

Research Study Informed Consent Document

Study Title for Participants: Testing the use of investigational drugs Atezolizumab and/or Bevacizumab with or without standard chemotherapy in the second-line treatment of advanced-stage head and neck cancers

Official Study Title for Internet Search on
<http://www.ClinicalTrials.gov>: **Protocol EA3202:** A Phase II/III trial of Chemotherapy + Cetuximab vs Chemotherapy + Bevacizumab vs Atezolizumab + Bevacizumab Following Progression on Immune Checkpoint Inhibition in Recurrent/Metastatic Head and Neck Cancers (NCT05063552)

Version Date: March 13, 2025

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 your head and neck cancer has come back or spread to other locations in the body.

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 drug combination is most effective to use for recurrent or metastatic head and neck cancer after the initial treatment doesn't work?

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

What is the usual approach to my recurrent or metastatic head and neck cancer?

The usual approach for patients with recurrent or metastatic head and neck cancer who are not in a study is treatment with surgery, radiation, or chemotherapy. There are several FDA-approved chemotherapy drugs that are commonly used in your type of cancer and include docetaxel, cetuximab, cisplatin and carboplatin. Sometimes, combinations of these treatments are used. Your doctor can explain which treatment may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for a few months or longer.

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

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

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

If you decide to take part in this study you will randomly be assigned to one of three groups. If assigned to the first group, you could get cisplatin or carboplatin in combination with docetaxel and cetuximab for 18 weeks, followed by cetuximab alone either weekly or biweekly for up to two years or until disease progression/unacceptable side effects.

In the second group, you could get either cisplatin or carboplatin in combination with docetaxel and bevacizumab for 18 weeks followed by bevacizumab alone every three weeks for up to two years or until disease progression/unacceptable side effects.

In the third group you will get atezolizumab and bevacizumab every three weeks for up to two years or until disease progression/unacceptable side effects.

After you finish your treatment, your doctor will continue to follow your condition for five years and watch you for side effects. After your study treatment is complete you will be receiving a phone call follow up every three months for the first two years, and then every 6 months for year's three to five.

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

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

Risks

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

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

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

- High blood pressure
- Tiredness
- Infection
- Bleeding

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

Benefits

There is evidence that the combination of bevacizumab and chemotherapy and the combination of bevacizumab and atezolizumab is effective in shrinking or stabilizing your type of cancer. It is not known if these new combinations are more effective than the current standard of care with chemotherapy and cetuximab at extending your life or extending your time without disease. This study will help the study doctors learn things that will help people in the future.

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

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

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. This may mean slowly stopping the study drugs so that there is not a sudden unsafe change, risk to your health, etc. 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 National Cancer Institute (NCI) Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor. The study sponsor is the organization who oversees the study.

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

What is the purpose of this study?

The purpose of this study is to compare the usual treatment alone or the usual treatment plus bevacizumab or a combination of bevacizumab and atezolizumab as a second-line therapy for head and neck cancers. The addition of study drugs could shrink or stabilize your cancer or stop it from growing. But, it could also cause side effects, which are described in the risks section below.

This study will help the study doctors find out if this different approach is better than the usual approach. To decide if it is better, the study doctors will be looking to see if the addition of bevacizumab to the usual treatment or bevacizumab in combination with atezolizumab increases the life of patients compared to the usual approach.

These chemotherapy drugs (cisplatin, carboplatin, docetaxel, and cetuximab) are already approved by the FDA for use in recurrent or metastatic head and neck cancer. But most of the time they are not used until other chemotherapy or immunotherapy stops working. There will be about 216 people taking part in the first part (phase II) portion of this study and about 214 people taking part in the second part (phase III) portion of this study.

What are the study groups?

This study has 3 study groups.

- **Group 1**

If you are in this group, you will get the standard chemotherapy used to treat this type of cancer (cisplatin or carboplatin, and docetaxel) plus cetuximab. You will get these drugs intravenously (IV) through a vein in the arm or through your port. Cisplatin/carboplatin and docetaxel can be administered either every 21 days or as a split dose on days 1 and 8 of every 21-day cycle. Cetuximab is administered on days 1, 8 and 15 of every 21-day cycle. After 6 cycles with these drugs, cetuximab alone will be given weekly or biweekly for up to two years.

There will be about 72 people in this group for the phase II portion and about 108 additional people in this group for the phase III portion of this study.

- **Group 2**

If you are in this group, you will get the standard chemotherapy used to treat this type of cancer (cisplatin or carboplatin, and docetaxel) plus bevacizumab. You will get these drugs intravenously (IV) through a vein in the arm or through your port.

