To: CIRB

From: Robert Mutter, M.D.

Date: August 6, 2024

Re: Amendment #6 (PVD 06/06/2024), for NCI protocol #10291: "A Phase 1b Study of Berzosertib in Combination with Radiation Therapy to Overcome Therapeutic Resistance in Chemotherapy Resistant Triple Negative and Estrogen and/or Progesterone Receptor Positive, HER2 Negative Breast Cancer"

SUMMARY OF CHANGES –
Model Informed Consent Document (PVD 08/06/2024)

I. PI Requested Changes:

#	Section	Comments
1.	General	Version date has been updated to match that of the revised protocol document

Research Study Informed Consent

Study Title for Participants: Testing the addition of an anti-cancer drug, berzosertib, in combination with a usual treatment (radiation therapy) for chemotherapy-resistant (breast cancer that did not benefit from chemotherapy) triple-negative and estrogen and/or progesterone positive, HER2 negative breast cancer

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Protocol 10291, "A Phase 1b Study of Berzosertib in Combination with Radiation Therapy to Overcome Therapeutic Resistance in Chemotherapy Resistant Triple Negative and Estrogen and/or Progesterone Receptor Positive, HER2 Negative Breast Cancer" (NCT # **04052555**)

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 been diagnosed with breast cancer, and there were cancer cells present in your surgical tissue after chemotherapy.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question:

What is the highest dose of berzosertib that can be given safely and tolerably (with manageable side effects) when added to radiation for chemotherapy resistant breast cancer and to determine the recommended Phase 2 dose?

We are doing this study because berzosertib has not previously been used in combination with radiation for breast cancer. We want to find out the highest dose of M6620 that can be given safely with radiation, so we can ultimately determine if this approach is better or worse than one of the usual treatment approaches of radiation alone for breast cancer in a future study. The usual approach is defined as care most people get for chemotherapy resistant breast cancer.

What is the usual approach to my chemotherapy resistant triple negative and estrogen and/or progesterone receptor positive, HER2 negative breast cancer?

The usual approach for patients who are not in a study is treatment with radiation alone sometimes followed by further chemotherapy or hormone 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 get M6620 through a vein in your arm twice weekly for 5 weeks and radiation therapy 5 days a week for 5-6 weeks, depending on what type of surgery you have had. Week 6 of radiation therapy will be given to you if you have had breast conserving surgery and may be given at your physician's discretion if you have had a mastectomy.

After you finish M6620 and radiation therapy, your doctor will continue to follow your condition and watch you for side effects weekly for 4 weeks after your last dose of radiation. After 4 weeks, your doctor will have the option to administer further chemotherapy or hormone therapy as part of the usual approach for your cancer. Your doctor will follow your condition and watch you for side effects at 12 months, 24 months, and 36 months after that. You will need to return to the clinic for these follow-up evaluations.

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.

There is a risk that you could have side effects from the M6620 and radiation therapy combination.

Some of the most common side effects of M6620 that the study doctors know about are:

M6620 may also make the side effects of radiation therapy worse, more frequent, or different than you would get with radiation alone, the usual approach for your cancer. In particular, the radiation skin reaction is likely to be worse with the combination of M6620 and radiation therapy compared with radiation alone. There could be more thickening or firming of the breast or chest wall on touch and for women with breast implants or expanders, there could be more hardness or tightness of the implant and negative changes in the way the breast implant looks or feels. Another side effect is possible radiation esophagitis (redness, pain, or swelling of the esophagus), pneumonitis (redness, pain, or swelling of the lungs), or pericarditis (redness, pain, or swelling of the tissue that surrounds the heart). Other possible side effects of radiation therapy are described in the section, "Side Effect Risks".

There may be some risks that the study doctors do not yet know about from M6620 and radiation therapy combination.

