Research Study Informed Consent Document - Screening

Study Title for Participants: Testing the combination of anti-cancer drugs talazoparib and temozolomide in people 12-17 years old with advanced stage rare cancers

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10490, "Rapid Analysis and Response Evaluation of Combination Anti-neoplastic Agents in Rare Tumors (RARE CANCER) Trial: RARE 2 Talazoparib and Temozolomide" (NCT05142241)

If the individual being asked to participate in this research study is a minor, the term "you" refers to "you and/or your child" throughout the remainder of this document; "we" means the doctors and other staff.

Overview and Key Information

What am I being asked to do?

We are asking you to undergo screening in order 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 a cancer that is considered rare and for which there is no standard treatment. You may also have changes in a gene that repairs damage to your DNA.

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 screening part of the study being done?

This screening part of the study is to find out if you are eligible for the research (treatment) part of the study. The treatment part of the study is being done to answer the following question:

- Can the combination of the two study drugs, talazoparib and temozolomide, make your type of rare cancer stop growing or shrink?

The purpose of this screening step is to find out if you fit the requirements for taking part in this treatment study. For some patients, this includes testing your tumor tissue to find out whether your tumor has abnormalities or changes in the *MGMT* gene that prevent this gene from carrying out its normal function. If you have already had this MGMT testing done, your genetic testing results will be reviewed to determine if you are eligible for one of the treatment groups of the study. Your study doctor or nurse will tell you if you need to have changes in the *MGMT* gene in order to join the treatment part of the study.

Your medical history and lab tests will also be reviewed to ensure that you meet all the study requirements. You may not be eligible for the treatment part of the study for several reasons unrelated to your cancer. If the results of the testing indicate that you are eligible to participate in the treatment part of the study, then your study doctor or nurse will discuss the study further with you and you will have the opportunity to decide whether you will participate in the treatment study.

What is the usual approach to my cancer?

The usual approach for patients who are not in a study is treatment with radiation, kinase inhibitor drugs, immunotherapy drugs, or chemotherapy drugs. There are no treatments that are FDA-approved for your health condition or proven to help patients with your health condition live longer, including radiation and chemotherapy.

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?

Participants in the screening step of the study are required to have testing of your tumor tissue to see if your *MGMT* gene has the abnormalities or changes required for this study. If you do not already have *MGMT* testing results or do not have tumor tissue available for testing, you and your doctor may decide to have a tumor biopsy done in order to participate in this screening step and determine if you are eligible for the treatment part of the study. Your doctor will send your tumor tissue to a laboratory for testing, if needed, and will discuss the testing results (either new or from the past) with you.

If the test results confirm that you meet all the study requirements, you will be asked to participate in the treatment part of the study and will receive another consent form that explains what will happen in that part of the study.

If we find that you do not meet all the study requirements, you will not be enrolled in the treatment part of the study and your doctor will discuss other options for your care.

There will be about 168 people taking part in the screening part of the study. There will be about 47 people taking part in the treatment part of the study.

What are the risks and benefits of taking part in this screening 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 the screening part of this study?" section.

If you choose to take part in this study, there is a risk that you may be asked sensitive or private questions which you normally do not discuss.

If you choose to take part in this study, there is a risk that your cancer may get worse while the screening tests are occurring.

Benefits

This screening study will help determine whether you could be eligible for the treatment part of the study. Otherwise, there will be no benefit to you.

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. However, once your tumor tissue sample has been sent to the testing laboratory, it may not be possible to stop the testing. If you decide to not participate in the study after the testing results are received, they may still be a part of your medical records, and they may possibly affect your future care. You can ask your study doctor whether this information will be included in your medical records.

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. Your study doctor will tell you about going off the study if:

- Your health changes and being part of the study is no longer in your best interest.
- New information becomes available, and the study is no longer in your best interest.
- You do not follow the study rules.
- You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (National Cancer Institute [NCI]). The study sponsor is the organization that 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 the screening step of this study is to find out if you fit the requirements for taking part in the treatment part of this study.

