To: Cancer Therapy Evaluation Program

From: Rory Shallis, M.D.

Date: December 11, 2024

Re: Amendment 6/Revision 11: "The PRIME Trial: PARP Inhibition in IDH Mutant Effectiveness Trial. A Phase II Study of Olaparib in Isocitrate Dehydrogenase (IDH) Mutant Relapsed/Refractory Acute Myeloid Leukemia andMyelodysplastic Syndrome."

SUMMARY OF CHANGES – Consent Document

I. CTEP Request for Amendment dated 10/1/2024 from Melissa M. McKay-Daily, Ph.D.

#	Section	Comments
1.	All	The date has been changed to match the current version of the protocol.

Research Study Informed Consent Document

Study Title for Participants: Using the Drug Olaparib to Treat Your Relapsed/Refractory Acute Myeloid Leukemia or Myelodysplastic Syndrome with a Isocitrate Dehydrogenase (IDH) mutation.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
Protocol 10264, "The PRIME Trial: PARP Inhibition in IDH Mutant Effectiveness Trial. A Phase II Study of Olaparib in Isocitrate Dehydrogenase (IDH) Mutant Relapsed/Refractory Acute Myeloid Leukemia and Myelodysplastic Syndrome", (NCT03953898)

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 acute myeloid leukemia or myelodysplastic syndrome that is not responding as expected to the current treatment. You can participate in this trial because your doctor found a change in the gene called the IDH (isocitrate dehydrogenase) gene.

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 control the progression of your acute myeloid leukemia or myelodysplastic syndrome by using the drug olaparib?

We are doing this study because we want to improve the treatment options for patients with acute myeloid leukemia and myelodysplastic syndrome. There is some evidence that olaparib may help patients with IDH mutations. This study will help us understand if this approach is better or worse than the usual approach for your acute myeloid leukemia or myelodysplastic syndrome. The usual approach is defined as care most people get for acute myeloid leukemia or myelodysplastic syndrome.

What is the usual approach to my acute myeloid leukemia or myelodysplastic syndrome?

For Patients with Myelodysplastic Syndrome

Most patients with high risk myelodysplastic syndrome start on treatment with the Food and Drug Administration (FDA) approved drugs azacitidine (Vidaza) or decitabine (Dacogen) and, for some, undergo an allogeneic stem cell transplant. For patients that progress after treatment, there is no standard approach - some patients receive only blood transfusions, others receive lower intensity chemotherapy to control the disease, or participate in a clinical trial. Intensive chemotherapy is also a reasonable alternative option for younger patients able to tolerate it.

For Patients with Acute Myeloid Leukemia

You may have already received one or several treatments before considering this trial. The usual treatments include chemotherapy, or targeted therapies like azacytidine, decitabine, or IDH inhibitors. All patients also receive supportive treatments like blood transfusions and antibiotics that do not treat the disease but help you as a patient. You should know that, for acute myeloid leukemia (AML) with IDH mutations, the FDA has approved ivosidenib and enasidenib. You may enroll on this trial before or after receiving those drugs. If you choose to participate in this trial, you will receive a study drug, olaparib, that may or may not work for you. In this situation, you will potentially be able to receive ivosidenib or enasidenib after olaparib if a new treatment is needed.

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 olaparib until your disease gets worse or the side effects become too severe.

After you finish your study treatment, you will continue to be seen by your study doctor who will follow your condition for 90 days and monitor you for side effects from the drug. Most of the follow up will be in the clinic with your doctor. With both acute myeloid leukemia and myelodysplastic syndrome most patients require other support such as blood transfusions a few times a week, so these visits will likely not increase the frequency of your routine visits to the clinic.

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 olaparib may not treat your disease as well as we expect. For most patients on this trial there is no standard usual treatment, except for patients with acute myeloid leukemia who have not already received an IDH inhibitor. For these patients olaparib may not work as well as the IDH inhibitor.

There is also a risk that you could have side effects from olaparib. These side effects may be worse and may be different than you would get with the usual approach for acute myeloid leukemia or myelodysplastic syndrome.

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

- Anemia, which may require blood transfusion
- Diarrhea, nausea, vomiting
- Tiredness
- Loss of appetite

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

Benefits

This drug (olaparib) has been used to treat people other types of cancer such as certain types of ovarian cancer. It has also been tested in living human cells and mice that are injected with human acute myeloid leukemia and myelodysplastic syndrome. It is unlikely that it will work in everyone with your cancer. 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 means that you should discuss stopping the drug with your doctor *before* you stop taking it. 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), 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 good and bad effects of the drug called olaparib. Olaparib may or may not treat your cancer, and it could also cause side effects, which are described in the risks section below. The study doctors hope to learn if the study drug will decrease, or at least stabilize, your disease from getting worse.

