To: CTEP Protocol and Information Office

From: [redacted]

Date: November 10, 2022

Re: Amendment to NCI Protocol 10398: A Phase 2 Study of Anti-PD-L1 Antibody (Atezolizumab) in Chondrosarcoma and Clear Cell Sarcoma

This amendment is in response to [redacted] notice regarding atezolizumab drug information updates. The only change to the consent forms is the version date.

Thank you for your consideration.

I. ICD Changes:

#	Section	Comments
1.	Footer	Updated the version date.

Research Study Informed Consent Document

Study Title for Participants: Testing Atezolizumab in People ≥18 Years Old with Clear Cell Sarcoma or Advanced Chondrosarcoma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: NCI Protocol 10398 "A Phase 2 Study of Anti-PD-L1 Antibody (Atezolizumab) in Chondrosarcoma and Clear Cell Sarcoma"

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 advanced clear cell sarcoma or chondrosarcoma that is not curable by surgery and for which there is no standard treatment. People with your type of advanced cancer usually don't have effective treatment options, including radiation and 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?

The main reason this study is being done is to answer the following question:

- Does the study drug, atezolizumab (MPDL3280A), cause your cancer to shrink by at least one-quarter compared to its present size?

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your chondrosarcoma or clear cell sarcoma. The usual approach is defined as

care most people get for chondrosarcoma or clear cell sarcoma that is not curable by surgery. Atezolizumab has not been approved by the FDA for your type of cancer.

What is the usual approach to my clear cell sarcoma or chondrosarcoma?

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

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer, but you may want to receive comfort care to help relieve your symptoms.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will get atezolizumab through a vein in your arm (IV) once every 3 weeks (21 days). The Study Team will monitor your cancer and your safety. You will continue to get doses of atezolizumab for as long as your cancer does not get worse, the side effects are tolerable, you agree to stay on study, and the study doctor agrees it is still in your best interest to take part in the study.

After you stop atezolizumab treatment, your doctor will continue to follow your condition for 90 days from your last treatment date or until you start a new treatment. During those 90 days, your doctor will watch you for side effects. This follow up will consist of three telephone calls from the Study Team: one call between Day 27 and Day 30 after the last dose of atezolizumab, one call between Day 57 and Day 60 after the last dose of atezolizumab, and one call between Day 87 and Day 90 of after the last dose of atezolizumab.

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

There is also a risk that you could have side effects from the atezolizumab. 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:

- Tiredness
- Infection
- Anemia (tiredness from low red blood cell counts)
- Diarrhea, nausea, vomiting
- Difficulty swallowing
- Fever
- Flu-like symptoms including body aches
- Allergic reaction
- Loss of appetite
- Pain in back
- Cough, shortness of breath, stuffy nose
- Itching, acne, rash

Atezolizumab may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Hormone gland problems (e.g., problems with control of metabolism, growth, stress response, blood pressure, sexual organs, pain, temperature, and blood sugar)
- Pain in belly
- Pain or swelling of the joints
- Rash that develops on skin, nails, scalp and inside of mouth or vagina that may be painful

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

Benefits

There is evidence that drugs similar to atezolizumab that affect your immune system might be effective in shrinking your type of cancer. It is not possible to know now if atezolizumab will shrink your cancer compared to the usual approach. 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 at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely; your doctor can help you with this. 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 (the National Cancer Institute). The study sponsor is the organization who oversees the study. The study may be stopped by the sponsor if they determine the drug is not working.

You may be able to continue treatment with atezolizumab if it is helping you feel better, even if tests suggest that your cancer is getting worse. If you meet the criteria for remaining on treatment, your doctor will discuss with you the potential risks and benefits of continuing treatment.

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

What is the purpose of this study?

The purpose of this study is to test the good and bad effects of the drug called atezolizumab. Atezolizumab could shrink your cancer, but it could also cause side effects, which are described in the risks section below. The study doctors hope to learn if the study drug will shrink your cancer by at least one quarter compared to its size. We also plan to test the effect of the study drug on immune cells in your tumor, in the tissue around your tumor, and in your blood.

