Research Study Informed Consent Document

Study Title for Participants: A Study Combining the Peposertib (M3814) Pill With Standard Chemotherapy In Patients With Platinum-Resistant or Ineligible Ovarian and Related Cancers With An Expansion In High Grade Serous Ovarian Cancer and Low Grade Serous Ovarian

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol P10324, A Phase I/Ib Dose Escalation Study of Pegylated Liposomal Doxorubicin (PLD) With Peposertib (M3814) in Platinum-Resistant or Ineligible Ovarian and Related Cancers with Planned Expansions in High Grade Serous (HGSOC) and Low Grade Serous Ovarian Cancer (LGSOC) (NCT04092270)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have ovarian cancer that has progressed (gotten worse) or recurred (come back) after receiving at least one prior line of chemotherapy that included a platinum-based chemotherapy (either carboplatin or cisplatin), and you have not yet received an anthracycline chemotherapy (either doxorubicin or pegylated liposomal doxorubicin) for treatment of your cancer.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

Is it safe and tolerable to combine the study drug peposertib (M3814) with the standard chemotherapy pegylated liposomal doxorubicin, and what is the best dose of peposertib (M3814) for this combination in women with recurrent ovarian cancer?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your ovarian cancer. The usual approach is defined as care most people get for ovarian cancer.

What is the usual approach to my ovarian cancer?

The usual approach for patients that have experienced a recurrence or progression of their disease who are not in a study is treatment with surgery, hormonal therapy, biologic therapy, or chemotherapy. Sometimes combinations of these drugs are used. There are several chemotherapy drugs approved by the FDA that are commonly used. When patients are treated with FDA approved drugs for recurrent ovarian cancer the time until their cancer next progresses is generally between 3 and 12 months. Your doctor can explain which treatment may be best for you. If your cancer is platinum sensitive, your doctor may recommend that you receive platinum-based chemotherapy or a PARP inhibitor based on your genetic makeup instead of joining this study. If this is your first platinum-sensitive recurrence or progression you may be foregoing treatment known to increase life expectancy. If this is your second platinum-sensitive recurrence or progression, you may be foregoing treatments which are known to be effective. You should discuss all available options with your doctor.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will be treated with intravenous (IV) pegylated liposomal doxorubicin in combination (PLD) with a pill therapy called peposertib (M3814). You will continue to receive the study drugs until your disease becomes worse, your study doctor believes it is no longer working for you, or you desire to discontinue the study drugs. You may choose to stop doses at any time.

After you finish doses on the study, your doctor will continue to follow your condition and watch you for side effects. You will be asked to return to clinic 30 days after you complete doses for a side effect assessment. If you stop doses before your cancer progresses, then you will be asked to continue to have imaging performed every 2 or 3 months until time of progression.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the combination of pegylated liposomal doxorubicin with peposertib (M3814) may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer. Combining the two study drugs, peposertib (M3814) with PLD, can result in greater side effects of those currently experienced by each drug individually.

There is also a risk that you could have side effects from the peposertib (M3814) and or chemotherapy.

These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- Possible side effects of pegylated liposomal doxorubicin (PLD):
  - Nausea and vomiting
  - Low blood counts
  - Hair thinning
  - Rash
  - Mouth sores
  - Discoloration of the urine to a red or orange color
  - Weakening of the heart muscle (rare)
  - Hand-foot syndrome (palmar-plantar dysesthesia)
  - Fever
  - Weakness, tiredness
  - Bruising, bleeding

- Possible side effects of peposertib (M3814) include:

There may be some risks that the study doctors do not yet know about. The combination of PLD and peposertib (M3814) could lead to heightened risks or a new side effects.

