

To: CTEP Protocol and Information Office

From: Timothy Yap, MD, PhD

Branch: Investigational Drug Branch, CTEP, DCTD, NCI

Date: 09/08/2023

Re: Amendment #11 of Protocol #10329: "Phase I Sequential Trial of Agents Against DNA Repair (STAR)"

SUMMARY OF CHANGES – Consent

I. PI Initiated Changes

#	Section	Comments
1.	<u>Throughout and title page</u>	<p>PI Response: The protocol version date was updated on the Title Page and throughout the document on the headers.</p> <p>Old Text: November 14, 2022</p> <p>New Text: September 8, 2023</p>

Research Study Informed Consent Document

Study Title for Participants: Testing the sequential combination of the anti-cancer drugs Olaparib followed by Advasosertib (AZD1775) in patients with advanced solid tumors with selected mutations and PARP resistance.

Official Study Title for Internet Search on <http://www.ClinicalTrials.gov>: P10329, “Phase I Sequential Trial of Agents against DNA Repair (STAR)” (NCT: NCT04197713)

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 an advanced solid tumor.

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 two questions:

1. Which doses of olaparib and AZD1775 are best to give people when these drugs are given sequentially (one at a time)?
2. What side effects does sequential olaparib and AZD1775 have on the body?

We are doing this study because we want to find out if it's safe to take olaparib and AZD1775 on different schedules from the usual approach. The usual approach is defined as care most people get for their advanced solid tumor.

What is the usual approach to my advanced solid tumor?

The usual approach for patients who are not in a study is treatment with surgery, radiation, or chemotherapy drugs which are Food and Drug Administration-approved. Sometimes, combinations of these treatments are used. 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 drugs olaparib and AZD1775. You will take olaparib twice a day (by mouth), and AZD1775 once a day (by mouth). You will take your medication on this schedule:

- Olaparib for five days (Days 1-5)
- No medication for two days (Days 6 and 7)
- AZD1775 for five days (Days 8-12)
- No medication for two days (Days 13 and 14)
- Olaparib for five days (Days 15-19)
- No medication for two days (Days 20 and 21)
- AZD1775 for five days (Days 22-26)
- No medication for two days (Days 27 and 28)

This schedule from Day 1 through Day 28 is called a cycle. You will repeat this cycle continuously for up to 2 years, or until:

- your disease gets worse,
- the side effects become too severe,
- you want to stop participating.

After you finish your study treatment, your doctor will continue to follow your condition for every 3 to 6 months via phone calls (which may last approximately 5 minutes) for up to 2 years, will set up clinic visits as needed, and watch you for side effects and cancer progression.

You will be given a Study Drug Diary that you will have to maintain and update during each cycle. You will have to bring it to each visit along with the bottle and any remaining study drug. Note that olaparib is sometimes called AZD2281, and it may be labelled this way on the bottle. Be careful not to confuse the olaparib (aka, AZD2281) bottle with the other drug, AZD1775.

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

You are being asked to participate in a study where the primary objective is to find the dose where it is expected that there is a one-in-four chance you will experience either a particularly concerning severe reaction, a life-threatening reaction, or treatment-related death within the first 28 days. We want to make sure you know about a few other 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 you could have side effects from the study drugs, olaparib and AZD1775. These side effects may be worse and may be different than you would get with the usual approach for your tumor.

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

1. Diarrhea
2. Nausea
3. Vomiting
4. Loss of appetite
5. Tiredness

These side effects are associated with both drugs, except loss of appetite, which is currently only known to be associated with olaparib. There may be some risks that the study doctors do not yet know about.

Benefits

There is some evidence in human cells and animals that using olaparib and AZD1775 one after the other may shrink or stabilize your cancer as successfully as using them together, with fewer side effects, but we do not know if this will happen in people. It is unlikely that 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:

1. Your health changes and the study is no longer in your best interest.
2. New information becomes available and the study is no longer in your best interest.
3. You do not follow the study rules.
1. For women: You become pregnant while on the study.
2. 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 two drugs called olaparib and AZD1775 to see which dose of each is the most tolerable when they are given sequentially (*i.e.*, one after another). This study tests different doses of the drug to see which dose is most tolerable (*i.e.*, has the fewest or least bothersome side effects) for people, and whether they are tolerable when taken sequentially. There will be up to 54 people taking part in this study.

Olaparib has been approved by the Food and Drug Administration for some women with ovarian cancer or breast cancer.

We don't know if AZD1775 works to treat cancer in people.