Cisplatin/carboplatin and docetaxel can be administered either every 21 days or as a split dose on days 1 and 8 of every 21-day cycle. Bevacizumab is administered once every cycle (21 days). This group will receive 6 cycles. After 6 cycles with these drugs, bevacizumab alone will be given every 21 days for up to two years.

There will be about 72 people in this group for the phase II portion and about 108 additional people in this group for the phase III portion of this study.

- **Group 3**

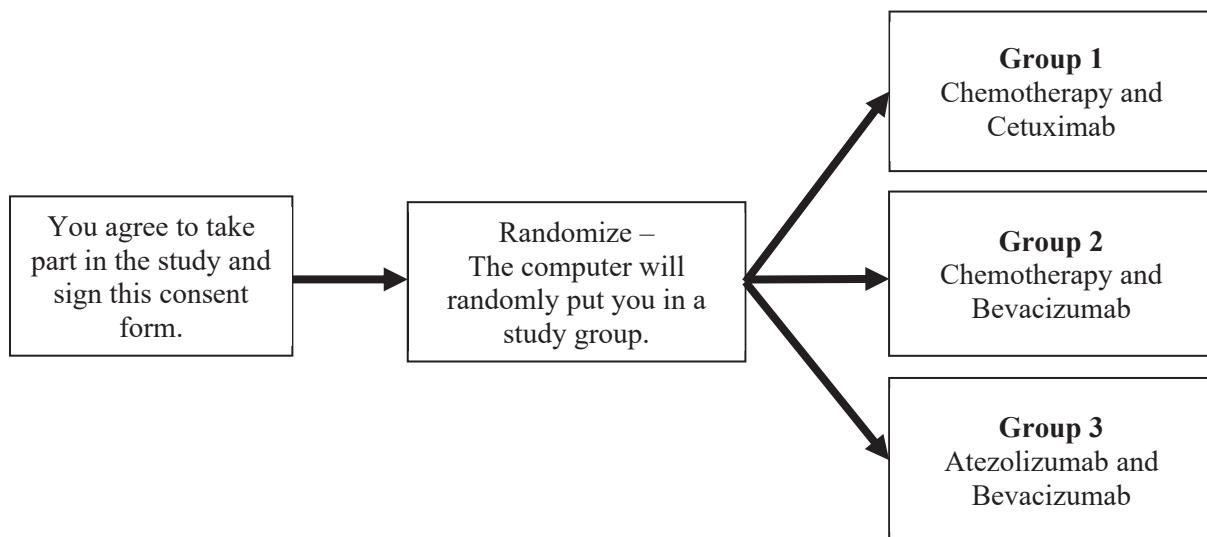
If you are in this group, you will get both bevacizumab and atezolizumab. You will get these drugs intravenously (IV) through a vein in the arm or through your port the first day of each cycle. Each cycle lasts 21 days. This group will have cycles every 21 days until progression or for up to two years.

There will be about 72 people in this group for the phase II portion and about 108 additional people in this group for the phase III portion of this study.

We will use a computer to assign you to one of the study groups. This process is called “randomization.” It means that your doctor will not choose and you cannot choose which study group you are in. You will be put into a group by chance. You will have an equal chance of being in Group 1, Group 2, or Group 3.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right.

Based on the outcome of the phase II portion, group 2 or group 3 will be moving forward to the phase III portion of the study, to be compared with group 1.



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.

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

General Risks

If you choose to take part in this study, there is a risk that the study approach may not be as good as the usual approach for your cancer or condition 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 bevacizumab and 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 6 months after the last dose of study treatment if you are in group 2 or 3 and for 2 months after the last dose of study treatment if you are in group 1.

Side Effect Risks

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

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

Here are important things to know about side effects:

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

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

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.

- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at the combination of the usual drugs used to treat this type of cancer as well as two study drugs. The different combinations of drugs may increase your side effects or may cause new side effects.

Drug Risks

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

Possible Side Effects of Bevacizumab (CAEPR Version 2.5, May 2, 2018)

COMMON, SOME MAY BE SERIOUS

In 100 people receiving bevacizumab (rhuMAb VEGF), more than 20 and up to 100 may have:

- High blood pressure which may cause headaches, dizziness, blurred vision

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving bevacizumab (rhuMAb VEGF), from 4 to 20 may have:

- Anemia which may require blood transfusion
- Infection, including collection of pus in the belly or rectum
- Abnormal heartbeat which may cause palpitations or fainting
- Pain in the belly, rectum, chest, joints, muscles, or tumor
- Low appetite, constipation, diarrhea, heartburn, nausea, vomiting, or dehydration
- Bleeding from multiple sites including the vagina or nose
- Internal bleeding which may cause black tarry stool, blood in vomit, coughing up blood, or blood in urine
- Blockage of internal organs which may cause vomiting or inability to pass stool
- Sores in the mouth
- Allergic reaction during or after infusion of bevacizumab which may cause fever, chills, rash, itching, hives, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Low white cell count that may increase the risk of infection
- Damage to the jawbone which may cause loss of teeth
- Delay in healing of wounds or spontaneous opening of wounds
- Weight loss, tiredness, or dizziness
- Muscle weakness
- Headache

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving bevacizumab (rhuMAb VEGF), from 4 to 20 may have:

- Numbness, tingling or pain in the fingers or toes
- Hoarseness, stuffy nose, or cough
- Dry skin
- Swelling and redness of the skin
- Blood clot in limbs or lungs which may cause swelling, pain, shortness of breath
- Leakage of protein in the urine, which can rarely lead to damage to the kidney

RARE, AND SERIOUS

In 100 people receiving bevacizumab (rhuMAb VEGF), 3 or fewer may have:

- Clots in the arteries, causing stroke (which may cause paralysis or weakness) or heart attack (which may cause chest pain or shortness of breath). This risk is significantly increased in patients who are elderly or with history of diabetes
- Heart failure which may cause shortness of breath, swelling of ankles, and tiredness
- Bowel perforation (a tear in the bowel) that can cause pain or bleeding and require surgery to repair
- A tear or hole (fistula) in internal organs such as the nose, throat, lungs, esophagus, rectum, or vagina. These conditions may cause serious infections or bleeding and require surgery to repair
- Sores in the throat
- Flesh-eating bacteria syndrome, an infection in the deep layers of skin
- Damage to organs (bone, lungs, others) which may cause loss of motion
- Bleeding in the tumor, brain, belly or lungs which may cause confusion, blood in stool or coughing up blood
- Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
- Kidney damage which may require dialysis
- Redness, pain or peeling of palms and soles

Additional Notes on Possible Side Effects for Bevacizumab:

- Risk in pre-menopausal women: more likely to develop menopause when taking bevacizumab.

Risk Profile for Atezolizumab (MPDL3280A) (CAEPR Version 2.5, November 18, 2024)

COMMON, SOME MAY BE SERIOUS

In 100 people receiving atezolizumab (MPDL3280A), more than 20 and up to 100 may have:

- Tiredness
- Infection

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving atezolizumab (MPDL3280A), 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 (MPDL3280A), 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 inflammation and heart failure. Symptoms and signs of heart problem may include: shortness of breath, swelling of the ankle 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.
- Damage to organs in the body when the body produces too many white cells
- Swelling of the brain (meningitis/encephalitis), which may cause headache, confusion, sleepiness, seizures, and stiff neck.
- Abnormal movement of the facial muscles
- Swelling of the spinal cord
- Problem of the muscle (myositis, rhabdomyolysis), 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.
- Swelling or tenderness of blood vessels.

Possible Side Effects of Cisplatin (Table Version Date: April 20, 2015)

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Cisplatin, more than 20 and up to 100 may have:

- Nausea, vomiting,
- Infection, especially when white blood cell count is low
- Anemia which may cause tiredness, or may require blood transfusions
- Bruising, bleeding
- Kidney damage which may cause swelling, may require dialysis
- Hearing loss including ringing in ears

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving Cisplatin, from 4 to 20 may have:

- Hair loss
- Change in taste
- Diarrhea
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Confusion
- Difficulty with balance
- Numbness and tingling of the arms and legs
- Blurred vision or changes in ability to see colors (especially blue or yellow)

RARE, AND SERIOUS

In 100 people receiving Cisplatin, 3 or fewer may have:

- Cancer of bone marrow caused by chemotherapy later in life
- Seizure

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

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Carboplatin, more than 20 and up to 100 may have:

- Hair loss
- Vomiting, nausea
- Infection, especially when white blood cell count is low
- Anemia which may cause tiredness, or may require blood transfusions
- Bruising, bleeding

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Carboplatin, more than 20 and up to 100 may have:

- Belly pain

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving Carboplatin, from 4 to 20 may have:

- Diarrhea, Constipation
- Numbness and tingling in fingers and toes
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Changes in taste
- Changes in vision

RARE, AND SERIOUS

In 100 people receiving Carboplatin, 3 or fewer may have:

Damage to organs which may cause hearing and balance problems

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

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Docetaxel, more than 20 and up to 100 may have:

- Swelling of the body
- Hair loss
- Change in nails
- Rash, itching
- Vomiting, diarrhea, nausea, constipation
- Sores in mouth which may cause difficulty swallowing
- Infection, especially when white blood cell count is low
- Anemia which may require blood transfusions
- Bruising, bleeding
- Tiredness
- Numbness and tingling of the arms and legs
- Fever
- Absence of menstrual period
- Swelling and redness of the arms, leg or face
- Pain

