Research Study Informed Consent Document

Study Title for Participants: Testing the combination of MLN4924 (pevonedistat), carboplatin, and paclitaxel in patients with advanced non-small cell lung cancer (NSCLC) who have previously been treated with immunotherapy

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10266, A Phase 2 Study of MLN4924 (pevonedistat) in Combination with Carboplatin and Paclitaxel in Advanced NSCLC Previously Treated with Immunotherapy (NCT# TBD)

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 non-small cell lung cancer (NSCLC) that did not respond to immunotherapy (type of treatment that makes parts of your immune system work harder to attack the cancer) and platinum-based chemotherapy (such as carboplatin-based chemotherapy).

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:

Can we lower the chance of your NSCLC growing or spreading by adding a new drug (study drug) to the usual combination of drugs (carboplatin and paclitaxel)? The study drug MLN4924 (pevonedistat) is not approved by the Food and Drug Administration (FDA) for the treatment of your disease).

Cancer treatment resistance occurs when cancers that have been responding to a therapy (shrinking or not spreading) suddenly begin to grow or they don't respond at all. In other words, the cancer cells are resisting the effects of the cancer treatment, such as the immunotherapy and carboplatin-based chemotherapy.

We are doing this study because we want to find out if this approach of adding MLN4924 (pevonedistat) to carboplatin and paclitaxel can lead to a cancer response again and whether this is better or worse than the usual approach for your NSCLC. The usual approach is defined as care most people get for NSCLC. Blood samples will be taken to evaluate how the drug works and tissue (if available) will be analyzed for markers that may help identify which patients may be more likely to benefit from the study drug.

What is the usual approach to my NSCLC?

The usual approach for patients with NSCLC who have progression of cancer following immunotherapy and carboplatin-based chemotherapy who are not in a study is chemotherapy with one drug alone such as docetaxel or pemetrexed, if not previously received, or gemcitabine. The drug combinations of Docetaxel and Pemetrexed as well as Docetaxel and Ramucirumab are FDA approved for this indication. Gemcitabine is not approved by the FDA for this indication, but may be used given its activity in NSCLC and approval by the FDA in combination with platinum as an initial treatment for advanced NSCLC.

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 receive the study drug MLN4924 (pevonedistat), the chemotherapy drug carboplatin, and the chemotherapy drug paclitaxel until your disease becomes worse, your study doctor believes it is no longer working for you, or you decide to discontinue study therapy. After you finish taking the study drugs, your doctor will continue to watch you for side effects and follow your condition with clinic visits every 3 months for 1 year, then every 6 months until 5 years from end of treatment if your NSCLC has not progressed. If your NSCLC does progress, your doctor will be follow your condition with phone calls every 3 months for 1 year, then every 6 months until 5 years from the time of progression.

At any time after the 4 cycles of therapy, your study doctor may continue with a) carboplatin, paclitaxel, and MLN4924 (pevonedistat); or b) continue carboplatin and MLN4924 (pevonedistat) without paclitaxel; or c) only observe you on study. You will take dexamethasone

(steroid) and anti-nausea medications to prevent or decrease the risks of side effects such as nausea and drug reaction.

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 the study drug MLN4924 (pevonedistat), the platinum-based therapy drug carboplatin, and the chemotherapy drug paclitaxel may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

There is a risk that you could have side effects from the combination of the study drugs MLN4924 (pevonedistat), carboplatin, and paclitaxel. These side effects may be worse and may be different than you would get with the usual approach for NSCLC.

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

- Anemia
- Constipation, diarrhea, nausea, and vomiting
- Tiredness, fever
- Loss of appetite
- Pain
- Dizziness, headache
- Shortness of breath
- Chills
- Anorexia
- Soreness
- Achiness
- Increase in liver enzymes

There may be some risks that the study doctors do not yet know about.

