SUMMARY OF CHANGES -- Consent

NCI Protocol #: 10191

Local Protocol #: Dana-Farber/Harvard Cancer Center Protocol #19-715

Protocol Version Date: August 24, 2024

Protocol Title: A Phase 2 Study of M6620 (VX-970, berzosertib) in Combination with Carboplatin compared with Docetaxel in Combination with Carboplatin in Metastatic Castration-Resistant Prostate Cancer

Informed Consent Version Date: August 24, 2024

ICD Changes (from version February 1, 2021)

Additional changes by Principal Investigator dated August 24, 2024

#	Section	Comments
1.	Header	Version date updated

Research Study Informed Consent Document

Study Title for Participants: Comparing the combination of a new targeted therapy drug, M6620 (VX-970, berzosertib) (targeting DNA damage repair), and the chemotherapy drug carboplatin to the usual care of carboplatin and docetaxel in patients with metastatic (cancer that has spread) castration-resistant prostate cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: A Phase 2 Study of M6620 (VX-970, berzosertib) in Combination with Carboplatin compared with Docetaxel in Combination with Carboplatin in Metastatic Castration-Resistant Prostate Cancer, Protocol #10191

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have metastatic castration-resistant prostate cancer that is no longer responding to standard hormonal drugs and a chemotherapy drug known as a "taxane" (docetaxel, cabazitaxel or paclitaxel).

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 increase the likelihood of shrinking your prostate cancer by adding a new drug, called M6620 (VX-970, berzosertib), to a commonly used chemotherapy drug for prostate cancer, called carboplatin?

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

What is the usual approach to my cancer?

The usual approach for patients who are not in a study is treatment with carboplatin in combination with docetaxel. Some patients may also be candidates for FDA-approved therapies including chemotherapy drugs, an immune therapy, or a radiation therapy.

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 either get a usual approach of carboplatin with a chemotherapy drug called docetaxel or a study approach of carboplatin with M6620 (VX-970, berzosertib), until your disease gets worse or the side effects become too severe. If you are initially treated with the usual approach of carboplatin and docetaxel and your disease gets worse, you may later be given the study approach of carboplatin and M6620 (VX-970, berzosertib) as long as you continue to meet the eligibility requirements of the study.

After you finish your study drug dosing, your doctor will continue to follow your condition for up to 42 days to watch you for side effects.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach for your cancer at shrinking or stabilizing your cancer.

There is also a risk that you could have side effects from the study approach. These side effects may be worse and may be different than you would get with the usual approach for your cancer

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

- Anemia, Tiredness
- Diarrhea, Nausea, Vomiting
- Headache, Flushing
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Infection which may cause painful and frequent urination

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

Benefits

There is evidence that this combination of carboplatin and M6620 (VX-970, berzosertib) is effective in shrinking and/or stabilizing different types of cancer such as ovarian, melanoma, and head and neck cancer, but we do not know if this will happen in patients with your type of cancer. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study are 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.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (the National Cancer Institute). 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 compare any good and bad effects of using the investigational drug M6620 (VX-970, berzosertib), a drug targeting the response to DNA damage, in combination with carboplatin, as compared with the usual care approach combination of carboplatin along with docetaxel for patients with metastatic castration-resistant prostate cancer. The addition of M6620 (VX-970, berzosertib) to the usual carboplatin chemotherapy could shrink your cancer, but it could also cause side effects.

This study will allow the researchers to know whether this different approach is better, the same, or worse than the usual approach. To be better, M6620 (VX-970, berzosertib) should increase the likelihood of tumor shrinkage by about 20% as compared to the standard chemotherapy combination. Carboplatin is not FDA-approved for use alone in prostate cancer but is commonly used in combination with docetaxel when docetaxel stops working on its own. There will be about 142 people taking part in this study.

M6620 (VX-970, berzosertib) is a type of targeted cancer therapy that targets an enzyme in cancer cells called ATR. ATR plays an important role in repairing damage to DNA caused by various forms of stress to the cells, thus allowing cancer cells to repair the DNA in an effort to fix themselves. M6620 (VX-970, berzosertib) stops cancer cells with high levels of stress from fixing themselves (by blocking their ability to repair damaged DNA) so that they are unable to survive. Carboplatin is a chemotherapy drug that is commonly used in many cancer types including ovarian and other gynecologic cancers, lung cancers, and bladder cancers, and in combination with docetaxel in metastatic castration-resistant prostate cancer. Carboplatin is known to lead to stress in cancer cells, causing DNA damage. In the presence of M6620 (VX-970, berzosertib), cancer cells are unable to repair this DNA damage and undergo cell death. Therefore, we expect that M6620 (VX-970, berzosertib) in combination with carboplatin will be more toxic to cancer cells than either drug alone.

