SUMMARY OF CHANGES – Consent

NCI Protocol #: 10382

Protocol Version Date: March 18, 2025

Protocol Title: A Phase I/II Trial Evaluating the Safety and Efficacy of Eribulin in Combination with Copanlisib in Patients with Metastatic Triple Negative Breast Cancer

Informed Consent Version Date: March 18, 2025

#	Section	Changes
1.	Running header	Updated protocol version date to 03/18/2025
2.	How will information about me be kept private?	Updated gender to sex.

Research Study Informed Consent Document – Phase 1

Study Title for Participants: Testing the addition of copanlisib to eribulin for advanced-stage triple negative breast cancer**.**

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10382, A Phase I/II Trial Evaluating the Safety and Efficacy of Eribulin in Combination with Copanlisib in Patients with Metastatic Triple Negative Breast Cancer (NCT04345913)

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 metastatic triple negative breast cancer (TNBC).

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:

What is the highest dose of copanlisib dihydrochloride and eribulin in combination that can be safely taken in triple negative breast cancer that has spread?

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

What is the usual approach to my metastatic triple negative breast cancer?

The usual approach for patients who are not in a study is treatment with chemotherapy like eribulin. Eribulin is approved by the FDA for treatment of metastatic TNBC. Your doctor can explain which treatment may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for a few months or longer.

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 get the study drug copanlisib in combination with eribulin until your disease gets worse or the side effects become too severe.

After you finish your study treatment, your doctor will continue to follow your condition and the study team will watch you for side effects. They will also check on you every 3 months for a total of 3 years after treatment by phone and/or by reviewing your medical chart.

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 study treatment may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from the study drugs. 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:

- Fatigue
- Elevated blood sugar
- Nausea
- Diarrhea
- Low blood counts that can increase the risk of infection

There may be some risks that the study doctors do not yet know about. There may be risks that are serious and even life threatening

Benefits

There is some evidence in living animals that this treatment can shrink or stabilize cancer, but we do not know if this will happen in people. It is unknown if this treatment will 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. 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 (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 good and bad effects of adding a specific drug, copanlisib, to the usual therapy of eribulin. The combination of copanlisib and eribulin has been tested in animals, but has not been tested in people. This study tests different doses of the drug to see which dose is safer for people. There will be up to 18 people taking part in this phase of the study. Overall, there will be about 106 patients taking part in this study. "Dose" is defined as the amount of drug you get, (amounts such as 45 mg or 60 mg).

Copanlisib is an inhibitor of a protein called phosphoinositide-3-kinase (PI3K). PI3K is often changed [or mutated] in cancer cells and causes resistance to treatment. Copanlisib is already approved by the FDA to treat another type of cancer, but it is not approved for the treatment of breast cancer. Eribulin is approved by the FDA for treatment of metastatic TNBC.

What are the study groups?

This consent form covers the first part of this study. During this part of this study, different people will get different doses of the study drug copanlisib and one of the usual treatment drugs eribulin. Copanlisib and eribulin will be administered in the clinic on the same day. Your dose of the drugs and how often you will get the drugs will depend on when you enroll and what side effects other participants have had. Both copanlisib and eribulin will be given either through a vein in your arm or the port that your doctor has placed under your skin to deliver medications into a vein on either the first and eighth day of each cycle (each cycle will be 21 days) or on the first and 15th day of each cycle (each cycle will be 28 days). See the patient study calendar for more information.

The first three people taking part in this study will get the lowest dose. If the drugs cause serious side effects, the schedule of when the doses of copanlisib and eribulin are given will be adjusted for the next group of study participants. If the drug does not cause serious side effects, the next group of people in the study will get a higher dose. 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 lowered. Once this dose is found, this part of the study is stopped.