What are the study groups?

There are two parts in this study: 1) a dose escalation part and, 2) a dose expansion part. Your doctor will tell you which part you are in. Everyone will get both AZD1775 and olaparib.

1. In the dose escalation part of this study, the first 3 people will get the starting doses of olaparib and AZD1775. If the drugs don't 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 to monitor as they increase the dose. The doses will continue for every new group until there are serious side effects that require the dose to be lower. Once this intolerable dose is found, the dose escalation is stopped.
2. In the dose expansion part of this study, there will be a screening step, where we will test whether you or your tumor have a change in specific genes, which will allow you to join

the study. In this part of this study, the highest dose found in Part 1 (*i.e.*, the highest dose with manageable side effects) will be given to 24 more people: 12 people with changes in the BRCA genes and 12 people with changes in DNA Damage Repair (DDR) genes (*BRIP1*, *FANCA*, *PALB2*) or Cyclin E amplification. This will help study doctors better understand the side effects that may happen with this drug.

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 counts done weekly during the first cycle of treatment.
- Physical exams done every other week during the first two cycles.
- An electrocardiogram (ECG, performed in triplicate if your doctor thinks it's necessary) before you begin the study, at the start of the second cycle and every cycle thereafter of treatment, and at any time deemed necessary by your physician.

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. Your previous testing results will be used to determine if you have a change in your genes. If you have not undergone testing, a piece of tissue from your previous surgery will be used for the test. If a piece of tissue is not available from your previous surgery, we will perform a biopsy to obtain tissue. This genetic testing is optional if you are in the dose escalation group, and required if you are in the dose expansion group. The study doctors do not know if changes in your genes will determine your response to treatment using different doses and schedules of olaparib and AZD1775.

Finding these changes would not affect your treatment in this study. However, they could affect your health in other ways. If there are changes found that could cause health problems, then your study doctor may discuss your options with you. 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 try to contact you several times.
4. You will require another genetic test to confirm the results. This test must be paid for at your own expense.
5. If it is confirmed that there are changes found that could cause health problems, then your doctor will discuss your options with you. We strongly suggest that you also talk to a genetic counselor. Genetic counseling services must be paid for at your own expense.

It is more likely, however, that you will not be contacted by us about a medically important finding. Even if we do not contact you, it does not mean that your genes do not contain changes that are important to your health. Researchers are always learning about new and medically important changes in genes and some information may be learned in the future. Researchers will only decide to contact you about genetic test results at the time your DNA 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.

You will need to have some tumor biopsies and blood samples taken before and during the study.

Blood samples for research purposes will be taken for the study at four separate time points. Here is a timeline of when you will have to have blood samples taken:

1. Before you begin the study drugs
2. Cycle 1, Day 12
3. At each time you test for the spread of cancer
4. If your disease gets worse

Tumor biopsies will be taken for the study at up to three separate time points (two time points are mandatory, one is optional). If your tumor cannot be accurately measured in size, you will not have to undergo the mandatory biopsies. Here is a timeline of when you will have to have tumor samples taken:

1. Before you begin the study drugs
2. Cycle 1, Day 12
3. If your disease gets worse. This biopsy is optional.

The study biopsy takes small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer. Genetic material (DNA, RNA) will be obtained from your tumor and blood samples. They will be used to evaluate changes in your DNA and RNA that may occur during treatment, and may indicate if you will or will not respond to treatment.

Your study doctor may 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. If there is not enough tissue left over from your biopsy, your study doctor will need to do another biopsy to get this tissue. This tumor sample will be taken before you begin the study drugs.

If there is any leftover specimen, it may be stored for biobanking and later use. This will be discussed in the section under “Optional studies.”

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 blood samples and tumor biopsies 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 sequential treatment with olaparib and AZD1775 may not be as good as the usual treatment for your cancer in 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.
- Missing time from work and family activities.

The use of olaparib and AZD1775 used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 3 months after you have completed the study.

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

Genetic Testing Risks

The genetic test used in this study will test your tumor for genetic changes. These changes also may 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.

Genetic tests of normal tissue can reveal information about you and also 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.

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. You may sign a separate consent form for the study biopsy that describes the risks in more detail.

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 olaparib and AZD1775 used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

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

Here are important things to know about side effects:

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 using two study drugs sequentially instead of simultaneously. The aim of this study is to reduce the side effects you may normally experience if taking the drugs simultaneously. 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.