This chemotherapy drug, olaparib, is already approved by the FDA for use in ovarian cancer. But, most of the time it is not used until other drugs stop working. There will be about 46 people taking part in this study.

Another purpose is for the study doctors to learn if patients with IDH mutations are more sensitive to treatment with olaparib. A blood test that is routinely checked is necessary to find this mutation. All patients taking part in this study will need to take this test.

What are the study groups?

Patients with acute myeloid leukemia and myelodysplastic syndrome with particularly abnormal genes (IDH genes) who have received other types of therapy may be eligible for this study.

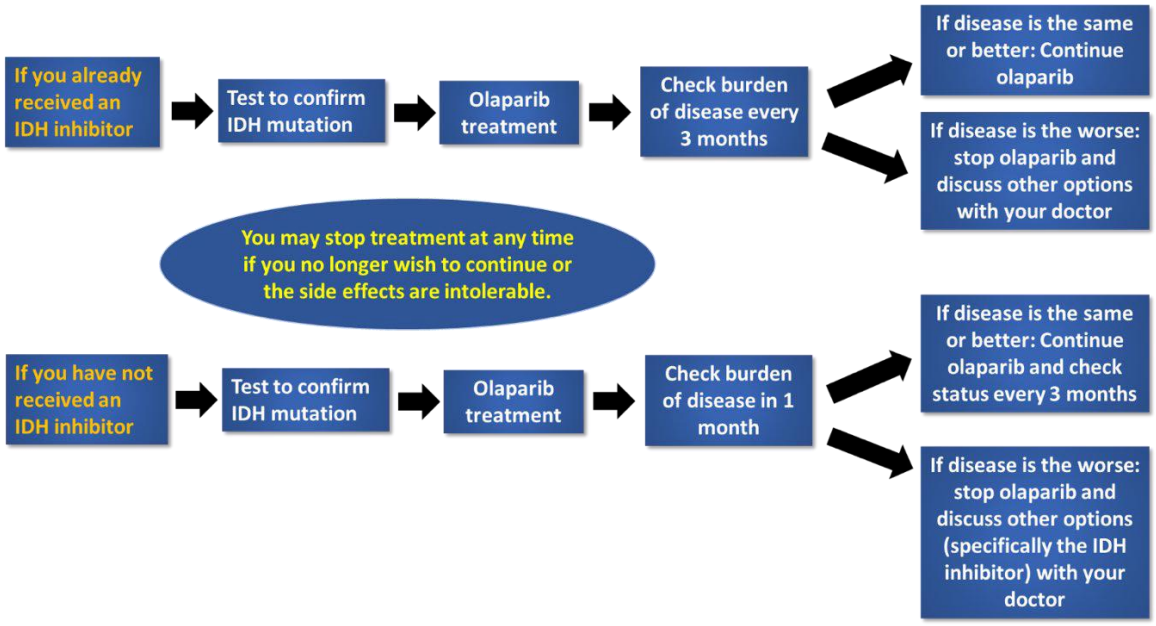
Screening:

This study has a screening step, which will consist of collecting a sample of your bone marrow, like the biopsy you had when your cancer was diagnosed. The purpose of this step is to test your cancer to find out if it has a specific mutation. If it does and you meet all the study requirements, then we can assign you to treatment. Please know that your eligibility for this trial may have been determined in part on the basis of a laboratory-developed test that has not been reviewed by the FDA. If we find that your cancer does not have the mutation that is needed for this study, then your doctor will discuss other options for your care.

Treatment:
All patients enrolled on this study will get the study drug olaparib. Olaparib is a tablet that you will need to take twice a day on each day of the cycle. Each cycle lasts 28 days. You will receive treatment as long as you continue to benefit, or at least 12 cycles. You should not consume grapefruit, grapefruit juice, or Seville oranges while taking olaparib. See the study calendar for more information.

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

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



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.

- A swab of the inner lining of your cheek (buccal swab) done at enrollment.
- Blood tests done:
  - twice weekly during Week 1 of the first cycle of treatment,
  - once weekly during Weeks 2, 3, and 4 of the first cycle of treatment,
  - once per cycle starting on the second cycle of treatment,
  - and at discontinuation of therapy.
- Physical exams are done weekly during the first cycle and the beginning of every cycle.
- Bone marrow biopsies every 3 months, and at discontinuation of therapy.

This study will use genetic tests that may identify changes in the genes in your 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 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 may require another genetic test to confirm the presence of an IDH mutation if not done in the last month. 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 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.