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

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:

- Blood tests to see how your blood is clotting before you begin the study.
- Blood test to check your average blood sugar over the last few months before you begin the study.
- Blood test done weekly on treatment days to check your blood sugar.
- On Day 1 of Cycle 1 for all patients receiving copanlisib: Blood tests to check your blood sugar before you receive each dose of copanlisib and extra tests after you receive the first dose of copanlisib.
- Electrocardiogram (ECG) to check how your heart is functioning before you begin the study and on Day 1 of Cycle 2.
- Blood test to check your cholesterol before you begin the study and every 4 cycles.
- Blood test to see whether you have hepatitis before you begin the study.
- Urine sample to check how much protein is in your urine before you begin the study.
- Pregnancy tests in women of childbearing potential conducted during screening and every 3 cycles thereafter.

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 your biopsy when you were diagnosed with cancer. This sample is a required part of the study. This tissue will be tested for mutations or markers that may predict response to therapy. You and your study doctor will have the results of this testing prior to being able to enroll in this study.

Tumor biopsy for research: Small pieces of cancer tissue removed by surgery (biopsies) will be taken for the study before you begin treatment. This is like the biopsy you had that helped diagnose your cancer. This sample is required if there are cancer sites that can be biopsied safely, in order for you to take part in this study because the research on the sample is an important part of the study. There is also a research biopsy on Day 1 or 2 of Cycle 2. The tissue collected will be used for research to look for some specific genetic mutations or markers in the cancer cell that might predict response to treatment. If you agree, any specimen leftover will be stored for biobanking. This will be discussed in the section on optional studies.

Blood collection for research: Blood samples will be taken at the following time points:

- Before you begin treatment
- Cycle 2 Day 1
- Every 9 weeks (±7 days) when your tumor is checked
- When your disease gets worse but before you begin a different treatment

The blood samples are required in order for you to take part in this study because the research on the sample is an important part of the study. The blood will be collected at the same time as routine blood draws when possible to minimize the number of extra needlesticks you have. The blood collected will be used for research to study whether specific markers in the blood may be associated with treatment response. If you agree, any specimen leftover will be stored for biobanking. This will be discussed in the section on optional studies.

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. You and your study doctor will not get any results of this testing.

A patient study calendar is attached at the end of this document. It shows how often these 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 treatment may not be as good as the usual approach 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 study 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 3.5 months (men only) or 1 month (women only) 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

As part of this study, we are also studying a genetic test. The test is designed to find out if your tumor has the genetic changes that may suggest better response in this study. Once we know if your tumor has certain genetic changes or not, you will be able to enroll in the study.

Because this genetic test is still being studied, there is a risk that the test results may be wrong.

The genetic test used in this study will test your tumor and normal tissue for genetic changes. We will study genetic changes in your tumor including genes in PIK3CA and PTEN.

Biopsy Risks

Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection, significant bleeding, or collapsing of the lung can occur.

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. Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

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.

Diarrhea is a common side effect associated with copanlisib. You should notify your doctor immediately at the first sign of poorly formed or loose stools or an increased frequency of bowel movements. Loperamide (Imodium) should be kept on hand and should be taken as recommended by your doctor.

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:

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 a 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 Copanlisib Dihydrochloride
(Table Version Date: April 2, 2023)

COMMON, SOME MAY BE SERIOUS In 100 people receiving copanlisib dihydrochloride (BAY 80-6946 dihydrochloride), more than 20 and up to 100 may have:
• Diarrhea • Tiredness • Infection, especially when white blood cell count is low • High blood pressure which may cause headaches, dizziness, blurred vision

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving copanlisib dihydrochloride (BAY 80-6946 dihydrochloride), from 4 to 20 may have:
• Anemia which may require blood transfusion • Sores in the mouth which may cause difficulty swallowing • Nausea, vomiting • Bruising, bleeding • Loss of appetite • Pain • Damage to the lungs which may cause shortness of breath • Rash

RARE, AND SERIOUS In 100 people receiving copanlisib dihydrochloride (BAY 80-6946 dihydrochloride), 3 or fewer may have:
• Change in the heart rhythm • Swelling and redness of the skin • Itching

Possible Side Effects of Eribulin Mesylate (Table Version Date: August 9, 2018)

