Vanderbilt University Institutional Review Board
Informed Consent Document for Research

Principal Investigator: Vandana G. Abramson, MD **Revision Date:** 9/11/2020
Study Title: BRE 15136: A Phase II trial of atezolizumab (anti-PDL1) with carboplatin in patients with metastatic triple negative breast cancer
Institution/Hospital: Vanderbilt University Medical Center NCT03206203

This informed consent applies to Adults.

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study. Anyone you authorize to receive your medical record will also get this note.

1. What is the purpose of this study?

You are being asked to take part in this research study because you have breast cancer that has spread to areas of your body outside of your breast.

The purpose of this study is to test how well the combination of study drugs, carboplatin and atezolizumab, keeps your cancer from growing compared to taking carboplatin only. You will be given carboplatin with atezolizumab or carboplatin alone (a computer decides). If you receive only carboplatin, at some time in the future, if your cancer starts to grow, you may be able to receive atezolizumab. If you receive carboplatin and atezolizumab, you will be removed from the study if your cancer becomes worse.

Carboplatin is an FDA approved drug that is administered intravenously.

The study drug atezolizumab is an investigational drug. This means that it has not been approved by the Food and Drug Administration (FDA) for breast cancer. Atezolizumab is also called MPDL3280A. Atezolizumab works to assist your immune system in fighting cancer cells. It is now being tested as a possible therapy against solid tumors and hematologic malignancies for humans.

About 106 people will take part in this study. About 37 people from Vanderbilt will take part in this study.

2. What will happen and how long will you be in the study?

If you give your consent to be in this study by signing this form, you will have tests and procedures (called "**screening**") done. These are done to reduce the risks of taking part in this study and to make sure it is okay for you to be in the study.

Biospecimens will be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.

It is possible that after these tests are reviewed, you will not be able to be in the study. There may be other reasons why you cannot be in this study. These reasons will be discussed with you by your study doctor or the clinic staff.

Screening
After you have signed this consent, the screening tests listed below will be done within 28 days of your first dose of study drugs. Some of the tests listed below must be done less than 7 days of your first dose of the study drugs. If they were done too long before that, they may need to be repeated. Your doctor/study team will discuss this with you.

- You will have a complete physical exam and your current symptoms will be reviewed. Physical examination will include examination of major body systems including neurologic, cardiac, respiratory, gastrointestinal, and skin. You will be asked about your medical and cancer history including any past treatments or surgeries for your disease. Your performance status (your ability to carry out your daily activities) will be assessed. Your vital signs (height, weight, temperature, breathing rate, blood pressure, pulse and oxygen saturation) will also be recorded. You will be asked about any medicines you are taking including over-the-counter medicines, vitamins, or herbal treatments.
- You will have an ECG (electrocardiogram). This is a test to measure how your heart beats and this test may detect some abnormal heart conditions. Sticky pads will be put on your chest for this test and wires will be attached from the pads to an ECG machine. It is possible the sticky pads will irritate your skin and may cause a small amount of pain upon removal. You will be asked to lie still for about five minutes before the test.
- You will have a body CT Scan of your chest, abdomen, and pelvis, and a bone scan. These are described in the "scans" section of the consent.
- **Blood Collection** (4-5 tablespoons in total will be collected at the screening visit):
    - Blood will be drawn for the Vanderbilt lab to check your health and blood sugar levels (white blood cell count, differential, hemoglobin, platelet count, sodium, potassium, chloride, bicarbonate, BUN, creatinine, glucose, calcium, and magnesium, SGOT, SGPT, and total serum bilirubin, albumin, total protein, and INR).
    - If you are randomized to receive atezolizumab, blood will be drawn to assess thyroid function after screening. About 1 teaspoon of blood will be drawn for this test.
    - Blood will be drawn to test your blood for HIV, active or past exposure to hepatitis B, and hepatitis C. About 4 teaspoons of blood will be drawn for these tests.
- Only Women Able to Have Children: A pregnancy test will be done for women who can have children. The test will be done using a blood sample. The test must be negative for you to take part in the study. Women who are pregnant or breast feeding may not take part in the study. About 1 teaspoon of blood will be drawn.
- You will be asked to provide a piece of stored breast tumor sample from previous biopsies or surgeries you may have had in the past before you joined this study. If archived tumor samples are unavailable, a new tumor biopsy will be required. These samples can be used to study breast cancer. They will help researchers better understand the reasons for cancer development, growth, spread, and its response to treatment.
- You will be asked to have a biopsy of your disease. This biopsy will be done on an area of your body where your cancer has spread (area of disease outside of the breast). These samples will be used to test the gene signature of your tumor and for other research purposes. Having this biopsy is required to take part in this study. Your research doctor will tell you what area(s) of your body can be biopsied. Your research doctor, with your input and consent, will select only one area to biopsy. This is the case even if your breast cancer has spread to multiple areas. Before the biopsy, you will discuss the procedure with the doctor who will perform the biopsy. You will be asked to sign a separate consent form with the doctor that performs the procedure. You will sign only after an explanation of the potential risks. If you do not have any disease that is safely accessible, you will not have to undergo a biopsy. Also, if enough tissue is not obtained during a biopsy, you will not have to have it repeated.