The purpose of the treatment part of this research study is to test the good and bad effects of the study drugs called talazoparib and temozolomide. Talazoparib and temozolomide could shrink or stabilize your cancer, but they could also cause side effects, which are described in the risks section of the treatment study consent. The study doctors hope to learn if the study drug will shrink or stabilize your type of cancer. We also plan to test the effect of the study drug in the tissue around your tumor, and in your blood.

Talazoparib and temozolomide have already been approved by the FDA to treat other cancers, but the combination has not been approved by FDA.

There will be about 168 people taking part in the screening part of the study. There will be about 47 people taking part in the treatment part of the study.

What are the study groups?

This study has a screening step. The purpose of this step is to see if you are eligible for the treatment study. If you meet all the study requirements, then we can assign you to the treatment part of the study. The screening step includes testing your tumor to find out if it has specific abnormalities or changes in the *MGMT* gene. If it does and you meet all the study requirements, then we can assign you to treatment based on these changes. If we find that your tumor does not have the genetic changes that are needed for this study, then your doctor will discuss other options for your care. The *MGMT* gene screening test is not approved by the FDA in your disease.

What exams, tests, and procedures are involved in the screening part of 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 the screening for this study but may not be included in the usual care. We will use them to find out if you are eligible for the treatment part of the research study.

These exams, tests, and procedures to check your eligibility include:

- A test on your tumor tissue to see if its *MGMT* gene has specific abnormalities or changes needed for this study.
    - 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. The tissue is needed to look for changes in the *MGMT* gene. You and your study doctor will get the results of this testing.
    - If there is not enough tissue left over from your biopsy, your study doctor will need to do another biopsy to get this tissue for the screening step of this study. The study biopsy takes small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer. The biopsy is needed to look for changes in the *MGMT* gene. You and your study doctor will get the 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. This will be described further in the 'Optional Studies' section at the end of this document.

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

General Risks

For some patients, the screening part of 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.

If you choose to take part in this study, there is a risk that your cancer may get worse while the screening tests are occurring.

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.

Genetic Testing Risks

As part of this study, we are also studying a genetic test for some patients. The test is designed to find out if your tumor has the abnormalities or changes in the *MGMT* gene that are needed for some patients on this study. If it does, we will assign you to a study group based on the genetic changes in your tumor.

Because this genetic test is still being studied, there is a risk that the test results may be wrong. If the test results are wrong, you may be included in this study even though it may not offer the best treatment option for you. Or, you may not be included in this study even though it may offer a good treatment option for you.

What are my responsibilities in the screening step of 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.

What are the costs of taking part in the screening step of this study?

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

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety and see if you are eligible for the study.
- 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.

You will not pay for the costs of the genetic testing of your tissue sample performed by the laboratory.

If screening shows you are eligible to participate in the treatment part of the study, any costs related to being part of the study will be discussed along with details of your treatment in a second consent form for the treatment study.

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 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 Dr. Alice Chen at (240) 781-3320.

For questions about your rights while in this study, call the NIH Office of Human Subjects Research Protections (OHSRP) at (301) 402-3713.

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 if you need to be tested for changes in the *MGMT* gene. These studies are separate from the main study described above. These optional studies will not benefit your health. The researchers leading this optional study hope the results will help other people with cancer in the future. For some of

these studies, the results will be added to your medical records and you and your study doctor will know the results.

Taking part in these optional studies is your choice. You can still take part in the screening step of this study even if you say "no" to 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 these studies for any reason, you can still take part in the screening step of this study.

At the end of this consent form, circle your choice of "yes" or "no" for each of the following studies.

Optional sample collections and known laboratory studies

Optional Study #1 - biopsy to collect tumor tissue for MGMT testing

If you need testing of your tumor tissue to see if the *MGMT* gene has the abnormalities or changes required for this study and you do not already have tumor tissue available for testing, you and your doctor may decide to have this optional tumor biopsy done in order to participate in this screening step and possibly be eligible for the treatment part of the study. Your doctor will send your tumor tissue to the laboratory for testing and will discuss the testing results with you.