COMMON, SOME MAY BE SERIOUS In 100 people receiving eribulin mesylate (E7389; Halichondrin B Analog), more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Constipation, nausea • Tiredness • Infection, especially when white blood cell count is low • Loss of appetite • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving eribulin mesylate (E7389; Halichondrin B Analog), from 4 to 20 may have:
• Pain • Diarrhea, vomiting • Sores in the mouth which may cause difficulty swallowing • Swelling of arms, legs • Fever • Swelling and redness of the area of radiation • Bruising, bleeding, weight loss • Dizziness, headache • Changes in taste • Feeling of "pins and needles" in arms and legs • Muscle weakness • Numbness, tingling or pain of the arms and legs • Difficulty sleeping • Cough, shortness of breath, sore throat • Rash

RARE, AND SERIOUS In 100 people receiving eribulin mesylate (E7389; Halichondrin B Analog), 3 or fewer may have:
• Change in the heart rhythm

Additional Drug Risks

The study drug could interact with other drugs such as antibiotics, herbal medication and anti-seizure medication. Your study doctor will give you a wallet card that lists your study medications. Share this information with your family members, caregivers, other health care providers, and pharmacists.

Patients with diabetes may need to increase or change their diabetic medications to better control their diabetes.

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

These drugs have not been used in combination and there may be unknown risks.

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: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** 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 treatment. Use an acceptable birth control method such as the barrier method (condoms, diaphragms, or cervical caps), birth control, or abstinence for the duration of your study participation and for 3.5 months (men only) or 1 month (women only) after your last day of study treatment.

Acceptable Birth Control Methods:

- Condoms **with spermicide** AND one of the following:
    - Oral contraceptive or hormonal therapy (*e.g.*, hormone implants, skin patches, intravaginal device, hormone shots).
    - Placement of an intra-uterine device (IUD; *e.g.*, Mirena®).
    - Vasectomy, with participant assurance that the vasectomy was successful.
    - Tubal occlusion (*i.e.*, getting your tubes tied).
- Total sexual abstinence, when this is in line with your usual and/or preferred lifestyle. **Periodic abstinence** (*e.g.*, calendar, ovulation), the rhythm method, **and withdrawal are not acceptable methods of contraception**.

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 cancer. 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 cost of eribulin
- the costs of getting the copanlisib and eribulin ready and giving it to you.
- your insurance co-pays and deductibles.
- the ECG before you begin study treatment and on Day 1 of Cycle 2.

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 biopsies before you begin study treatment and on Day 1 or 2 of Cycle 2.
- The research blood draws before beginning study treatment, on Day 1 of Cycle 2, every 9 weeks (±7 days) when your tumor is checked, and when your disease gets worse but before you start another treatment.
- The blood tests to check your average blood sugar (for all patients) before you enroll in the study and blood sugar tests after you receive the first dose of copanlisib on Day 1 of Cycle 1.
- Urine sample to check how much protein is in your urine before you begin the study.
- Blood test to check your cholesterol before you begin the study and every 4 cycles.
- Blood test to see whether you have hepatitis before you begin the study.

You or your insurance provider will not have to pay for the copanlisib 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 agent 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, and email address if appropriate*).

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 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 collect your tumor tissue and blood for research on evaluating the changes in your DNA and RNA that occur during treatment. Researchers will obtain genetic material (DNA and RNA) from both your tumor cells and your blood. Your DNA and RNA will be used for genomic sequencing, which is sequencing of all or part of your DNA. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems. The genomic sequencing will be done by an NCI-supported laboratory in Frederick, Maryland, known as the National Clinical Laboratory Network (NCLN) Genomics Laboratory at the Frederick National Laboratory for Cancer Research. The laboratory will compare the genomic sequences from your tumor and blood cells to identify how they differ. The differences between genomic sequences of your tumor and blood cells may be important to understand why you did or did not respond to the treatment you received. Researchers hope to find potential "biomarkers" (changes present in tumor tissue that predict how patients with your type of cancer may respond to current or future treatments). This optional study may improve the ability to select future treatments or treatment combinations for others in the future. This optional study will not affect the cancer treatment or approach that you receive.

Neither you nor your study doctor will be informed when the genetic sequencing research will be done. You and your study doctor will not receive reports of these studies, as they are intended for research purposes only and cannot be used to plan treatment.