Benefits

There is some evidence in animals and living human cells that adding M6620 to the usual approach of radiation alone can kill breast cancer more effectively than radiation alone or shrink or stabilize breast cancer for longer than the usual approach alone. However, we do not know if this will happen in people. It is unlikely that adding M6620 to the usual approach will help you live longer than the usual approach alone. This study may help the study doctors learn things that may help other people in the future.

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

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

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

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

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

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

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (NCI). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to test the safety and tolerability of the investigational study drug M6620 when used in combination with radiation therapy. We are also trying to determine the Phase 2 dose. This study tests different doses of the drug to see which dose is safer for people. There will be up to 42 people taking part in this study.

What are the study groups?

There are two parts in this study, a **dose escalation part** and a **dose expansion part**. Your doctor will tell you which part you are in.

In the **dose escalation part** of this study, different people taking part in this study will get different doses of the study drug M6620.

The first three patients taking part in this study will get the lowest dose of M6620. If the drug does not cause serious side effects, the next patients taking part in the study will get a higher dose. The study doctor will watch each patient carefully as the dose is increased. The doses will continue to increase until people have serious side effects that require the dose to be lowered or the dose has been increased 3 times without any serious side effects that required the dose to be lowered. Once this dose is found, which is called the maximum tolerated dose, the study is stopped.

In the **dose expansion part** of this study, the highest dose with manageable side effects will be given to 12 more people. This will help study doctors better understand the side effects that may happen with this drug.

Treatment schedule: You will receive radiation therapy 5 days a week for 5-6 weeks, depending on the type of surgery you had. You will also get M6620 through a vein in your arm twice weekly [redacted] See the study calendar for more information.

You will not be able to get additional doses of M6620. This drug is not approved by the FDA for treatment of your disease or any other and is therefore considered "investigational".

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 and serum chemistry done before your treatment begins and weekly during M6620 and radiation therapy combination.
- Physical exams done weekly after the completion of radiotherapy for four weeks.

This study will use genetic tests that may identify changes in the genes in your DNA. Your genes carry information about you and your family, from the color of your eyes to health conditions for which you may be at risk, such as certain kinds of cancer.

Finding these changes would not affect your treatment in this study. However, they could affect your health in other ways. If the changes in your genes were inherited, the changes could also affect the health of your family members.

You and your family may want to know about any genetic test findings that may be important to your health. You may use this form to grant us permission in advance to give this information to your doctor. If a genetic test result about you seems to be medically important and you have granted us permission to contact you, the following steps will occur:

1. Researchers will study the result further to decide if it may be medically important to you or your relatives.
2. The research laboratory that performed the genetic test will contact your doctor about the finding. The research laboratory, which will not have any identifying information about you, will provide your doctor with a code number assigned to your genetic test sample.
3. Your doctor will use the code number to identify you, and will then contact you about the medically important finding. Your doctor may 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:

- Your study doctor will need to use some of the tissue left over from your biopsy when you were diagnosed with cancer (before you had chemotherapy) and from when you had surgery to remove your tumor (after you had chemotherapy). You and your study doctor will not get the results of this testing. These samples are a required part of the study.

- Blood samples (about 3 ½ tablespoons) will be taken prior to start of treatment, during the third week of study treatment, at the end of treatment, four weeks after the end of study treatment, and at 12 months. Researchers will obtain genetic material (DNA and RNA) from your tumor tissue and blood samples. Your tumor's DNA and RNA will be sequenced to evaluate the tumor and changes in the tumor that may have occurred during chemotherapy. You and your study doctor will not get any results of this testing. These samples are a required part of the study.