Benefits

There is some evidence in cell models and animal models that adding peposertib (M3814) to the usual approach of treatment with pegylated liposomal doxorubicin can shrink or stabilize ovarian cancer for longer than the usual approach alone. However, this is only laboratory data. We do not know if this will happen in people. It is unlikely that this combination will help you live longer than the usual approach alone. This study may help the study doctors learn things that may help other people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (NCI). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to test the safety and tolerability (side effects) of a drug called peposertib (M3814) in combination with pegylated liposomal doxorubicin. Pegylated liposomal doxorubicin has already been approved by the FDA for treatment of patients with recurrent ovarian cancer. Peposertib (M3814) has been tested in animals and patients with other types of cancer, but has not been tested in people with ovarian cancer before. This study tests different doses of peposertib (M3814) in combination with pegylated liposomal doxorubicin to see which dose is safest and most tolerable for people. There were 21 people who took part in the first part of this study (the dose escalation part), and up to another 28 will be taking part in the second part or the expansion part, which will further assess the safety of the recommended dose determined in the dose finding part.

Another purpose of the study is to determine if your cancer is shrinking or getting worse. This will be done using the usual standard of care procedures (radiographic imaging).

Another purpose is to check the level of the study drugs in your blood (Pharmacokinetics). In addition, another objective of the study is for genetic research to see if the study drug combination may work best in certain people and to measure for tumor cells in the blood.

What are the study groups?

There are two parts in this study, a dose escalation part and a dose expansion part. You are being asked to take part in the expansion part. The dose of the study drugs you receive will depend on when you enroll in the study.

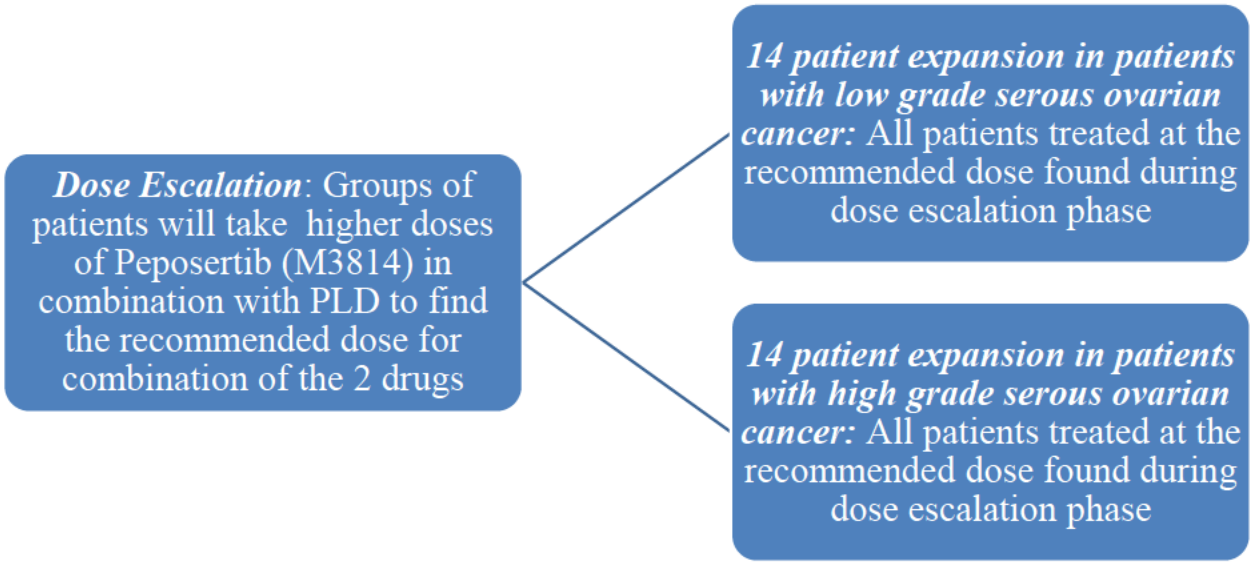
In the dose escalation part of this study, different people will get different doses of the study drug peposertib (M3814) by mouth, in combination with IV pegylated liposomal doxorubicin. The first 3 people taking part in this study will take the lowest dose twice each day for 28 days. If the drug does not cause serious side effects, the next group in the study will take a higher dose twice each day for 3 weeks and then not take any doses for 1 week. If the drug still does not cause serious side effects, the next groups in the study will take a higher dose twice each day for 1 week and then not take any doses for 3 weeks. The study doctor will watch each group carefully as they increase the dose. The doses will continue to increase for every new group until people have serious side effects that require the dose to be lower. Once this dose is found, the dose escalation is stopped. This first part has been completed.