Benefits

It is unlikely that the study drug combination will work in everyone with your cancer or help you live longer. 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. This may mean slowly stopping the study drugs so that there is not a sudden unsafe change or risk to your health. 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.
- For women: 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 (National Cancer Institute [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 good and bad effects of the drug MLN4924 (pevonedistat). MLN4924 (pevonedistat) plus carboplatin and paclitaxel could shrink your cancer, but it could also cause side effects, which are described in the risks section. The study doctors hope to learn if MLN4924 (pevonedistat) plus carboplatin and paclitaxel will reduce the size of your cancer.

Carboplatin and paclitaxel have already been approved by the FDA to treat cancer, including NSCLC.

There will be about 25 people taking part in this study.

What are the study groups?

In this study, you will get the usual chemotherapy drugs carboplatin and paclitaxel. You also will get the study drug MLN4924 (pevonedistat).

Treatment schedule: You will get MLN4924 (pevonedistat) through a vein in your arm on the first, third, and fifth day of each cycle over 1 hour. You will get carboplatin through a vein in your arm over 30 to 60 minutes and paclitaxel over 3 hours through a vein in your arm on the first day of each cycle. Each cycle lasts 21 days. Beyond Cycle 4, you will continue to receive treatment as long as it is working and you are tolerating treatment. See the study calendar for more information.

Due to the potential for a drug reaction and nausea, dexamethasone will be given prior to receiving the first dose of MLN4924 (pevonedistat) and paclitaxel,. On days when only MLN4924 (pevonedistat) is given, patients will receive dexamethasone immediately before receiving treatment. Anti-nausea medications (will be given prior to chemotherapy and after chemotherapy to prevent or reduce the risk of nausea and/or vomiting.

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 treatment, including preventing and managing side effects.

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

- Physical exams done more frequently, on Days 1, 3 and 5 during the first cycle of treatment,
- A blood or urine pregnancy test at screening and on Day 1 of the every cycle, if you are a woman of child-bearing potential,
- At screening, an echocardiogram or radionuclide angiography, an imaging test that allows doctors to visualize your heart functions
- A blood sample and a urine sample to make sure you are healthy enough for this study.
- An EKG, which is an electrocardiogram, a test used to record the electrical activity of your heart, done at screening, if and when your disease gets worse, and at 4 weeks after the last dose of study drugs

This study will use genetic tests that may identify changes in the genes in your tumor DNA. 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 there are changes found that could cause health problems, then your study doctor will discuss your options with you.

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

- You will have a blood test on Day 1 before you begin treatment and 6 hours after you receive treatment. These tests will be used in the future to test who will benefit from treatment with MLN4924 (pevonedistat).
- You will have a blood test on Day 1 before you begin treatment, immediately at the end of treatment, and 3, 12 (optional), 24 and 48 hours after treatment. These tests will be used to determine how the study drug, MLN4924 (pevonedistat), is processed by your body.
- You will have blood tests done on Cycle 1 Day 1, Cycle 3 Day 1 and when your treatment stops working in order to collect blood for research on circulating tumor cells to predict whether researchers can tell if MLN4924 (pevonedistat) has the demonstrated effect on the DNA repair pathway.

A patient Study Calendar is attached at the end of this document. It shows how often these tests, exams, 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 MLN4924 (pevonedistat) may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

You also may have the following discomforts:

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

The drugs used in this study 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 4 months after you have completed the study.

Genetic Testing Risks

The genetic test used in this study will test your tumor and normal tissue for genetic changes. 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.

Blood Draw Risks

Some of the risks from drawing blood from your arm may include pain, bruising, light-headedness, and rarely, infection. For most people, needle punctures to get blood samples do not cause any serious harm.

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 drugs.