Researchers will also look at changes in proteins in the tumor to look at how the tumor may respond to treatment.

Samples for known future studies:

I agree that my samples and related health information may be used for the laboratory (*study or studies*) described above.

YES NO

Unknown future studies

If you choose to take part in this optional study, tumor tissue and blood samples will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by Nationwide Children's Hospital in Columbus, Ohio,) 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 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. An additional optional biopsy will be performed after your disease gets worse but before you begin a different treatment. For the biopsy procedure, the study doctor will use a needle to take pieces of your tumor. This process may be repeated several times in the same appointment in order to get enough tissue.
2. Any leftover over tissue and blood samples from the mandatory collections will also be sent to the biobank.
3. Your samples will be stored in the biobank. 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.
4. Researchers can only get samples from the biobank after their research has been approved by experts. Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer Institute, will review each request. There will also be an ethics review to ensure that the request is necessary and proper. 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.
6. Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.

What are the risks in this optional sample collection?

- The most common risks related to a biopsy are a small amount of bleeding at the time of the procedure, bruising, and pain at the biopsy site. Pain can be treated with regular pain medications. Rarely, an infection, significant bleeding, or collapsing of the lung can occur.
- 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 sex; 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, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), 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, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*).

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 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

Patient Study Calendar

Phase 1	Screening	Before you begin study treatment	Cycle 1		Cycle 2		Cycle 3+		When you stop study treatment	To be conducted at each 3-month follow-up visit for up to 3 years[7]
			D1	D8[3]	D1	D8[3]	D1	D8[3]		
Pre-study procedures, including informed consent and demographics	X									
Leftover tumor tissue from your previous biopsy tissue	X									
Fresh tumor biopsy (mandatory if your tumor tissue is safely accessible)		X			X[4]					
Optional Fresh tumor biopsy (if your tumor tissue is safely accessible)									X	
Physical exam with an assessment of how well you perform every-day tasks	X		X	X	X	X	X		X	
Vital signs (blood pressure, height, weight)	X		X	X	X	X	X	X	X	
Concomitant medications	X	X ---------- X[9]								
Side effects assessment		X ---------- X[9]								
Blood draws for complete blood count and general health status	X		X	X	X	X	X	X	X	
Blood draw to test how well your blood sugar is controlled	X									
Testing blood sugar (glucose) levels	X		X[5]	X	X	X	X	X		
Blood test to see whether you have hepatitis	X									
Blood test to check your cholesterol	X						Every 4 cycles			
Pregnancy test	X[8]						X[8]			

Phase 1	Screening	Before you begin study treatment	Cycle 1		Cycle 2		Cycle 3+		When you stop study treatment	To be conducted at each 3-month follow-up visit for up to 3 years[7]
			D1	D8[3]	D1	D8[3]	D1	D8[3]		
ECG[6]	X				X					
Eribulin [1]			X	X	X	X	X	X		
Copanlisib [2]			X	X	X	X	X	X		
Medical imaging scans for tumor measurements	X						Every 9 weeks (±7 days)			X[9]
Blood collection for research purposes (mandatory)		X			X		Every 9 weeks (±7 days)		X	
Urine sample to check how much protein is in your urine	X									

1. Eribulin: dose as assigned
2. Copanlisib: dose as assigned
3. Day 8 procedures may happen on Day 15 instead.
4. Tumor biopsy may occur on Day 1 or Day 2 of Cycle 2.
5. On Cycle 1 Day 1, Blood tests to monitor blood sugar for all patients receiving copanlisib will be done before administration of copanlisib, 1 hour after the start of the copanlisib infusion, 1 hour after the end of the infusion, and 2 hours after the end of the infusion
6. ECG will be performed at baseline and on Day 1 of Cycle 2.
7. If you are removed from study due to unacceptable side effects(s) will be followed until the side effect stops getting worse or gets better . If this happens, you will be contacted for the first time within 3 days of when the side effect(s) started.
8. Pregnancy tests will be conducted in women of childbearing potential at screening and every 3 cycles thereafter
9. If you are removed from study because your disease gets worse, you will not have to return for any follow-up visits, but the study team will perform chart checks for the above specified time frame.