In the dose expansion part of this study, the highest dose with manageable side effects will be given to 14 more people with low grade serous ovarian cancer and 14 more people with high grade serous ovarian cancer. This will help study doctors better understand the side effects that may happen with this drug and its effects in patients with high grade and low grade serous ovarian cancer. You are being asked to take part in this part of the study.

Dosing schedule: You will get pegylated liposomal doxorubicin through a vein in your arm on the first day of each cycle. Each cycle lasts 28 days. In combination with this, you will take peposertib (M3814) by mouth twice daily [redacted]. On treatment days, you will wait until you are in clinic to take the peposertib (M3814) pills. The peposertib (M3814) pills should be taken twice daily, approximately 12 hours apart. See the study calendar for more information.

You will not be able to get additional doses of the study drug (peposertib (M3814)). This drug is not approved by the FDA for treatment of your disease.

Study Schema:



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care. We will use them to carefully follow the effects of the study drug, including preventing and managing side effects.

These exams, tests, and procedures to monitor your safety and health include:

- Blood counts and blood chemistry to confirm the normal function of your organs.
- Pregnancy testing if you are a woman of childbearing potential to ensure you are not pregnant.
- Physical exams done weekly during the first two weeks of treatment.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

Your study doctor will need to use some of the tissue left over from a prior biopsy or surgery done for your cancer in the past. This sample is a required part of the study. This tissue will be used to see what genes carry mutations in your tumor tissue. You and your study doctor will not get the results of this testing.

Mandatory blood samples will also be taken for the study for the dose escalation and dose expansion groups.

If you are in the dose escalation group, the first blood sample will be collected before you begin the study drug and additional blood samples will be collected over multiple time points on the first day (9 total times over an 8-hour period) of dosing as well as day 2 (1 time), day 8 (9 times over 8 hours) and day 15 (1 time) of the first cycle of treatment. During the second cycle of treatment, blood samples will be collected over multiple time points on the first day (9 total times over an 8 hour period) of dosing as well as day 2 (1 time), day 8 (1 time) and day 15 (1 time). These blood samples will help the researchers check the level of the study drugs peposertib (M3814) and PLD in your blood at various time points (pharmacokinetics). We will also collect blood samples during Weeks 1 and 3 during Cycle 1 to see if the amount of tumor cells in your blood changes with time. A total of approximately 120 mL of blood (8 tablespoons) will be collected on the study.

If you are in the dose expansion group, the first blood sample will be collected before you begin the study drug and additional blood samples will be collected over multiple time points on the first day (a total of 3 times) of dosing as well as day 2 (1 time), day 8 (1 time), and day 15 (1 time) of the first cycle of treatment. These blood samples will help the researchers check the level of the study drugs peposertib (M3814) and PLD in your blood at various time points (pharmacokinetics). We will also collect blood samples during Weeks 1 and 3 during Cycle 1 to see if the amount of tumor cells in your blood changes with time. A total of approximately 40 mL of blood (2 tablespoons) will be collected on the study.

Researchers will obtain genetic material (DNA and RNA) from your tumor tissue and blood samples. Your DNA and RNA will be sequenced to evaluate changes in your DNA and RNA that may occur during treatment. Tumor and blood genetic studies are mandatory so that the results can provide as much information as possible to potentially help future patients. You and your study doctor will not get any results of this testing.

This study will use genetic tests that may identify changes in your tumor DNA (genes). Your genes carry information about you and your family, from the color of your eyes to health conditions for which you may be at risk, such as certain kinds of cancer.

Finding these changes would not affect your treatment in this study. However, they could affect your health in other ways. If the changes in your genes were inherited, the changes could also affect the health of your family members.