Another purpose of this study is for study doctors to learn if a biomarker test is helpful to decide which patients are likely to respond to the study approach and/or the usual approach of carboplatin in combination with docetaxel chemotherapy. A biomarker is a measurable substance that is known to be associated with a certain condition and can indirectly show how well a specific drug regimen is working. A biopsy of a metastatic tumor prior to starting on therapy will be used for the biomarker test, and you have the option to contribute further to the research by undergoing another biopsy after completion of the study (see “Optional studies that you can choose to take part in” located at the end of the consent form). In addition, blood tests will be taken for research studies at certain intervals before, during and after your drug dosing on trial. The study doctors do not know if using the biomarker test is better, the same, or worse than if treatments were chosen without using the biomarker test.

What are the study groups?

Participants will be enrolled in one of two groups. In both groups, a drug dosing cycle is 21 days.

- **Group 1**

  If you are in this group, you will receive the usual approach with docetaxel chemotherapy in combination with carboplatin chemotherapy (unless you have contraindications to treatment with docetaxel, in which case you will be treated with carboplatin alone). You will get Docetaxel as an infusion into your vein over approximately one hour followed by Carboplatin as a 30 minute infusion on day 1. Drug dosing will be repeated every 21 days. See the study calendar for more information.

  If docetaxel and carboplatin are not effective for your cancer, you can later be treated with the investigational approach of M6620 (VX-970, berzosertib) with carboplatin. You may need to have imaging studies repeated and you will need to continue to meet the eligibility requirements of the study in order to switch to the investigational approach.

  There will be about 71 people in this group.

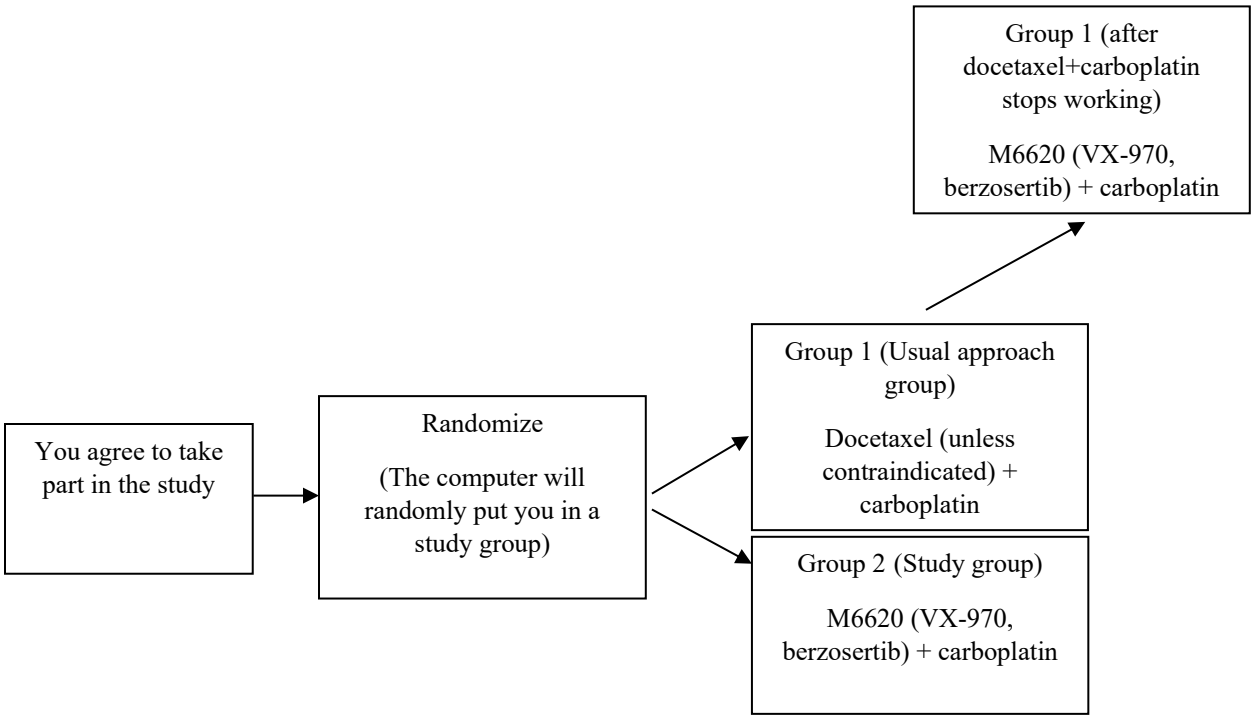
- **Group 2**

  If you are in this group, you will receive an investigational approach using the study drug M6620 (VX-970, berzosertib) in combination with carboplatin. You will receive carboplatin as a 30- minute infusion into your vein on day 1. On days 2 and 9 you will receive M6620 (VX-970, berzosertib) as an infusion into your vein over approximately one hour. This cycle of study drug dosing will be repeated every 21 days. See the study calendar for more information.