- Your samples will be used for 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. The genomic sequencing will be done by an NCI-supported laboratory in Frederick, Maryland, known as the Molecular Characterization (MoCha) Laboratory at the Frederick National Laboratory for Cancer Research. The laboratory will compare the genomic sequences from your tumor and blood cells to identify how they differ. The differences between genomic sequences of your tumor and blood cells may be important to understand why you did or did not respond to the treatment you received. Researchers hope to find potential "biomarkers" (changes present in tumor tissue that predict how patients with your type of cancer may respond to current or future treatments). This study may improve the ability to select future treatments or treatment combinations for others in the future. This study will not affect the cancer treatment or approach that you receive. Neither you nor your study doctor will be informed when the genetic sequencing research will be done. Your genomic sequence will also be stored in a secure NIH database for future use.

- If you agree, any genetic material left over after genomic sequencing will be stored ("biobanked") at a biorepository run by the Nationwide Children's Hospital in Columbus, Ohio, and supported by the NCI. Your samples may be used for potential future research studies. Health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will also be stored for future use. We do not know what research may be done in the future using your samples. 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. Additional information can be found in the ***Optional studies that you can choose to take part in*** section of this form.

- You will also need to give skin swabs for research on how radiation affects the bacteria that live on your skin (your skin "microbiome") and how that relates to side effects you may experience. Swabs will be collected from skin that received radiation and from the skin that did not receive radiation. Swabs will be collected: at baseline, at the end of your study treatment, and 4 weeks after the end of your study treatment. You and your study doctor will not get the results of this testing. These samples are a required part of the study.

If you are an English speaker and choose to take part in this study, you will be asked to fill out a form with questions about your physical well-being. Researchers will use this information to learn more about how cancer and cancer treatment affects people.

Since these forms are being used for research, the responses you provide will not be shared with your study doctor. If you have any serious health issues or other concerns, please talk with your doctor or nurse right away.

You will be asked to fill out this form eight times:

- Prior to receiving study treatment
- During Week 3 of study treatment

- At the end of study treatment
- At 2 weeks following your last study treatment
- At 4 weeks following your last study treatment
- Yearly for up to 3 years following completion of study treatment

Each form will take about 10 minutes to complete. The forms will ask about things like physical well-being, fatigue, and overall quality of life. You don't have to answer any question that makes you feel uncomfortable.

A patient study calendar is attached at the end of this document. It shows how often these exams, tests, and/or procedures will be done.

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

General Risks

If you choose to take part in this study, there is a risk that the combination of berzosertib and radiation may not be as good as the usual approach for chemotherapy resistant triple negative breast 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 combination of M6620 and radiation 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 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 blood (normal tissue) and tumor for genetic changes that may predict for greater benefit or increased side effects from the study drug. 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. Your doctor will talk with you about what the tests results may mean for you and your family.

He or she also may suggest you talk with a genetics counselor to learn more. You or your insurance plan would have to pay for visits to a genetic counselor.

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.

Skin Swab Risks

Some of the risks from swabbing the skin include irritation at the site where we obtained the swab.

Side Effect Risks

The combination of M6620 and radiation used in this study may affect how different parts of your body work such as your liver, kidneys, 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 combination of M6620 and radiation.

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.