You and your family may want to know about any genetic test findings that may be important to your

health. You may use this form to grant us permission in advance to give this information to your doctor. If a genetic test result about you seems to be medically important and you have granted us permission to contact you, the following steps will occur:

1. Researchers will study the result further to decide if it may be medically important to you or your relatives.
2. The research laboratory that performed the genetic test will contact your doctor about the finding. The research laboratory, which will not have any identifying information about you, will provide your doctor with a code number assigned to your genetic test sample.
3. Your doctor will use the code number to identify you, and will then contact you about the medically important finding. Your doctor may make try to contact you several times.
4. You will require another genetic test to confirm the results. This test must be paid for at your own expense.
5. If it is confirmed that there are changes found that could cause health problems, then your doctor will discuss your options with you. We strongly suggest that you also talk to a genetic counselor. Genetic counseling services must be paid for at your own expense.

It is more likely, however, that you will not be contacted by us about a medically important finding. Even if we do not contact you, it does not mean that your genes do not contain changes that are important to your health. Researchers are always learning about new and medically important changes in genes and some information may be learned in the future. Researchers will only decide to contact you about genetic test results at the time your DNA (genes) is initially sequenced. You will not be contacted or consented for any research done using your samples in the future, and you will not receive any reports or information about any medically important findings learned in the future. Also, sometimes the meaning of genetic test results can be uncertain, and we may not know for sure what the results mean for your future health. Sharing an uncertain genetic test result with you could offer little benefit, no benefit at all, or could even be harmful.

Results from genetic testing will not be a part of your medical records, unless the results are confirmed by additional testing that you agreed to. See “Who will see my medical information?” for laws and risks in protecting your genetic information.

A patient study calendar is attached at the end of this document. It shows how often these tests and procedures will be done.

What risks can I expect from taking part in this study?

General Risks

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

You also may have the following discomforts:

- Spend more time in the hospital or doctor’s office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in some future studies.

The drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 3 months after you

have completed the study.

This study will use a sample of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Genetic Testing Risks

The genetic test used in this study will test your tumor and normal tissue for genetic changes and see if they relate to your response to the study drug. Changes found in your normal tissue may be passed down in families. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down.

Genetic tests of normal tissue can reveal information about you and also about your relatives. Your doctor will talk with you about what the tests results may mean for you and your family. He or she also may suggest you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for visits to a genetic counselor.

Side Effect Risks

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

There is also a risk that you could have other side effects from the study such as weakening of the heart muscle, the study doctor will check your heart strength using an echocardiogram.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects.
2. Some side effects may go away soon, some may last a long time, and some may never go away.
3. Some side effects may make it hard for you to have children.
4. Some side effects may be mild. Other side effects may be very serious and even result in death.

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

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

This study is looking at a combination of the usual drug used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

Drug Risks

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of M3814 (peposertib)
CAEPR Version 1.2, June 12, 2024

POSSIBLE, SOME MAY BE SERIOUS
[redacted]

Possible Side Effects of Liposomal Doxorubicin
Table Version Date: March 16, 2017

COMMON, SOME MAY BE SERIOUS In 100 people receiving Liposomal Doxorubicin, more than 20 and up to 100 may have:
• Rash • Redness, pain or peeling of palms and soles • Vomiting, nausea, constipation or diarrhea • Sores in mouth which may cause difficulty swallowing • Weakness, tiredness • Infection, especially when white blood cell count is low • Anemia which may require blood transfusions • Bruising, bleeding • Fever

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Liposomal Doxorubicin, from 4 to 20 may have:
• Hair loss • Heart attack or failure which may cause chest pain, shortness of breath, swelling of ankles, cough • Swelling and redness at the site of the medication injection • Loss of appetite • Blockage of the bowels • Headache • Dry eye • Reaction during or following infusion of the drug

RARE, AND SERIOUS In 100 people receiving Liposomal Doxorubicin, 3 or fewer may have:
• Hepatitis which may cause yellow eyes and skin

RARE, AND SERIOUS In 100 people receiving Liposomal Doxorubicin, 3 or fewer may have:
• Severe blood infection • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Cancer of bone marrow caused by chemotherapy

Other Possible Drug Risks

[redacted]

Additional Drug Risks

The study drug could interact with other drugs or food including making one or more of your medications or the study medications work better or worse. [redacted] before the first administration of peposertib (M3814) and while you are a part of this study. Your study doctor will give you a drug information handout and wallet card that lists these possible interactions. Share this information with your family members, caregivers, other health care providers, and pharmacists.