  There will be about 71 people in this group.

We will use a computer to assign you to one of the study groups. This process is called "randomization." It means that your doctor will not choose, and you cannot choose which study group you are in. You will be put into a group by chance. You will have an equal chance of being in Group 1 or Group 2.

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 approach, including preventing and managing side effects.

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

- Blood tests on day 1 and day 9 of every 21-day drug dosing cycle
- CT scan of chest, abdomen and pelvis every 3 cycles while on study
- Bone scan every 3 cycles while on study
- Test of the electrical activity of your heart (EKG) before the study begins

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 a biopsy for the study prior to starting on study drug dosing. The study biopsy takes small pieces of cancer tissue from your body guided by CT imaging. This is like the biopsy you had that helped diagnose your cancer. This biopsy will be used for genetic and molecular testing to help the researchers understand which patients are more likely to respond to the usual approach and to the investigational approach. 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.
- Blood samples are also required for research studies. The first sample of less than 1 tablespoon of blood will be collected before you begin the study drugs. You will then have less than 1 tablespoon of blood taken for research studies on the day of starting your first drug dosing cycle, approximately every 3 cycles thereafter, and at the completion of study drug dosing.

Researchers will obtain genetic material (DNA) from your tumor tissue and blood samples. Genetic traits, or "variants," in the DNA derived from normal cells in your blood are referred to as **germline** variants, which you inherited from your biological parents and can pass down to your offspring. These genetic variants 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 participation in this study. However, they could affect your health in other ways.

Genetic changes in tumor's DNA are referred to as **somatic** variants, which define the biological properties of your tumor and might help determine whether your tumor would respond to certain drugs. This research will include DNA sequencing to identify variants in all genes in your normal cells and your cancer cells – this is referred to as whole exome sequencing. Genetic testing and other studies from the research biopsy will be used to understand which patients respond to the study drugs and which patients do not.

Your privacy is very important, and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. The results of the genetic testing from your research biopsy and from blood samples taken over the course of the study will not be available to the you and your physician.

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

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.

- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. Men treated or enrolled on this study must agree to use adequate contraception before the study begins, for the duration of study participation, and 6 months after completion of be given the study drugs. Should a woman become pregnant or suspect she is pregnant while her partner is participating in this study, she should inform her treating physician immediately. 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 6 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 and normal tissue for genetic changes in your whole genome. Changes found in your normal tissue may be passed down in families. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. Genetic tests of normal tissue can reveal information about you and also about your relatives. The results of these tests will not be returned to you or your study doctor.

Your 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/

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

Any of the specimen left over may be stored for biobanking. This will be discussed in the section under “Optional studies”.

Side Effect Risks

The drugs used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.
There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

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

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

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at a combination of the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

Drug Risks

The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 1 – Possible side effects of carboplatin and docetaxel are listed in the tables below. These drugs are part of the usual approach for treating this type of cancer:

Possible Side Effects of Carboplatin
(Table Version Date: March 24, 2015)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, more than 20 and up to 100 may have:
• Hair loss

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, more than 20 and up to 100 may have:
• Vomiting, nausea • Infection, especially when white blood cell count is low • Anemia which may cause tiredness, or may require blood transfusions • Bruising, bleeding • Belly pain
OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, from 4 to 20 may have:
• Diarrhea, Constipation • Numbness and tingling in fingers and toes • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Changes in taste • Changes in vision

RARE, AND SERIOUS In 100 people receiving Carboplatin, 3 or fewer may have:
• Damage to organs which may cause hearing and balance problems

Possible Side Effects of Docetaxel
(Table Version Date: July 21, 2015)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Docetaxel, more than 20 and up to 100 may have:
• Swelling of the body • Hair loss • Change in nails • Rash, itching • Vomiting, diarrhea, nausea, constipation • Sores in mouth which may cause difficulty swallowing • Infection, especially when white blood cell count is low • Anemia which may require blood transfusions • Bruising, bleeding • Tiredness • Numbness and tingling of the arms and legs • Fever • Absence of menstrual period • Swelling and redness of the arms, leg or face