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Docetaxel, more than 20 and up to 100 may have:

- Watering, itchy eyes

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving Docetaxel, from 4 to 20 may have:

- Severe skin rash with blisters and peeling which can involve inside of mouth and other parts of the body
- Belly pain
- Kidney damage which may require dialysis
- Blood clot which may cause swelling, pain, shortness of breath
- Abnormal heart rate
- Shortness of breath, wheezing
- Chest pain

RARE, AND SERIOUS

In 100 people receiving Docetaxel, 3 or fewer may have:

- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Cancer of bone marrow (leukemia) caused by chemotherapy

Patients should be aware that Docetaxel may cause them to become intoxicated from the alcohol it contains. Patients should avoid driving, operating machinery, or performing other activities that are dangerous within one to two hours after the infusion of Docetaxel. In addition, some medications, such as pain relievers and sleep aids, may interact with the alcohol in the Docetaxel infusion and worsen the intoxicating effects.

Possible Side Effects of Cetuximab (Table Version Date: January 19, 2016)

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Cetuximab, more than 20 and up to 100 may have:

- Change in nails
- Swelling and redness of the area of radiation
- Rash, itching, dry skin, acne
- Diarrhea, constipation, nausea, vomiting, loss of appetite, weight loss
- Sores in mouth which may cause difficulty swallowing
- Infection, especially when white blood cell count is low
- Difficulty sleeping

COMMON, SOME MAY BE SERIOUS

In 100 people receiving Cetuximab, more than 20 and up to 100 may have:

- Headache, tiredness
- Numbness and tingling of the arms and legs
- Blurred vision
- Shortness of breath, cough
- Fever
- Pain

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving Cetuximab, from 4 to 20 may have:

- Hair loss
- Severe skin rash with blisters and can involve inside of mouth and other parts of the body
- Blood clot which may cause swelling, pain, shortness of breath
- Allergic reaction or infusion reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat

RARE, AND SERIOUS

In 100 people receiving Cetuximab, 3 or fewer may have:

- Heart stops beating
- Kidney damage which may require dialysis
- Scarring of the lungs
- Severe blood Infection
- Sudden death

Additional Drug Risks

Patients are not permitted to receive chronic daily treatment with aspirin or NSAIDs known to inhibit platelet function or to use direct oral anticoagulant therapies due to bleeding risk with the study agents. Patients must also not be on immunosuppressive medication with some exceptions due to concerns for decreased responsiveness to the atezolizumab experimental arm. 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 FDG PET/CT 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 FDG PET/CT that you get in this study will expose you to more radiation than you get from everyday background radiation. The amount of radiation from this scan is the same as 3.3 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.

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

What are my responsibilities in this study?

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

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

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 treatment.

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 of getting the bevacizumab and 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 or your insurance provider will not have to pay for the bevacizumab or 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 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.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research including the Imaging and Radiation Oncology Core (IROC).

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 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).

For questions about your rights while in this study, call the _____ (*insert IRB contact*) Institutional Review Board at _____ (*insert telephone number*).

Optional studies that you can choose to take part in.

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

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

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

Optional sample collections for storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person’s response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Unknown future studies

If you choose to take part in this optional study, a sample of tissue from your previous biopsy and three additional blood samples will be collected and stored. Storing samples for future studies is called “biobanking.” The biobank is being run by ECOG-ACRIN 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.

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

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

- 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 just be in your tumor tissue. These are called somatic changes. Changes may also be in your normal tissue and passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

If only tumor tissue is sequenced, we will not know if a genetic change in your tumor is also in your normal tissue. This is why sometimes both normal tissue and tumor tissue are sequenced. This helps researchers understand if a genetic change happened only in your cancer tissue, or in your normal tissue as well.

What is involved in this optional sample collection?

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 prior surgery or biopsy** will be sent to the biobank. About 2 tablespoons of blood will be collected from a vein in your arm at the following times: prior to starting study treatment, about 2-4 weeks after starting treatment, and about 6-8 weeks after starting study treatment.
2. Your sample will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

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

Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for this optional sample collection, your tissue could be used up.

Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.

In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: <https://www.genome.gov/10002328/>

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

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

You will not benefit from taking part.

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

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

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, (*insert name of study doctor for main trial*), at (*insert telephone number of study doctor for main trial*), who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

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

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

Samples for unknown future studies:

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

YES

NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study.

Participant's signature _____

Date of signature _____

Signature of person(s) conducting the informed consent discussion _____

Date of signature _____