levels in your blood on day 1, day 6 and day 8 (optional) of cycle 1 and on day 1 of cycles 2-4 (up to a little more than 1 tablespoon at each timepoint).
- Blood and hair to study:
  - how well your tumor responds to treatment on day 1, 6 and 7 of cycle 1 and on day 1 of cycle 2 (hair samples).

- how your body responds to treatment on day 1, day 6, day 7 of cycle 1, on day 1 of cycle 2 and when your disease progresses (blood sample – up to 3 and a half tablespoons at each timepoint). Blood for certain tests may not be collected if no hair sample was obtained.

- Tumor biopsy:
  - We will ask you to provide samples of your tumors from previous surgeries or biopsies if available. We also may perform three optional tumor biopsies before treatment, on day 4 or 6 and between days 7 and 14 of cycle 1. Please see Risks from Biopsy section for the risks of biopsy. You will be asked to sign a separate consent each time you agree to have an optional biopsy. You can participate in the study even if you decide not to undergo the biopsy procedures. Samples will be used to study how well your tumor responds to treatment, all of your tumor genes and how well they are working.

I agree to participate in the additional research testing described above.

_____ Yes _____ No

Initials Initials

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

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

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

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

When you are finished taking the drugs (treatment)

Approximately 30 days after you have finished taking the study drug, you will be asked to return to Clinical Center for a safety follow up visit. At this visit, you will be asked questions about your health, get a physical exam and undergo blood tests.

If you have been taken off treatment for reasons other than worsening of your disease, you will continue to have imaging studies approximately every 9 weeks until worsening of your disease. You can have these studies at home institution and send us results.

If you are unable to return for these visits, we will obtain the information from you by telephone or e-mail.

Once you stop coming to Clinical Center for safety visits and your scans, we will call or e-mail you every 6 months to ask you about your general well-being.

HOW LONG WILL THE STUDY TAKE?

You will come for study treatments every 21 days until your disease gets worse or you have unacceptable side effects at which time we will stop treatment.

Visits will range from 4-8 hours in length.

After stopping treatment, we would like to see you in the NIH Clinical Center one month later and follow you after that for the rest of your life by telephone or e-mail.

If you stop treatment for reasons other than worsening of your disease, we would like to invite you for imaging studies approximately every 9 weeks until worsening of your disease.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have up to 65 people take part in this study.

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

The drug 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 be testing your blood and will let you know if changes occur that may affect your health.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last longer.
- Some side effects may be serious and may even result in death.

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

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

Risks of Rucaparib

VERY COMMON In 100 people receiving rucaparib, more than 10 may have:

• Nausea
• Feeling tired
• Low blood counts (red blood cells, white blood cells, and platelets). Sometimes fever occurs with the low blood counts. These low blood count effects may be more likely to occur after multiple cycles of treatment.
  o A low red blood cell count may make you feel tired or dizzy. If you feel dizzy while taking rucaparib, you should avoid potentially hazardous tasks such as driving or operating machinery.
  o A low white blood cell count puts you at higher risk for bacterial or viral infections. Having a high temperature or fever while your white blood cell count is low is a life threatening medical emergency and you must proceed to the nearest emergency room as soon as possible.
  o A low platelet count affects the ability of your blood to clot and could lead to bleeding events. Symptoms include but are not limited to easy bruising, prolonged bleeding from cuts, blood in stools or urine, or nose bleeding.
• A low phosphate level in your blood. Usually there are no symptoms but if the levels are critically low, you may notice trouble breathing, confusion, muscle weakness, and/or irritability.
• Increase in cholesterol. If your cholesterol increases significantly, your doctor may prescribe a medicine to lower your cholesterol level.
• Changes in kidney and liver function blood tests that may indicate a sudden decrease in your kidney or liver function. Changes in liver function blood tests can also indicate liver injury caused by various medications. These blood test changes will be evaluated by your study doctor along with any other side effects that you are experiencing as well as other test results.
• Changes in your sense of taste.
• Stomach-related effects such as constipation, vomiting, diarrhea, decreased appetite, stomach pain (epigastric pain), and indigestion.
• Difficulty breathing possibly from an inflammation of the lungs that may or may not be caused by a bacterial or viral infection.
• Dizziness
• Sensitivity to sunlight.
• Fever sometimes can occur independent of a low blood count.