Rarely, there are problems getting enough supplies of the study drug. If that happens, your doctor will talk with you about your options.

Additionally, it is possible that addition of peposertib (M3814) to PLD will cause additional side effects to occur.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments (see Dose Expansion and Dose Escalation Calendars).
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.
- Write down in your medication diary when you take the study drug at home.

For women: Do not get pregnant or breastfeed while taking part in this study. In order to enter this study, if you are a woman of childbearing potential, you must have a pregnancy test to confirm that you are not pregnant. This test will be performed before you enter the study.

For all: If you are able to become pregnant, then you must agree to use adequate contraceptive precautions prior to study entry, for the duration of study treatment and for 6 months after completing study treatment. Also routine pregnancy testing will be performed during treatment in those patients able to become pregnant. Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 6 months after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your ovarian cancer. This includes:

- the costs of tests, echocardiograms, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- Pregnancy testing (only in women who are able to become pregnant)
- the costs of getting the peposertib (M3814) ready and giving it to you.
- PLD and associated costs of its administration
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The extra blood taken for research tests.
- The blood taken for pharmacokinetic testing, to check the level of the drug in your blood.
- Research testing done with the tissue from your previous biopsy

You or your insurance provider will not have to pay for the peposertib (M3814) while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical

treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

There are laws that protect your genetic information. However, there is a risk that someone could get

access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor [redacted].

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

Optional storage of sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Unknown future studies

If you choose to take part in this optional study, any of your tumor tissue or blood samples left over from the genomic sequencing will be stored. Storing samples for future studies is called "biobanking." The biobank is being run by the Nationwide Children's Hospital in Columbus, Ohio, and is supported by the NCI. Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use. Your genomic sequence will also be stored in a secure NIH database for future use. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we do not know what research may be done in the future using your tumor tissue and blood samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- Future research studies may include genomic sequencing.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample collection?

If you agree to take part, here is what will happen next:

1. Your samples will be stored in the biobank. The samples are leftover samples from your previously collected blood and tissue. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
2. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
3. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information. Only your study doctor and a few study researchers will have access to the master list linking the code numbers to names. The biobank and the genomic sequencing laboratory will receive your samples with the following information only: your sample code number; your age, race/ethnicity, and gender; your type of cancer; any previous treatments you received for your cancer; and the treatment you will receive for this current study.
2. Researchers who study your samples and information will not know who you are. They also must agree that they will not try to find out who you are. The researchers must be trained in the handling of private information. Any researcher who wants to study your stored samples and genetic information must apply and be approved to do so.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

There are no costs to you or your insurance for exams, tests, and procedures done for research purposes only; these include the biobanking of your specimen(s). You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, Dr. Rachel Grisham, at 646-888-4653, who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I need my tissue or blood samples to be returned?

Tumor tissue or blood samples that remain in the biobank can be returned if needed for medically necessary events or procedures to assure appropriate medical care, such as for DNA or RNA analysis. Specimens may also be returned if tissue is needed to determine eligibility for enrollment in a research protocol or clinical trial. Every effort will be made to facilitate medically necessary events or procedures to assure appropriate medical care for a patient with a serious or life-threatening illness.

Tumor tissue or blood samples and genetic material (DNA and RNA) that is no longer in the biobank or that has already been given to or used by researchers cannot be returned. No samples will be returned for matters related to patients needing or wanting genetic testing to determine medically important risks.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, Dr. Rachel Grisham, at 646-888-4653.

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for unknown future studies:

I agree that my left-over samples and related health information may be kept in a biobank for use in future health research.

YES NO

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled “yes”.