If you decide to take part in this study, you will have to keep loperamide (Imodium) on hand, and take it at the first symptom of diarrhea.

Possible Side Effects of Olaparib (AZD2281) (Table Version 2.5, July 1, 2021)

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 the lungs which may cause shortness of breath

Possible Side Effects of AZD1775 (Table Version 2.7, Date: April 27, 2020)**COMMON, SOME MAY BE SERIOUS**

In 100 people receiving AZD1775 (adavosertib), more than 20 and up to 100 may have:

- Diarrhea, nausea, vomiting
- Tiredness

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving AZD1775 (adavosertib), from 4 to 20 may have:

- Anemia which may require blood transfusion
- Pain
- Constipation, heartburn
- Sores in the mouth which may cause difficulty swallowing
- Swelling of the body
- Fever
- Infection, especially when white blood cell count is low
- Bruising, bleeding
- Weight loss, loss of appetite
- Dehydration
- Dizziness, headache
- Difficulty sleeping
- Cough, shortness of breath
- Rash

RARE, AND SERIOUS

In 100 people receiving AZD1775 (adavosertib), 3 or fewer may have:

- Abnormal heartbeat
- Bleeding from multiple sites
- Internal bleeding which may cause black tarry stool, blood in vomit
- Damage to the liver
- Change in the heart rhythm
- Bleeding in the brain which may cause confusion

Additional Drug Risks

The study drug AZD1775 has a risk of infection in the blood, which can be severe. Your study doctor will discuss this risk with you.

The study drug could interact with other drugs and food, including antibiotics such as clarithromycin, certain foods (such as grapefruit juice), or herbal preparations (such as St. John's wort). Your study doctor will give you a drug information handout and wallet card that lists these possible interactions. Share this information with your family members, caregivers, other health care providers, and pharmacists.

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

What are my responsibilities in this study?

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

1. Keep your study appointments.
2. Write down in your medication diary when you take the study drug at home.
3. 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. If you are a woman of childbearing potential, you must agree to use an adequate method of contraception during the study and until 6 months after the last treatment.
- **For men:** Do not father a baby while taking part in this study. You must be either surgically or biologically sterile, or agree to use an adequate methods of contraception during the study until 3 months after the last treatment.
- **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 tumor. 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 the olaparib and AZD1775 ready and giving it to you.
- your insurance co-pays and deductibles.

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

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

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

- Research tumor biopsies.
- Research blood sampling.
- Health-monitoring blood tests and the ECGs.

You and/or your insurance provider will not have to pay for the study drugs olaparib and AZD1775 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 drugs now or in the future. This would include any organization helping the company with the study.
- The National Cancer Institute Central Institutional Review Board, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the groups it works with to review research.
- The National Cancer Institute 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 National Cancer Institute web site at <http://cancer.gov/> for more information about studies or general information about cancer. You may also call the National Cancer Institute 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 an optional study that you can choose to take part in. It is separate from the main study described above. This optional study will not benefit your health. The researchers leading this optional study hope the results will help other people with solid tumors. The results will not be added to your medical records and you will not know the results.

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

Circle your choice of “yes” or “no” for the following study:

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.

Unknown future studies

If you choose to take part in this optional study, samples from your previous blood samples and tumor biopsies will be collected and 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 National Cancer Institute. 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 blood and tumor samples. This means that:

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

If you choose to take part in this optional study, any of your tumor tissue or blood samples left over from the genomic sequencing will be stored. Storing samples for future studies is called "biobanking." The biobank is being run by the Nationwide Children's Hospital in Columbus, Ohio, and is supported by the National Cancer Institute. 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.

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

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- Future research studies may include genomic sequencing.

- You will not get reports or other information about any research that is done using your samples.

What is involved in this optional sample collection?

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

1. Samples of tissue will be collected from the optional extra biopsy when your disease gets worse. Any leftover samples from the research biopsies collected will be sent to the biobank. 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. 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, 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 gender; your type of cancer; any previous treatments you received for your cancer; and the treatment you will receive for this current study.
2. Researchers who study your samples and information will not know who you are. They also must agree that they will not try to find out who you are. The researchers must be trained in the handling of private information. Any researcher who wants to study your stored samples and genetic information must apply and be approved to do so.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

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

You will not benefit from taking part.

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

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

There are no costs to you or your insurance for exams, tests, and procedures done for research purposes only; these include the biopsy, DNA/RNA sequencing, and other molecular analyses and biobanking of your specimen. 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:

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

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

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

Study Calendar