VERY COMMON In 100 people receiving rucaparib, more than 10 may have:
• Difficulty sleeping • Constipation • Fatigue or weakness

FREQUENT In 100 people receiving rucaparib, more than 1 and less than 10 may have:
• Rash. Some rashes may be itchy, painful, or cause no symptoms at all. • Itchy skin • Infection. Low white blood cells may put you at risk for an infection that may lead to sepsis (chain reaction throughout your body which injures or damages tissues and organs) or shock (a sudden drop in blood pressure with loss of consciousness and/or possible seizures, including the possibility of death). • Redness, swelling, and pain on the palms of the hands and/or the soles of the feet. Sometimes blisters appear. • When a small amount of drug leaks out of the blood vessels, it damages the surrounding tissues. Symptoms may include tingling, burning, redness, flaking, swelling, blistering, and sores of the hands and feet due to the increased friction and heat your extremities are exposed to. If you experience these symptoms, apply ice packs and elevate hands and feet, then contact your study doctor immediately for treatment • Stomach cramps, loss of appetite, constipation, vomiting, inability to have a bowel movement or pass gas, swelling of the abdomen caused by a blockage in the intestines. • Blood in the urine. • Inflammation or sores along the inner surface of the mouth • You could have allergic reactions to the study drug, such as itching, skin rash, facial swelling, and/or a severe or sudden drop in blood pressure. A sudden drop in blood pressure could lead to shock with loss of consciousness and/or possible seizures, including the possibility of death. If you have any of the above symptoms, seek medical attention right away.

LESS FREQUENT In 100 people receiving rucaparib, up to 1 may have:
• Myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) have been reported in participants treated with rucaparib. MDS is a pre-cancerous condition where

LESS FREQUENT In 100 people receiving rucaparib, up to 1 may have:
the bone marrow is not as good at producing blood cells (red and/or white blood cells and/or platelets). People with MDS need transfusions (red blood cells and/or platelets) and/or other treatments. In some cases, MDS can progress to AML, which is a cancer of the bone marrow where more abnormal and immature white blood cells (also called blasts) are made than normal white blood cells. People with AML need treatment with chemotherapy and/or a bone marrow transplant. Participants may develop AML without first being diagnosed with MDS.

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Based on other research studies and animal studies, the following are potential risks that we will monitor:

- Embryofetal toxicity (risks to your unborn baby)
- An irregular heart rhythm that can be seen on an electrocardiogram related to a disturbance in how the heart's bottom chambers (ventricles) send signals
- Development of a new cancer

Risks from PLX038

COMMON
• Low white blood cells which can increase the risk of infection that may lead to sepsis (chain reaction throughout your body which injures or damages tissues and organs) or shock (a sudden drop in blood pressure with loss of consciousness, including the possibility of death). Having a high temperature or fever while your white blood cell count is low is a life threatening medical emergency and you must proceed to the nearest emergency room as soon as possible. • Low red blood cell count which can give you shortness of breath, weakness fatigue • A low platelet count which can cause easy bruising or bleeding • Diarrhea • Abdominal Pain • Inflammation (swelling and redness) of the large bowel (colon) • Decreased blood level of potassium • Dehydration

POTENTIAL SIDE EFFECTS BASED ON ANIMAL STUDIES:
• Diarrhea

- Nausea
- Vomiting
- Decreased appetite
- Hair loss
- Dark spots of the cornea, the transparent front part of the eye, which may cause loss of vision. Small spots appeared in the eyes of some monkeys that were administered PLX038. After stopping the drug, the spots may or may not go away
- Liver damage

RARE, AND SERIOUS

- Allergic reaction to the drug or one of the ingredients in the drug. An allergic reaction may include a rash, wheezing, shortness of breath, heart palpitations, swelling of the face and lowered blood pressure. Rarely, allergic reactions can be life threatening or can cause death.