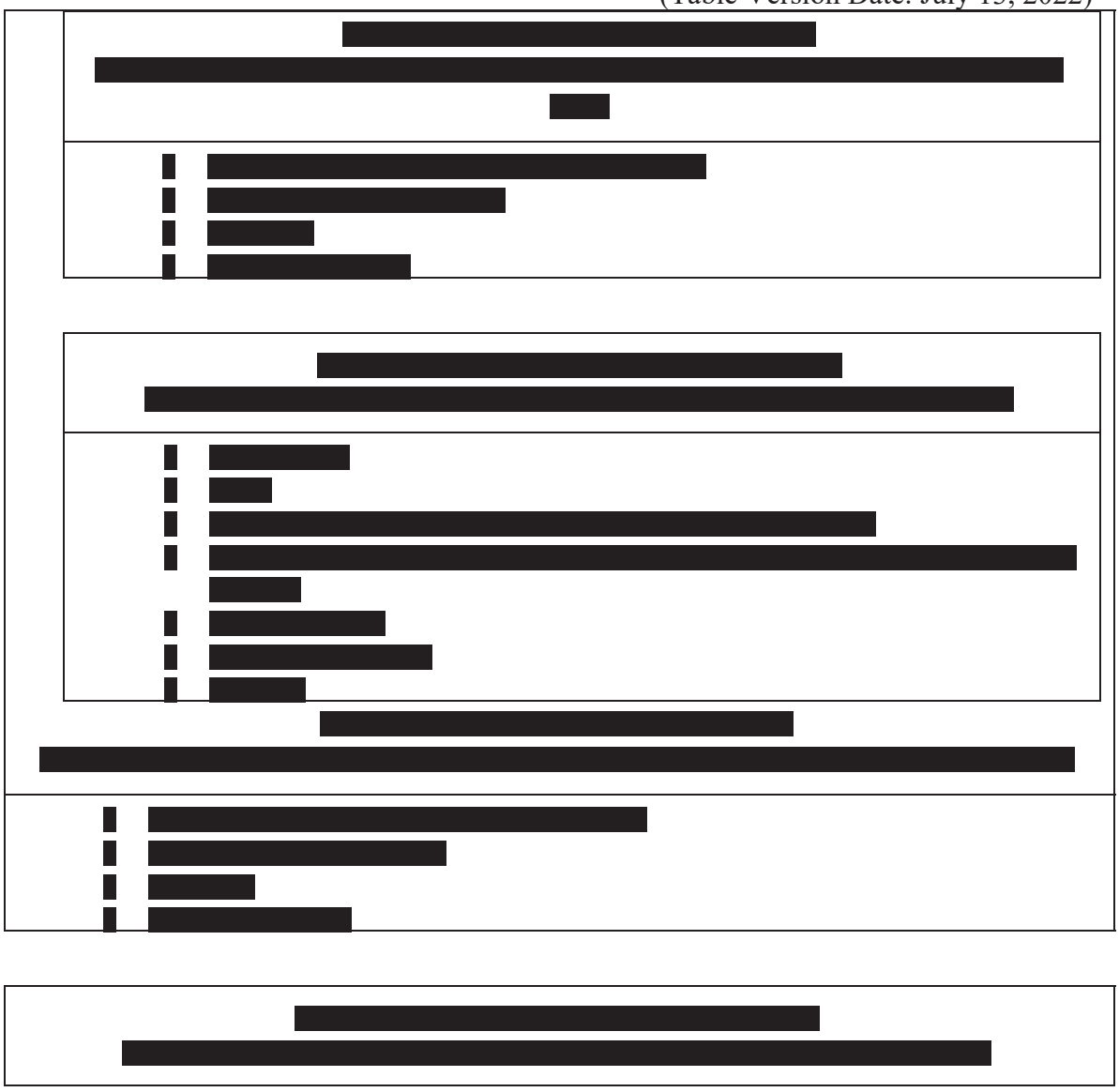
This study is looking at a combination of the usual approach used to treat this type of cancer (radiation alone) plus a study drug, M6620. This different combination of therapies may increase your side effects or may cause new side effects.

Drug Risks

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

Possible Side Effects of M6620 (VX-970, berzosertib)

(Table Version Date: July 13, 2022)



[redacted]

Additional Drug Risks

[redacted]

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

Possible Side Effects of Radiation Therapy

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, 10 to 100 may have:
• Reddening of the skin during treatment and for several weeks following treatment • Tanning of the skin lasting months and may be permanent • Slightly smaller breast size or change in the way the breast or chest wall look or feels • Mild thickening or firming of the breast on touch • Tiredness and weakness during treatment and for several weeks following treatment • Swelling of the arm, breast or chest wall • Peeling of the skin in the area treated with radiation • Mild pain at the site of radiation treatment requiring over the counter pain relievers • Sore throat or esophagus • For women with breast implants or expanders, side effects could also include hardness or tightness of the implant and negative changes in the way the breast implant looks or feels