COMMON, SOME MAY BE SERIOUS In 100 people receiving Docetaxel, more than 20 and up to 100 may have:
• Pain • Watering, itchy eyes

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Docetaxel, from 4 to 20 may have:
• Severe skin rash with blisters and peeling which can involve inside of mouth and other parts of the body • Belly pain • Kidney damage which may require dialysis • Blood clot which may cause swelling, pain, shortness of breath • Abnormal heart rate • Shortness of breath, wheezing • Chest pain

RARE, AND SERIOUS In 100 people receiving Docetaxel, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Cancer of bone marrow (leukemia) caused by chemotherapy

Patients should be aware that Docetaxel may cause them to become intoxicated from the alcohol it contains. Patients should avoid driving, operating machinery, or performing other activities that are dangerous within one to two hours after the infusion of Docetaxel. In addition, some medications, such as pain relievers and sleep aids, may interact with the alcohol in the Docetaxel infusion and worsen the intoxicating effects. Docetaxel can also rarely lead to serious eye disorders, including an eye disorder called cystoid macular edema, so you should let your doctor know about any changes in your vision.

Study Group 2 – Possible side effects of M6620 (VX-970, berzosertib) are listed in the table below, and possible side effects of carboplatin are listed above. The combination of M6620 (VX-970, berzosertib) with carboplatin is the investigational approach being tested in this study:

[redacted]

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.

Additional Drug Risks

The study drug could interact with other drugs. Specifically, [redacted]. 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.

Imaging Risks

The CT scans and bone scans that you get in this study will expose you to low amounts of radiation. Every day, people are exposed to low levels of radiation that come from the sun and

the environment around them. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans and bone scans that you get in this study will expose you to more radiation than you get from everyday background radiation. The amount of radiation from a CT scan of the Chest, a CT of the Abdomen and Pelvis, and a bone scan is the same as approximately 2 years, 3 years, and 1.5 years of background radiation, respectively. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation.

As part of the CT scans that you get in this study, iodine will be injected into your vein. Some people are allergic to iodine. Let your study doctor know if you have an allergy to iodine or seafood or if you have kidney problems.

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.

Do not father a baby while taking part in this study – adequate contraception must be used before and during the study and for 6 months after the last dose of study medication. Tell your study doctor right away if you think that your partner has become pregnant during the study or within 6 months after your last dose of study drugs.

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 prostate cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the study drugs 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:

- The biopsy at the beginning of the study.
- Blood samples for genetic testing before, during and at the completion of the study
- The test of the electrical activity of your heart (EKG) before the study begins

You or your insurance provider will not have to pay for the M6620 (VX-970, berzosertib) 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 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 (the National Cancer Institute) and any company supporting the study (maker of M6620 (VX-970, berzosertib)) now or in the future
- The 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 NCI's Experimental Therapeutics Clinical Trials Network (ETCTN) and the groups it works with to conduct research

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, we don't know what research may be done in the future using your information. This means that:

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

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

For questions about your rights while in this study, call the _____ *(insert name of 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 this optional study hope the results will help other people with prostate cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in 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.

Known future studies

If you choose to take part in this optional study, researchers will collect an additional biopsy specimen after you complete drug dosing on study. This biopsy specimen will undergo the same genetic and molecular testing as the pre-treatment biopsy specimen in order to understand the changes that allow a cancer to become resistant to the study drugs. The researchers ask your

permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for similar research studies that were performed on the biopsy performed at trial entry.

Unknown future studies

If you choose to take part in this optional study, extra tissue from your biopsy will be collected and stored. Storing samples for future studies is called "biobanking." The biobank is being run by the NCI Biorepository. 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.

We don't know what research may be done in the future using your tissue 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 sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems.
- 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, a sample of tissue will be collected at the end of the study from an optional extra biopsy. Here are the steps involved:

1. Blood tests will be performed (if they have not been already performed) to confirm that your blood has the ability to clot normally
2. You will sign the standard surgical consent form from the institution where the biopsy procedure takes place.
3. The research biopsy is done through guidance by CT imaging in a similar way to your pre-treatment biopsy and biopsies done for diagnosis.
4. Your sample 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.
5. 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.
6. 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?

- Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. Rarely, an infection can occur. You will sign a separate consent form before the biopsy is taken. This will be a standard surgical consent form from the institution where the biopsy procedure takes place.
- 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.
2. Researchers 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 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 researchers 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 have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)*

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for known future studies:

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

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 _____