Getting medical treatment right away may keep these problems from becoming more serious. Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Risks from Biopsy

This procedure usually causes only brief discomfort at the site from which the biopsy is taken. Risks of biopsy may include bleeding, injury to internal organs, and infection. Rarely, these complications from biopsy could result in hospitalization and require additional medical care. Risks of sedation will be described at the time of procedure.

Risks from Blood Collection

Side effects of blood draws include pain and bruising in the area where the needle was placed, lightheadedness, and rarely, fainting. When large amounts of blood are collected, low red blood cell count (anemia) can develop.

Risks associated with Hair Collection

You may feel some light pain and discomfort from hair collection.

What are the risks related to pregnancy?

If you are capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. For a portion of the study, you will need to use effective birth control methods and try not to become pregnant. Your study team will provide additional details on how long this will be required and what methods may be used. 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 while you are in the study. If you think or know you have

become pregnant during the restricted period, please contact the research team member identified at the top of this document as soon as possible. If you plan to become pregnant in the future, you must agree to use appropriate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry, for the duration of study treatment and for 6 months after treatment.

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

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

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

During your participation in this research study, you may be exposed to radiation from up to 5 CTs and 3 CT guided biopsies each year. The amount of radiation exposure from these procedures is equal to approximately 7.9 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 the roughly the same amount of radiation as 26.3 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 0.8 out of 100 (0.8%) and of getting a fatal cancer is 0.4 out of 100 (0.4%).

Risks from CT scans

If contrast dye is used, there is a risk for allergic reaction to the dye. If you are allergic to or sensitive to medications, contrast dye, iodine, or shellfish, please notify your study doctor. If you have had kidney failure or other kidney problems in the past, please notify your study doctor.

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.

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 include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer.

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

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

WHAT OTHER OPTIONS ARE THERE FOR YOU?

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

- choose to be treated with surgery, radiation or with 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.

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

DISCUSSION OF FINDINGS

New information about the study

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

Return of research results

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

These include:

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

Since the analyses that we perform in our laboratory are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing, the genetic changes that we find may or may not be valid. Therefore, we do not plan to inform you of all of the genetic results of testing on your tissue and blood that is performed in our research lab. However, in the unlikely event that we discover a finding believed to be clinically important based on medical standards at the time we first analyze your results, we will contact you. This could be many years in the future. We will ask you to 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 therapy for the following reasons:

- if your disease worsens or comes back during treatment
- if you become pregnant
- if you have side effects from the treatment that your doctor thinks are too severe
- if the PLX038 and rucaparib become unavailable
- if new information shows that another treatment would be better for you
- if the study is stopped for any reason

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

After the therapy is stopped, we would like to see you for a safety visit approximately one month after stopping therapy.

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

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

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

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to 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 cancer, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

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

_____ Yes _____ No

Initials Initials

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

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

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your 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.

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

Will Your Genomic Data Be Shared Outside of This Study?

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

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

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

How Long Will Your Specimens and Data be Stored by the NIH?

Your specimens and data may be stored by the NIH indefinitely.

Risks of Storage and Sharing of Specimens and Data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your 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.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

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

You will not receive compensation for participation in this study.

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

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

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

Will taking part in this research study cost you anything?

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

- If some tests and procedures 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.

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.

The NIH and the research team for this study are using PLX038 developed by ProLynx LLC through a joint study with your study team and the company. The company also provides financial support for this study.

Clovis Oncology, Inc. is providing rucaparib for this study to NIH without charge. No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested. However, there are some research partners not associated with the NIH working on this study who may receive payments or benefits, limited by the rules of their workplace

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 of National Cancer Institute.
- Qualified representatives from ProLynx LLC and Clovis Oncology, Inc., the pharmaceutical companies who produce PLX038 and rucaparib.

In most cases, the NIH will not release any identifiable information collected about you without your written permission.. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

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

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

Certificate of Confidentiality

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

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

The Certificate does not protect your information when it:

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

4. is disclosed with your consent.

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

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

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical 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.

POLICY REGARDING RESEARCH-RELATED INJURIES

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

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Anish Thomas, M.D., 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 to the oral should sign below if either:

1. **A short- form consent process only: 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: _____.