Participant's signature

Date of signature

Signature of person(s) conducting the informed consent discussion

Date of signature

Dose Escalation Group Calendar

		Cycle 1				Cycle 2				Cycle 3				Cycle 4 and beyond	
	Pre-Study	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	D1 of Subsequent cycles	Off Study Evaluation
Peposertib (M3814)[a]		X				X				X				X	
PLD[b]		X				X				X				X	
Pre-study procedures including informed consent, demographics, medical history, and height	X														
Concurrent medications	X	X----------X													
Physical exam, vital signs, weight, and assessment if how you perform everyday tasks and activities	X	X	X			X				X				X	X
Blood draws for complete blood count and general health status	X	X----------X													X
EKG (as your doctor indicates is necessary)	X														

		Cycle 1				Cycle 2				Cycle 3				Cycle 4 and beyond	
	Pre-Study	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	D1 of Subsequent cycles	Off Study Evaluation
Assessment of the size, shape, and position of the heart	X													Assessment will occur every 6 months or as your doctor indicates is necessary	X
Side effects evaluation		X----------												----------X	
Medical imaging scans for tumor measurements	X	Measurements taken every 8 weeks. After 6 months of treatment, this may increase to 12 weeks.													
Blood or urine collection for pregnancy test	X					X[f]				X[f]				X[f]	
Blood collection for research purposes to check the level of study drugs in your blood (Pharmacokinetics)		X[c]	X[d]	X[e]		X[g]	X[h]	X[i]							
Collection of tissue from your previous biopsies	X														
Blood collection for research purposes		X		X											

		Cycle 1				Cycle 2				Cycle 3				Cycle 4 and beyond	
	Pre-Study	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	D1 of Subsequent cycles	Off Study Evaluation

a: Peposertib (M3814): Dose as assigned, taken orally twice a day.

b: PLD: Dose: 40mg/m^2 IV

c: Blood collection will happen at various time points on Day 1 and 2.

d Blood collection will happen at various time points on Day 8.

e Blood collection will happen on Day 15.

f: If you are able to have children, you will take the pregnancy test at the start of each cycle.

g: Blood collection will happen at various time points on Day 1 and 2.

h: Blood collection will happen on Day 8.

i: Blood collection will happen on Day 15.

Dose Expansion Group Calendar

		Cycle 1				Cycle 2				Cycle 3				Cycle 4 and beyond	
	Pre-Study	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	D1 of Subsequent cycles	Off Study Evaluation
Peposertib (M3814)[a]		X				X				X				X	
PLD[b]		X				X				X				X	
Pre-study procedures including informed consent, demographics, medical history, and height	X														
Concurrent medications	X	X----------X													
Physical exam, vital signs, weight, and assessment if how you perform everyday tasks and activities	X	X	X			X				X				X	X
Blood draws for complete blood count and general health status	X	X----------X													X
EKG (as your doctor indicates is necessary)	X														

		Cycle 1				Cycle 2				Cycle 3				Cycle 4 and beyond	
	Pre-Study	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	D1 of Subsequent cycles	Off Study Evaluation
Assessment of the size, shape, and position of the heart	X													Assessment will occur every 6 months or as your doctor indicates is necessary	X
Side effects evaluation		X----------X													
Medical imaging scans for tumor measurements	X	Measurements taken every 8 weeks. After 6 months of treatment, this may increase to 12 weeks.													
Blood or urine collection for pregnancy test	X					X[f]				X[f]				X[f]	
Blood collection for research purposes to check the level of study drugs in your blood (Pharmacokinetics)		X[c]	X[d]	X[e]											
Collection of tissue from your previous biopsies	X														
Blood collection for research purposes		X		X											

		Cycle 1				Cycle 2				Cycle 3				Cycle 4 and beyond	
	Pre-Study	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12	D1 of Subsequent cycles	Off Study Evaluation

a: Peposertib (M3814): at the recommended dose, [redacted]

b: PLD: Dose: 40mg/m^2 IV

c: Blood collection will happen at various time points on Day 1 and 2.

d: Blood collection will happen on Day 8.

e: Blood collection will happen on Day 15.

f: If you are able to have children, you will take the pregnancy test at the start of each cycle.