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, 3 to 9 may have:
• Soreness or tightness in muscles of the chest wall or under the treated breast • Prominent thickening or firming of the breast or chest wall on touch • Severe pain at the site of radiation requiring prescription pain relievers • For women with breast implants or expanders, less likely risks could also include infection, severe pain, or severe hardness requiring removal or other surgery

RARE, AND SERIOUS In 100 people receiving radiation therapy, 2 or fewer may have:
• Cough or difficulty breathing due to lung inflammation • Inflammation of the heart muscle • Increased risk of heart disease • Rib fracture • Risk of developing another cancer

What are my responsibilities in this study?

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

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 6 months after your last dose of study 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 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 associated with getting radiation.
- the costs of getting M6620 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 cost of skin swabs for research
- the cost of the blood draws for research.
- the cost of getting your archival tissue for research.

You or your insurance provider will not have to pay for the M6620 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?

Information from your radiation plan will be stored. Researchers will use this information to learn more about why radiation therapy may cause side effects.

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 or the study treatment 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 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, and email address if appropriate*).

For questions about your rights while in this study, call the (*insert name of organization or center*) Institutional Review Board at (*insert telephone number*).

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

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

Circle your choice of “yes” or “no” for each of the following studies.

Optional sample collections for known research studies

If you choose to take part in this optional study, researchers will collect extra blood specimens for research on your immune cells and any identifiable tumor cells in your blood.

What is involved in this optional study?

If you agree to take part, additional blood samples will be collected from you. About 30 mL (2 tablespoons) will be drawn at each of the following timepoints: baseline; week 3 during study treatment; at the end of your study treatment; 4 weeks after the end of your study treatment; and 12 months after the end of your study treatment. About 150 mL (10 tablespoons) total will be taken for these optional research studies.

What is the risk of this optional study?

The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

How will information about me be kept private?

Your samples will be labeled with a code. The master list linking the code to your name and information will be kept separate from the samples and will be accessible only to your study doctor and a few study researchers. If research results are published, your name and 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?

You may withdraw your permission to use your samples by writing to your study doctor, (*insert name of study doctor for main trial*), at (*insert email for study doctor for main trial*). Then, any remaining samples will be destroyed or returned to your study doctor.

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*).

Samples for known studies:

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

YES NO

Optional storage of sample collections 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, any of your tumor tissue or blood samples left over from the genomic sequencing 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 NCI. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use. Your genomic sequence will also be stored in a secure NIH database for future use. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.

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

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

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may be 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.

What is involved in this optional study?

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

1. A sample from the tissue that was collected at the time of your biopsy or surgery to remove your cancer will be sent to the biobank. Leftover samples of blood obtained during this study will also be sent to the biobank.
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 study?

- 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 study?

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 study?

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 study?

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 retuned 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 study?

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

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

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

This is the end of the section about optional studies.

Contact for Future Research

I agree that my study doctor, or someone on the study team, may contact me or my doctor to see if I wish to participate in other research in the future.

YES NO

Contact for Medically Important Genetic Test Results

I agree that my study doctor, or someone on the study team, may contact me and my doctor if the laboratory finds a possible genetic test result that may be important to the health of me and/or my family members.

YES NO

Before you join this study, you may wish to talk with family members to see if they would like to learn of any genetic test results that may be important to their health. You have the right to decide how to handle sharing this information with your family members. However, if you were to become unable to share this information with family members due to illness or injury, or if you were no longer alive, please select and sign one of the options below on releasing genetic information to family members. Only genetic test results that may be medically important to your family members would be released.

Select and sign ONE option from below:

(1) **You have my permission** to release my genetic test results to **any and all** family members involved, in the event that I am unable to or have not survived to grant permission myself.

Participant's signature

Date of signature

Date of signature

(2) **You have my permission** to release my genetic test results or stored DNA **only** to the family members listed. Please write the name of the family member(s) in the space provided below.