Here are important things to know about side effects:

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

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

- If you notice or feel anything different, tell your study doctor. 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 new combination of study drugs. This 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 MLN4924 (pevonedistat)
(Table Version Date: August 10, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving MLN4924 (pevonedistat HCl), more than 20 and up to 100 may have:
• Diarrhea, nausea, vomiting • Tiredness, fever • Loss of appetite • Pain •

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving MLN4924 (pevonedistat HCl), from 4 to 20 may have:
• Anemia which may require blood transfusion • Infection, especially when white blood cell count is low which may cause painful and frequent urination • Bloating, constipation • Sores in the mouth which may cause difficulty swallowing • Chills • Swelling of arms, legs • Cold symptoms such as stuffy nose, sneezing, sore throat • Bruising, bleeding • Dehydration • Dizziness, headache • Muscle weakness • Numbness, tingling or pain of the arms and legs • Feeling of "pins and needles" in arms and legs • Worry, confusion • Difficulty sleeping • Cough, shortness of breath, wheezing • Nose bleed • Fluid around lungs • Increased sweating • ItchingLow blood pressure which may cause feeling faint

RARE, AND SERIOUS In 100 people receiving MLN4924 (pevonedistat HCl), 3 or fewer may have:
• Abnormal heartbeat • Kidney damage which may cause swelling, may require dialysis

Possible Side Effects of Carboplatin
(Table Version Date: October 23, 2018)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may require a blood transfusion • Vomiting, nausea • Pain • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, from 4 to 20 may have:
• Visual loss • Diarrhea, constipation, belly pain • Changes in taste • Numbness and tingling in fingers and toes

RARE, AND SERIOUS In 100 people receiving Carboplatin, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

Possible Side Effects of Paclitaxel
(Table Version Date: September 26, 2017)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, more than 20 and up to 100 may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require blood transfusions • Pain • Sores in mouth which may cause difficulty swallowing • Diarrhea, nausea, vomiting • Muscle weakness • Numbness, tingling or pain of the arms and legs • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Paclitaxel, from 4 to 20 may have:
• Abnormal heartbeat • Blood clot which may cause swelling, pain, shortness of breath • Damage to the lungs which may cause shortness of breath

RARE, AND SERIOUS In 100 people receiving Paclitaxel, 3 or fewer may have:
• Heart attack or heart failure which may cause shortness of breath, swelling of ankles and tiredness • A tear or hole in the bowels which may cause pain or that may require surgery • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Additional Drug Risks

The study drug MLN4924 (pevonedistat) could interact with other drugs. Certain other drugs can change how your body processes MLN4924 (pevonedistat). This could decrease the effect of MLN4924 (pevonedistat), or it could increase the side effects from MLN4924 (pevonedistat). 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. MLN4924 (pevonedistat) in combination with other drugs could cause an exacerbation of any side effect currently known to be caused by the other drug, or the combination may result in side effects never previously associated with either drug.

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

The injection of the radionuclide may cause some slight discomfort. Allergic reactions to the radionuclide are rare.

What are my responsibilities in this study?

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

- Keep your study appointments.
- 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.

For women: We do not know if the study drug MLN4924 (pevonedistat) will affect an unborn child. Therefore, women who are breast-feeding or pregnant will not be allowed to take part in this study. Due to unknown risks and potential harm to the unborn child/infant, you must agree

not to become pregnant, breastfeed a baby, or donate eggs (ova) during the study and for 4 months afterwards.

In order to enter this study, you must have a pregnancy test to confirm that you are not pregnant. This test will be repeated just before you start taking the study medication and then regularly throughout the study. If a pregnancy test during the study shows that you may be pregnant, you will be withdrawn from the study, the study treatment will end, and the pregnancy will be followed until its conclusion.

Unless you cannot have children because of surgery or other medical reasons (you had an effective tubal ligation, you had your ovaries or uterus removed, or you are post-menopausal), you must use one highly effective method of contraception and one additional effective (barrier) method of contraception at the same time from the time of signing the informed consent form, for the entire study drug treatment period, and for 4 months after receiving your last dose of study drug (see examples below). A postmenopausal state is defined as no menses (menstrual periods) for 12 months without an alternate medical cause.