Atezolizumab has already been approved by the FDA to treat other cancers but not for clear cell sarcoma or advanced chondrosarcoma.

There will be about 68 people taking part in this study.

What are the study groups?

The trial will test three groups of patients based on tumor types. The three groups are: (1) tumor that is clear cell sarcoma or has an *EWSR1/ATF1* or *EWSR1/CREB1* translocation, (2) grade 2 or 3 conventional chondrosarcoma, and (3) dedifferentiated chondrosarcoma. Each adult taking part in this study will receive the same dose that is used for standard of care with the study drug atezolizumab; children will get a lower unapproved dose. You will be able to receive additional doses of the drug for as long as you remain in the study.

Atezolizumab will be given in the outpatient setting, so you won't have to stay overnight in the hospital or clinic. The drug will be given by vein into your arm (IV). The first time you get the drug, it will take about 1 hour to give it to you. You will need to stay at the hospital for 2-3 hours after the first time you get the drug so that your doctor can monitor you. Later in the study, the study drug may be given to you over a period of 30 minutes instead. The study drug is given in cycles. Each cycle involves one dose of study drug every 21 days (on same day of each cycle) until you experience unacceptable side effects or your tumor grows. You will not receive any atezolizumab on the other 20 days of each cycle.

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.

- An electrocardiogram (EKG) and an echocardiogram (ECHO) to test your heart
- A pregnancy test in women who are able to become pregnant
- A CT scan or other imaging test such as ultrasound (an examination using sound waves) or MRI (an examination using magnetic field and radio waves) that detects your tumor

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.

1. You will need to have biopsies for the study:
    - The first biopsy will be at the start of the study, before you begin atezolizumab treatment.
    - The second biopsy will be collected near the beginning of Cycle 3, although it may be earlier if it looks like your cancer is getting better.

    The study biopsy takes small pieces of cancer tissue from your body. This is like the biopsy you had that helped diagnose your cancer. These study biopsies are done for research; they are not done as part of your medical care. The purpose of these biopsies is to compare your body's immune response against your tumor before and after treatment with the study drug. If the first biopsy is unsuccessful or the procedure has caused you harm, the second biopsy will not be done, but you may still remain in the study. You will not get the results of this testing. If you agree to take part in the study, you may need to sign a separate consent form for the study biopsy at the hospital or clinic where the biopsy is done.

One optional tumor biopsy may be collected for research purposes if your cancer gets worse or your tumor grows. There is more information about this optional biopsy in the "Optional biopsy collection for known laboratory studies" section near the end of this document.

2. You will need to have blood samples collected for the study. The researchers will use the samples to learn more about how atezolizumab works and which patients in the future might be most likely to respond to atezolizumab. They will also use some of your blood to learn which genes are only in your tumor and not in your normal blood. Each sample will be approximately 3 teaspoons of blood. They will be collected at the following times:
    - At the start of the study, before you begin atezolizumab treatment.
    - Before your second dose of atezolizumab (the first day of Cycle 2).
    - Before your third dose of atezolizumab (the first day of Cycle 3), or earlier if your doctor sees evidence that you are responding to the drug.
    - At the end of Cycle 3 and one at the end of Cycle 5.
    - Every 12 weeks after Cycle 5 for the rest of your first year. Then, every 18 weeks during your second year and every 24 weeks in the years after that.
    - If your cancer gets worse.
    - **For participants at the NCI,** additional blood samples will be required:
        - after two weeks of treatment (if you and your doctor agree to this collection),
        - at the start of every cycle, beginning with Cycle 2, and
        - if your cancer gets worse.

      Your study doctor can tell you if these blood collections are required for you. Each of these samples will be about 1 teaspoon of blood.

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

The mandatory research genetic tests used in this study will test genes in your tumor and your normal blood for genetic changes. Changes found in your normal blood 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. We will not tell you anything we learn about your genes from research done on this study.

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 atezolizumab 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 atezolizumab 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 5 months after your last atezolizumab dose.