What is involved in this optional sample collection?

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

1. A sample of tumor tissue will be collected from an optional extra biopsy and will be sent to the laboratory for *MGMT* testing.
2. Your sample will be stored at the laboratory. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until you request that they be transferred, or they are used for research or destroyed.
3. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.
4. If you meet all the study requirements to enroll in the treatment portion of this study, any biopsy tissue that remains after the MGMT testing is complete may be used as the baseline biopsy on the treatment portion of this study. If you do not meet all the study requirements, we can try to transfer any remaining biopsy tissue to another clinical study that you want to participate in, but we cannot guarantee that there will be enough tissue remaining for all studies.

Optional Study #2 - genomic testing of remaining tumor tissue

If testing of your tumor tissue shows that the *MGMT* gene does not have the abnormalities or changes required for this study and you still have more tumor tissue available for testing, you and your doctor may decide to have a genomic test performed on your remaining tumor

tissue. The results of this genomic sequencing will be added to your medical records and you and your study doctor will know the results.

Researchers will also know the results of your genomic sequencing. 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.

If you choose to take part in this optional study, researchers will collect a sample of your blood and a sample of your tumor tissue and use these samples to sequence 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.

What is involved in this optional sample collection?

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

1. About 1 tablespoon of blood will be collected from a vein in your arm. This blood sample and a sample from the tumor tissue that was collected at the time of your biopsy will be sent to the laboratory for genomic testing.
2. Your sample will be stored at the laboratory. 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. 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.

Optional Study #3 - additional MGMT testing of remaining tumor tissue

Researchers are trying to learn more about the MGMT genetic test done on your biopsy tissue to look for abnormalities and changes in the *MGMT* gene. They are studying other tests that look at the function of the *MGMT* gene and hope to learn which MGMT tests are best to use in patients.

If you choose to take part in this optional study, researchers will use a small sample of your tumor tissue to look at the function of the *MGMT* gene in your tumor. They will look at the proteins made by your tumor cells and use genetic sequencing research tests to read the RNA (**r**ibo**n**ucleic **a**cid) present in your tumor cells. RNA is similar to DNA (**d**eoxyribo**n**ucleic **a**cid) because they are both types of cellular "instructions" inside your tumor cells.

We will not give you any individual results from these tests. We will not add these research results to your medical record.

What is involved in this optional study?

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

1. A sample from the tumor tissue that was collected at the time of your biopsy will be sent to the laboratory for more MGMT testing.
2. Your sample will be stored at the laboratory. 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. 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 these optional sample collections?

General Risks:

- 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 laboratory for this optional sample collection, your tissue could be used up.

Risks of Optional Study 1:

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

Risks of Optional Study 2:

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.

Risks of Optional Studies 2 and 3:

- 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 laboratory scientists. 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.
2. The laboratory scientists who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
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 results of your genomic testing (optional study 2) will be given to your physician for use in your care.

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, Dr. Alice Chen, at (240) 781-3320, who will let the laboratory know. Then, any sample that remains in the laboratory 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 have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, Alice Chen, at (240) 781-3320.

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:

Optional Study #1 - biopsy to collect tumor tissue for *MGMT* testing

I agree to undergo the optional tumor biopsy collection and have my samples and related health information used for the laboratory studies described above.

YES NO

Optional Study #2 - genomic testing of remaining tumor tissue

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

YES NO

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

YES NO

Optional Study #3 - additional *MGMT* testing of remaining tumor tissue

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

YES NO

My signature agreeing to take part in the screening step for this 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 screening part of the study.

_____

Participant's signature

_____

Date of signature

_____

Signature of parent/guardian

_____

Date of signature

_____

Signature of person(s) conducting the informed consent discussion

_____

Date of signature