<table>
<tr><th>Highly effective methods</th><th>Additional effective (barrier) methods</th></tr>
<tr><td>Combined (estrogen and progestogen containing) hormonal contraception that inhibits ovulation to prevent pregnancy
Oral
Intravaginal
Transdermal</td><td rowspan="2">Male or female condom with or without spermicide(female and male condoms should not be used together)</td></tr>
<tr><td>Progestogen-only hormonal contraception associated with inhibition of ovulation
Oral
Injectable
Implantable</td></tr>
<tr><td>Intrauterine device (IUD) (inserted in the uterus)</td><td rowspan="3">Cap, diaphragm, or sponge with spermicide</td></tr>
<tr><td>Intrauterine hormone-releasing system (IUS)</td></tr>
<tr><td>Bilateral tubal occlusion (surgical procedure that prevents the sperm from reaching the eggs)</td></tr>
</table>

Highly effective methods	Additional effective (barrier) methods
Vasectomized partner (surgical procedure performed on males for birth control)	
Sexual abstinence	

For men: It is not known whether the study medication will affect sperm or an unborn baby. For this reason, to be in the study you must agree not to father a child or donate sperm during the study and for 4 months afterwards. However, if you have not had a vasectomy and are sexually active with any person who is pregnant, or could get pregnant, you must use a condom with spermicidal cream or jelly each time you have sex during the study and for 4 months after you stop taking the study medication. Even if you are surgically sterilized (*i.e.* have had a vasectomy) you must agree to use an appropriate method of barrier contraception (latex condom with a spermicidal agent) during the entire time when you are given the study drug, and for 4 months after you stop taking the study medication. You may also completely avoid having heterosexual intercourse.

If your partner should become pregnant, she should be under medical supervision during her pregnancy, and the baby should be under supervision after it is born. Your partner may be asked to give her consent to the collection of information related to both herself as well as the baby.

For all: If you or your partner does become pregnant while you are taking part in the study, you must tell your study doctor immediately. They will be able to advise you regarding the possible risks to your unborn child and discuss options for managing the pregnancy. You will be asked for the results of any tests and procedures carried out during your pregnancy and up to the birth. You may also be asked for the results from any evaluation of the baby after the birth.

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 NSCLC. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety and prevent and treat side effects.
- the costs of carboplatin and paclitaxel.
- the costs of getting the carboplatin, and paclitaxel ready and giving it to you.
- administration of MLN4924 (pevonedistat).
- 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 research blood tests done on Cycle 1 Day 1, before treatment and 6 hours after treatment , to look at the effects of MLN4924 (pevonedistat).
- The research blood tests done on Cycle 1 Day 1, Cycle 3 Day 1 and when your treatment stops working.
- The research blood tests done on Day 1 before treatment, immediately at the end of treatment and 3, 12 (optional), 24, and 48 hours after treatment.
- The echocardiogram or radionuclide angiography at the beginning of the study.
- The EKG done at the start of the study, when your treatment stops working, and 4 weeks after the last dose of study drug.

You or your insurance provider will not have to pay for the MLN4924 (pevonedistat) while you take part in this study. You may be billed for pharmacy dispensing charges.

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 _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

For questions about your rights while in this study, call the _____ *(insert name of 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 this optional study hope the results will help other people with cancer in the future.

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

Known future studies

If you choose to take part in this optional study, researchers will:

Use a sample of your tumor collected at the time of your initial surgery or biopsy to determine if your tumor has certain proteins that make it more responsive to treatment with MLN4924 (pevonedistat).

Use an additional sample of your blood collected at the same time as the required study collections on the first day of treatment, before treatment starts, and six hours after treatment, to determine who will benefit from treatment with MLN4924 (pevonedistat).