Participant's signature

Date of signature

(3) **You do NOT have my permission** to release my genetic test results or stored DNA to any family members. I request that this information be kept private.

Participant's signature

Date of signature

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 for Protocol 10291 – For mastectomy patients

	Before the Study	During the Study Treatment					After the Study Treatment		
		Week 1	Week 2	Week 3	Week 4	Week 5	Weekly for 3 weeks following end of treatment	At 4 weeks after the end of treatment	At 12 months, and then every year for up to 3 years
M6620[A]		X	X	X	X	X			
Radiation Therapy[B]		X	X	X	X	X			
Pre-study procedures including informed consent, demographics, medical history, height	X								
Physical exam	X	X	X	X	X	X	X	X	X
Pregnancy test[C]	X								
Concurrent meds, weight, and general well-being, vital signs	X	X	X	X	X	X	X	X	
General blood draw for health monitoring	X	X	X	X	X	X	X[D]		
Side Effect Evaluation	X	X----------							----------X	X
Tumor tissue collection[E]	X								
Blood draws for scientific study		X[F]		X		X		X	X[I]
Skin swabs		X[F]				X[G]		X	
Quality of life questionnaires		X[F]		X		X[G]	X[H]	X	X

	Before the Study	During the Study Treatment					After the Study Treatment		
		Week 1	Week 2	Week 3	Week 4	Week 5	Weekly for 3 weeks following end of treatment	At 4 weeks after the end of treatment	At 12 months, and then every year for up to 3 years

A: M6620: Dose as assigned; [redacted]
B: You will receive radiation 5 times a week
C: Pregnancy test for women of child bearing potential
D: Blood work only at Week 7 (2 weeks after end of treatment)
E: Left over tumor tissue from your previous biopsies- (i) when you were diagnosed with cancer and (ii) from when you had surgery to remove your tumor.
F: On Day 1 of week 1 prior to M6620 and radiation therapy
G: To be collected within 5 days of the last treatment (preferably on the last day of treatment)
H: Only at Week 7 (2 weeks after end of treatment)
I: At 12 months only

Study Calendar for Protocol 10291 – For lumpectomy patients

	Before the Study	During the Study						After the Study Treatment		
		Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Weekly for 3 weeks following end of treatment	At 4 weeks after the end of treatment	At 12 months, and then every year for up to 3 years
M6620[A]		X	X	X	X	X				
Radiation Therapy[B]		X	X	X	X	X	X			
Pre-study procedures including informed consent, demographics, medical history, height	X									
Physical exam	X	X	X	X	X	X	X	X	X	X
Pregnancy test[C]	X									
Concurrent meds, weight, and general well-being, vital signs	X	X	X	X	X	X	X	X	X	
General blood draw for health monitoring	X	X	X	X	X	X	X	X[D]		

	Before the Study	During the Study						After the Study Treatment		
		Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Weekly for 3 weeks following end of treatment	At 4 weeks after the end of treatment	At 12 months, and then every year for up to 3 years
Side Effect Evaluation	X	X----------X								X
Tumor tissue collection[E]	X									
Blood draw collections for scientific study		X[F]		X			X		X	X[I]
Skin swabs		X[F]					X[G]		X	
Quality of life questionnaires		X[F]		X			X[G]	X[H]	X	X

A: M6620: Dose as assigned; [redacted]
B: You will receive radiation 5 times a week
C: Pregnancy test for women of child bearing potential
D: Blood work only at Week 8 (2 weeks after end of treatment)
E: Left over tumor tissue from your biopsies- (i) when you were diagnosed with cancer and (ii) from when you had surgery to remove your tumor.
F: On Day 1 of week 1 prior to M6620 and radiation therapy.
G: To be collected within 5 days of the last treatment (preferably on the last day of treatment)
H: Only at Week 8 (2 weeks after end of treatment)
I: At 12 months only