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:

- Before you begin study treatment, you will need to have a bone marrow sample taken for the study. This provides small amounts of cancer tissue from your bone marrow, like the biopsy you had that helped diagnose your cancer. At this time, you will also have a blood sample taken. These samples are required of everyone to participate in the study.
- There are other studies that you can take part in, where we will collect more bone marrow and blood samples. Some of these will only be available to patients who have never been on a type of medication called an IDH inhibitor. Here is when these samples will be taken, which group they are for, and whether they are mandatory or optional:

When will the samples be taken?	**What kind of samples will be taken?**	**Is this required or optional?**
Before you begin study treatment	Blood	Required for everyone.
	Bone marrow	
End of Cycle 1	Blood	Required for everyone.
	Bone marrow	• Patients **without** prior treatment with an IDH inhibitor: Required • Patients **with** prior treatment with an IDH inhibitor: Optional.
End of Cycle 3	Blood	Required for everyone.
	Bone marrow	
End of Cycle 6	Blood	Required for everyone.
	Bone marrow	
End of Cycle 9	Blood	Required for everyone.
	Bone marrow	
End of Cycle 12	Blood	Required for everyone.
	Bone marrow	
	Blood	Required for everyone.

End of Treatment	Bone marrow	Optional for everyone.

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. If you agree to take part in the study, you may need to sign a separate consent form for the study biopsy at the hospital or clinic where the biopsy is done.

A patient study calendar is attached at the end of this document. It shows how often these tests, and/or 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 drug may not be as good as the IDH inhibitor that is FDA approved to stabilize or decrease your leukemia burden. If you have myelodysplastic syndrome (MDS), there is no alternate standard option that is FDA approved, however other trials may be available.

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.

Reproductive Risks

The olaparib 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.

Olaparib is associated with a significant risk of fetal toxicity. To participate to the study, you need to agree to use effective birth control methods. Effective birth control methods are defined as total abstinence for the duration of the study (starting at the day of the screening) or one of the combinations described below:

- Male partner with vasectomy **plus** male condom
- Female partner with her tubes tied **plus** male condom
- Copper IUD **plus** male condom
- Normal and low dose oral birth control pills **plus** male condom
- Cerazette-brand birth control pill (desogestrel) **plus** male condom
- Hormonal shot or injection **plus** male condom
- Etonogestrel-brand hormonal birth control implants **plus** male condom
- Norelgestromin transdermal ("the patch") system **plus** male condom

- Levonorgestrel intrauterine system (IUS) ("IUD") device **plus** male condom
- Intravaginal device **plus** male condom

Genetic Testing Risks

The genetic test used in this study will test your tumor for a genetic mutation in the IDH gene. This change is usually not passed down through your family, however, we may incidentally discover genetic changes that might be passed down to your children. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down.

Since this study is only testing tumor tissue, we will not know if a genetic change in your tumor is also in your normal tissue. If you want to find out if the change is in your normal tissue, then you will need to get other tests done outside of this study.

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

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.

Biopsy Risks

Common side effects of a bone marrow 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 or significant bleeding can occur. For patients receiving a sternal biopsy, which is uncommon for adults, collapsing of the lung can rarely occur. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

Side Effect Risks

"If you choose to take part in this study, there is a risk that the olaparib (AZD2281) may not be as good as theusual 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 future studies.

The olaparib (AZD2281) 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 will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

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.

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.

Risk Profile for Olaparib (AZD2281)

COMMON, SOME MAY BE SERIOUS In 100 people receiving olaparib (AZD2281), more than 20 and up to 100 may have:
• Anemia which may require blood transfusion • Pain • Diarrhea, nausea, vomiting • Tiredness • Loss of appetite

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving olaparib (AZD2281), from 4 to 20 may have:
• Bloating, constipation, heartburn • Sores in the mouth which may cause difficulty swallowing • Swelling of arms, legs • Cold symptoms such as stuffy nose, sneezing, sore throat • Infection which may cause painful and frequent urination • Infection, especially when white blood cell count is low • Dizziness, headache • Changes in taste • Cough, shortness of breath • Rash

RARE, AND SERIOUS In 100 people receiving olaparib (AZD2281), 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Bruising, bleeding • Cancer of bone marrow caused by chemotherapy • Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions • Damage to lungs which may cause shortness of breath • Blood clot

Additional Drug Risks
The study drug could interact with other drugs and food. We will need to carefully review all your medications to prevent drug interactions, and some drugs may need to be changed to minimize 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.