Genetic Testing Risks

As part of the research study, it is possible that you could learn that you have genetic risks for another disease or disability. This may be upsetting and, depending on what you learn, might create a need to make challenging decisions about how to respond.

Although your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, learning your research results could mean something about your family members and might cause you or your family distress. Before joining the study, it may be beneficial to talk with your family members about whether and how they want you to share your results with them.

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. Biopsies for this study might involve exposure to radiation from CT scans (see "Imaging Risks," below, for more information). You may sign a separate consent form for the study biopsy that describes the risks in more detail.

Blood Sample Risks

Possible side effects from drawing the blood sample include mild pain, bleeding, bruising, and infection at the site of the needle insertion. Fainting or light-headedness can sometimes occur, but usually last only a few minutes.

Side Effect Risks

The atezolizumab 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 drug.

Here are important things to know about side effects:

1. The study doctors do not know who will or will not have side effects. **If you experience diarrhea, it is important that you contact the study doctor immediately, even if the diarrhea is mild.**
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.

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 Atezolizumab

COMMON, SOME MAY BE SERIOUS In 100 people receiving atezolizumab, more than 20 and up to 100 may have:
• Tiredness • Infection

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving atezolizumab, from 4 to 20 may have:
• Anemia which may require blood transfusion • Diarrhea, nausea, vomiting • Difficulty swallowing • Fever • Flu-like symptoms including body aches • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Reaction during or following a drug infusion which may cause fever, chills, rash • Loss of appetite • Pain in back • Cough, shortness of breath, stuffy nose • Itching, acne, rash Atezolizumab (MPDL3280A) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting. • Pain in belly • Pain or swelling of the joints • Rash that develops on skin, nails, scalp and inside of mouth or vagina that may be painful

RARE, AND SERIOUS In 100 people receiving atezolizumab, 3 or fewer may have:
• Bruising, bleeding

Atezolizumab (MPDL3280A) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Heart problems including swelling and heart failure. Symptoms and signs of heart problems may include: shortness of breath, swelling of the ankles and body.
- A condition with high blood sugar which leads to tiredness, frequent urination or excessive thirst.
- Swelling and redness of the eye
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly.
- Swelling of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck.
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine.
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs.
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
- Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Skin: blisters on the skin, including inside the mouth (can be severe), rash with blisters, skin rash developing 1-8 weeks after a drug is given, which may be accompanied by fever, lymph node swelling and organ failure.

Additional Drug Risks

The study drug could interact with other drugs. 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 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 that you get in this study will expose you to more radiation than you get from everyday background radiation. The total amount of radiation from these scans is the same as (*insert estimate for local institution, e.g., 14 years' worth*) of background radiation. 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.

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 5 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 clear cell sarcoma or chondrosarcoma. 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 atezolizumab 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 biopsies for testing the effect of atezolizumab on your immune system (before starting treatment and before starting Cycle 3 [or earlier if there is evidence your cancer is shrinking]).
- The blood collections for genetic analysis (before starting treatment, before starting Cycle 3 [or earlier if there is evidence your cancer is shrinking], at the end of Cycle 3, at the end of Cycle 5, at every other tumor measurement visit after that [e.g., Cycle 9, Cycle 13, etc.], and if your disease gets worse).
- The blood collections (required for some participants) for testing the effect of atezolizumab on your immune system (at the time of any biopsy, on Day 15 of Cycle 1, before starting each new cycle, and if your disease gets worse).

You or your insurance provider will not have to pay for the atezolizumab while you take part in this study.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor and any company supporting the study or the study agent now or in the future. This would include any organization helping the company with the study.
- The NCI Central IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now we don't know what research may be done in the future using your information. This means that:

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

There are laws that protect your genetic information. However, there is a risk that someone could get access to your genetic information and identify you by name. In some cases, employers could use your genetic information to decide whether to hire or fire you. The study

doctors believe the risk of this happening is very small. However, the risk may increase in the future as people find new ways of tracing information. For more information about the laws that protect you, ask your study doctor.

Where can I get more information?