Unknown future studies

If you choose to take part in this optional study, your tumor sample will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run at the University of Wisconsin and is supported by the NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

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 don't know what research may be done in the future using your tumor 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.
- 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 or blood. These are called somatic changes. Changes may also be in your normal tissue or blood 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 changed 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. A sample from the tissue that was collected at the time your surgery or biopsy in addition to any leftover blood samples will be sent to the biobank.
2. Your samples will be stored in the biobank at the University of Wisconsin. 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.
3. Researchers can only get samples from the biobank after their research has been approved by experts.
4. Researchers will not be given your name or contact information.
5. 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.

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 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. 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, _____ *(insert name of study doctor[s])* at _____ *(insert telephone number and email address if appropriate*), 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 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 retuned 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 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, _____ *(insert name of study doctor[s])* at _____ *(insert telephone number and email address if appropriate*).
Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for known future studies:

I agree that my samples and related health information may be used for the laboratory study described above.

YES NO

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to learn about results from this study.

YES NO

Samples for unknown future studies:

I agree that my 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

Contact for Medically Important Genetic Test Results

I agree that my study doctor, or someone on the study team, may contact me and my doctor if the laboratory finds a possible genetic test result that may be important to the health of me and/or my family members.

YES NO

Before you join this study, you may wish to talk with family members to see if they would like to learn of any genetic test results that may be important to their health. You have the right to decide how to handle sharing this information with your family members. However, if you were to become unable to share this information with family members due to illness or injury, or if you were no longer alive, please select and sign one of the options below on releasing genetic information to family members. Only genetic test results that may be medically important to your family members would be released.

Select and sign ONE option from below:

(1) **You have my permission** to release my genetic test results or stored DNA **only** to the family members listed. Please write the name of the family member(s) in the space provided below

Participant's signature _____

Date of signature _____

Witness's signature _____

(2) **You do NOT have my permission** to release my genetic test results or stored DNA to any family members. I request that this information be kept private.

Participant's signature _____

Date of signature _____

Witness's signature _____

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 _____

Attachment 1: Study Calendar

	Before the Study	During the Study														After the Study		
		Cycle 1					Cycle 2			Cycle 3			Cycle 4+					
	Pre-study	Day 1	Day 3	Day 5	Day 8	Day 15	Day 1	Day 3	Day 5	Day 1	Day 3	Day 5	Day 1	Day 3	Day 5	At disease progression	4 weeks after last dose of study drug	Long term follow-up off-study treatment
Tumor tissue collection (optional)	X																	
MLN4924 (pevonedistat)—IV infusion		X	X	X			X	X	X	X	X	X	X	X	X			
Carboplatin—IV infusion		X					X			X			X					
Paclitaxel—IV infusion		X					X			X			X					
Pre-study procedures including informed consent, demographics, medical history, height, urine collection, clotting tests, optional tissue collection, and echocardiogram or radionuclide angiography	X																	
Physical exam, interval history, weight, and general well-being	X	X	X	X			X			X			X			X	X	
EKG (will be taken at pre-study, disease progression, 4 weeks after your last doses of study drug, and as your doctor indicates it is necessary.	X															X	X	
Concurrent meds	X	X	X	X			X			X			X			X		
Vital signs and blood draws for complete blood count and general health status	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

	Before the Study	During the Study														After the Study		
	Pre-study	Cycle 1					Cycle 2			Cycle 3			Cycle 4+			At disease progression	4 weeks after last dose of study drug	Long term follow-up off-study treatment
		Day 1	Day 3	Day 5	Day 8	Day 15	Day 1	Day 3	Day 5	Day 1	Day 3	Day 5	Day 1	Day 3	Day 5			
Pregnancy test	X	X					X			X			X			X		
Side effects evaluation		X----------															X	
Imaging to assess and measure tumors – CT or MRI scans for the chest and abdomen. CT scans of the pelvis should be done as clinically indicated.	X										X					X		
Blood draw for studying drug interactions- Before treatment, immediately at the end of treatment and 3, 12, 24, and 48 hours after treatment		X																
Blood draws for studying protein activity—before treatment begins and 6 hours after		X																
Blood draw to assess if tumor cells have shed		X								X						X		
Follow-up phone call from clinical study staff																		X