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.
- 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. **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 3 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 acute myeloid leukemia or myelodysplastic syndrome. 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 getting olaparib ready and giving it to you.
- your insurance co-pays and deductibles.
- The bone marrow aspirate samples at enrollment and after cycles 1, 3, 6, 9, 12, and at end of treatment.

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 – these tests will be covered by the study. These include:
- The swab of the inner lining of your cheek (buccal swab) at enrollment.
- Blood samples at enrollment, weekly during cycle 1, and after cycles 1, 3, 6, 9, 12, and at end of treatment.

You or your insurance provider will not have to pay for the olaparib 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.

These organizations include:

- 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.
- The medical team helping support the trial.

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 routinely get reports or other information about any research that is done using your information, but you may request it.

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 hopes the results will help other people with your condition 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 these optional 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 bone marrow biopsy aspirate (tumor sample), blood, and buccal swab for research on evaluating the changes in your gene sequence (DNA) and gene activity (RNA) that occur during treatment. The tests will be done by an NCI-supported laboratory in Frederick, Maryland, known as the Molecular Characterization (MoCha) Laboratory at the Frederick National Laboratory for Cancer Research. The laboratory will compare the genomic sequences from your tumor and normal cells to identify how they differ. 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.

Unknown future studies

If you choose to take part in this optional study, any of your bone marrow 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. 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.

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.

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.

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. A sample from the bone marrow aspirate that was collected at the time of at the start of treatment will be sent to the biobank. A sample of bone marrow aspirate will be collected from additional bone marrow biopsies while on treatment. Up to 6 biopsy procedures may be performed over the course of 1 year (at the start of treatment, at 1 month, at 3 months, at 6 months, at 9 months, at 12 months, and at discontinuation of therapy). For the biopsy procedure, the study doctor will use a needle to take pieces of your tumor. Blood will also be collected from a vein in your arm. Up to 3 tablespoons of blood will be collected at the start of treatment, at 1 month, at 3 months, at 6 months, at 9 months, at 12 months, and at discontinuation of therapy.
2. 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.
3. 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.
4. 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?

- 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 or significant bleeding may occur. In the rare circumstance as a sternal biopsy, collapsing of the lung can occur. The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- 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. 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, Dr. Thomas Prebet, at Yale University (203-727-7103).

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 studies described above.

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

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

	Before the Study	During the Study													After the Study
	Pre-Study	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycle 7	Cycle 8	Cycle 9	Cycle 10	Cycle 11	Cycle 12	End of Study	90 day follow-up
Olaparib [A]		X	X	X	X	X	X	X	X	X	X	X	X		
Pre-study procedures including informed consent, demographics, medical history, height, EKG, vital signs	X														
Physical exam	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Buccal swab (optional)	X														
Post-study procedures including, vital signs															X
Pregnancy test [B]	X														
Concurrent meds, weight, and general well-being	X	X	X	X	X	X	X	X	X	X	X	X	X		X
Blood draw for complete blood count [C]	X	X	X	X	X	X	X	X	X	X	X	X	X		X
General bloodwork [C] (serum chemistry)	X	X	X	X	X	X	X	X	X	X	X	X	X		X
General blood work [C] (blood clot test)	X	X	X		X		X		X		X		X	X	
Side Effect Evaluation		X	X	X	X	X	X	X	X	X	X	X	X		X
Blood draw for eligibility and studying protein levels (mandatory)	X	X		X			X			X			X	X	
Bone marrow collection for eligibility (mandatory)	X														
Blood draw for research studies required for everyone (mandatory)	X	X		X			X			X			X		
Blood draw and bone marrow collections for research studies for everyone (optional)														X	
Bone marrow collection for research studies required for everyone (mandatory)	X			X			X			X			X		

	Before the Study	During the Study													After the Study
	Pre-Study	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycle 7	Cycle 8	Cycle 9	Cycle 10	Cycle 11	Cycle 12	End of Study	Off Study
Bone marrow collection for research studies for patients **without** prior treatment with an IDH inhibitory (mandatory)		X													
Bone marrow collection for research studies for patients **with** prior treatment with an IDH inhibitory (optional)		X													

A: Olaparib: Dose as assigned every 12 hours. You will take the pills by mouth.
B: Pregnancy test for women of child-bearing potential.
C: Bloodwork will be done twice weekly during Week 1 of Cycle 1, weekly during Weeks 2-4 of Cycle 1, then once per cycle as noted.

Note: Each Cycle is 28 days.; Visit Windows: Cycle 1 – 3 (+/-1 day); Cycle 4 – 12+ (+/-3 days); EOT +/- 7 days; 90 f/u +/-14 days