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

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

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ (*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 center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

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 research 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 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 biopsy collection for known laboratory 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 extra (third) tumor biopsy if your disease comes back or shows signs of coming back. The researchers will use the tissue from this biopsy to:

1. Perform a specific, targeted sequencing test on your tumor tissue in a clinically approved laboratory.
    - **You and your doctor will receive the results of this test**. The results will be added to your electronic medical record and may be used to guide your medical care.
    - Your doctor will discuss these results with you and tell you about any gene variations that might make you able to take part in targeted therapy clinical trials in the future.
2. Study any changes in your immune system's response to your cancer.
    - This test is done for research only. **We will not give you any individual results from this test or add this information to your medical record.**
    - The researchers hope to learn how atezolizumab helps the immune system work against tumors.
3. Measure effects of your cancer or atezolizumab treatment on your tumor's genes.
    - This test is done for research only. **We will not give you any individual results from this test or add this information to your medical record.**
    - Your tumor contains genes, which serve as the "instruction book" for the cells that make up our bodies. Determining whether different tumor gene variations affect how atezolizumab works against tumors will help scientists understand which patients might respond best to this drug.

What is involved in this optional sample collection?

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

1. An additional, biopsy will be performed if your disease comes back or shows signs of coming back.
2. Your research samples will be stored with a coded identifier, not your name. Any personal data about you will also be stored in a sequence computer database with that

code identifier. Your sample will be stored by the researchers until they are used for research or destroyed. There is no limit on the length of time we will keep your samples and research information.
3. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- Typical risks of biopsy collection include, but are not limited to, bleeding, infection, pain and scarring. There is also some risk associated with radiation exposure if a CT scan is involved in the biopsy procedure.
- 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. 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 from this study who study your sample and information will know who you are. However, they will not share your identity with anyone else.
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.

However, if you choose to have this optional tumor biopsy before leaving the study, we will perform a specific, targeted sequencing test on this tumor tissue in a clinically approved laboratory, and you and your doctor will receive the results of this test. These results will also be added to your electronic medical record. Your doctor will discuss these results with you and tell you about any gene variations that might make you able to take part in targeted therapy clinical trials in the future.

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)*, at _____ (*insert telephone number of study doctor*), who will let the other researchers know. Then, any sample that remains in storage will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been 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 this optional study:

Samples for known future studies:

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

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

_____

Participant Study Calendar

Day	Participant Activity
Before starting study drug	• Check in at the _____ [*name of center*] • Medical history and physical exam, including ECOG Performance Status (an assessment of how you are doing with your daily living activities) • Echocardiogram and EKG to test your heart • Tumor measurements by CT/MRI or PET • Routine blood tests • Required blood draw for genetic research (all patients) • Required blood draw for research on the effects of the study drug (some patients only) • Pregnancy test for women who are able to become pregnant • Tumor biopsy will be required
Cycle 1 Day 1	• Go to _____ [*name of center*] • Routine blood tests • Atezolizumab will given through a vein over 1 hour, followed by observation at the _____ [*name of center*] for 2-3 hours
Cycle 1 Day 15	• Check in at the _____ [*name of center*] • Routine blood tests • Blood draw for research on the effects of the study drug (some patients only; optional)
Cycle 2 Day 1	• Go to _____ [*name of center*] • Medical history and physical exam • Routine blood tests • Required blood draw for genetic research (all patients) • Required blood draw for research on the effects of the study drug (some patients only) • Atezolizumab will given through a vein (about 30 minutes to 1 hour)
Cycle 3 and onwards, Day 1	• Go to _____ [*name of center*] • Medical history and physical exam • Routine blood tests • Required blood draw for research on the effects of the study drug (some patients only) • Atezolizumab will through a vein (about 30 minutes to 1 hour) • Tumor biopsy will be required at the start of Cycle 3
End of Cycle 3 and onwards	• Tumor measurement by CT/MRI or PET to measure any changes in the size of your tumors will be performed at the end of Cycle 3, and at the end of every 2 cycles after that (less often once you have been on study for >1 year) • Required blood draw for genetic research at the end of Cycles 3 and 5 and every 4 cycles after that (less often once you have been study for >1 year)