  Types of biopsy you may have depending on the location of your tumor:
  If your cancer has spread to your skin, you may be asked to provide a biopsy sample for research purposes. Skin biopsies can be performed by your research doctor or by a surgeon. For a skin biopsy, lidocaine will be injected in your skin to numb it. Lidocaine may burn or cause a rash, redness, or soreness where you get the shot. There is a risk that this drug may cause problems with heart rhythm. Then two small pieces of skin (about half a centimeter each) will be removed. Two to four stitches will be used to close the biopsy site. These will be taken out after a week. The procedure will take about 15-20 minutes.

If your cancer has spread to your lymph nodes, liver, or bone, you may be asked to provide three to six samples for research purposes. The biopsy will be done either by a surgeon or a radiologist. This is an outpatient procedure. You cannot to eat or drink anything starting the night before the procedure. Right before the procedure, a very small flexible hollow tube will be inserted into a vein in your arm. You will get medicines such as sedatives and painkillers through this tube. Depending upon the location of the cancer, a radiologist may use ultrasound or a CT scan to guide him/her to the correct place to take a piece of tissue. Next, a needle will be used to get samples. The procedure will take about 1 hour. Usually, no stitches are required. Afterwards, you will be observed in the recovery room for 2-6 hours, on average. You will also need to get a friend or family member to drive you home after the procedure.

How the Study Drugs are Given

If the screening tests show you can be in the study, then you will be asked to return to the cancer clinic for your first visit. The study doctor will let you know how much of each drug to take. A computer will decide whether you will go into the carboplatin only group or the carboplatin + atezolizumab group. This process is called "randomization," like flipping a coin to decide on a group. You and your doctor will be told which treatment you are assigned. For every 1 patient in the carboplatin + atezolizumab group, one patient will go to the carboplatin only group. If your disease worsens and you are in the carboplatin only group, you can "cross-over" to receive atezolizumab.

Carboplatin and atezolizumab are both a liquid solution given intravenously.

You will be administered carboplatin or the carboplatin and atezolizumab (if in the carboplatin + atezolizumab group) on day 1, cycle 1.

Photography

If you have skin rashes or lesions, the study doctor may take color photographs (digital images) and measurements to document your condition. Special care will be taken to shield your identity in these photographs, in accordance with local guidelines. If you have a tattoo(s), your tattoo(s) may be included and visible in the photographs (digital images). Tattoos may be considered unique and identifiable, so the photograph(s) (digital images) of your tattoo(s) may identify you in pictures. However, your eyes will be masked in an effort to protect your identity. All photographs will be treated in a secure and confidential manner at all times. If you choose not to allow photos to be taken of your lesions or rash, you will still be able to participate in the study

What will be done during Each Cycle

While you are taking part in the study, you will be asked to come to cancer clinic on day 1 of every cycle that you participate in this study. Each cycle is 21 days. When you come to the cancer clinic you may have the following things done:

- You will have a complete physical exam.
- Your performance status (your ability to carry out your daily activities) will be assessed.
- Your vital signs (weight, temperature, breathing rate, blood pressure, pulse and oxygen saturation) will be recorded.
- You will be asked about any medicines you are taking including over-the-counter medicines, vitamins, or herbal treatments.
- You will be asked about any changes in your health status that you may be experiencing.
- **Blood Collection** (4-5 tablespoons in total will be collected at these visits):
    - Blood will be drawn for the Vanderbilt lab to check your health and blood sugar levels (white blood cell count, differential, hemoglobin, platelet count, sodium, potassium, chloride, bicarbonate, BUN, creatinine,

glucose, calcium, and magnesium, SGOT, SGPT, and total serum bilirubin, albumin, total protein, and INR). .
  - If you are randomized to receive atezolizumab, blood will be drawn to assess thyroid function every 4 cycles.
  - Blood will be drawn for the Vanderbilt lab to check your blood for tumor cells. This test is called circulating tumor DNA. This will only be done on day 1 of cycle 1, day 1 of cycle 2, and at the end of treatment.
  - Blood will be drawn at cycle 1, day 1 and cycle 2 day 1 to collect mononuclear cells (to look at how the cells in the body respond to the study immunotherapy).
  - Blood will be drawn to test your blood for HIV, active or past exposure to hepatitis B, and hepatitis C, once every year that you are on the study. About 4 teaspoons of blood will be drawn for this test.
- A CT scan will be completed every 3 cycles. In addition, if bone metastases were present on the baseline studies, a bone scan will also be completed every 3 cycles.
- Study drug administration
- You will complete a biopsy questionnaire regarding your experience with the biopsies on cycle 2, day 1.

End of Study Visit

If your disease gets worse, you are having bad side effects, or you no longer wish to be in the study then you will have an end of study visit. This is to make sure you are okay after taking the study drug. The following things will be done at this visit:

- You will have a complete physical exam and your current symptoms will be reviewed. Your performance status (your ability to carry out your daily activities) will be assessed. Your vital signs (weight, temperature, breathing rate, blood pressure, oxygen saturation and pulse) will also be recorded.
- **Blood Collection** (3-4 tablespoons in total will be collected at the end of study visit):
  - Blood will be drawn for the Vanderbilt lab to check your health and blood sugar levels (white blood cell count, differential, hemoglobin, platelet count, sodium, potassium, chloride, bicarbonate, BUN, creatinine, glucose, calcium, and magnesium, SGOT, SGPT, and total serum bilirubin, albumin, total protein, and INR).
  - If you are randomized to receive atezolizumab, blood will be drawn to assess thyroid function every 4 cycles. About 1 teaspoon of blood will be drawn for this test.
  - Blood will be drawn for the Vanderbilt lab to check your blood for tumor cells. This test is called circulating tumor DNA. About 2 teaspoons of blood will be drawn for this test.
  - Blood will be drawn to collect mononuclear cells (to look at how the cells in the body respond to the study immunotherapy).
- You will have a biopsy of your disease if you are stopping the study. This biopsy will be done on an area of your body where your cancer has spread (area of disease outside of the breast).

Study Duration and Follow-up

You will keep taking the study drugs until:

- Your disease gets worse, or
- You get bad side effects from the treatment that you cannot tolerate, or
- You wish to stop the study, or
- You are not able to follow the requirements of the study
- You become pregnant
- The study is canceled

Because of these reasons, we cannot predict the length of time that you will be on study. You will be closely followed by the research nurse while on study and will be asked to come back to the cancer clinic for a follow up visit within 30 days (+/- 3 days) from your last dose of study drugs. If you are not able to return to the cancer clinic, then the research nurse will call you for this follow up. Any ongoing side effects or problems will be reviewed.

Please note that if you are in the carboplatin only group and your disease worsens, you can "cross-over" to receive atezolizumab.

If you are still experiencing bad side effects from the treatment, then you may be followed by the research nurse every 3 months until the side effect has gotten better.

We may follow-up your health status by reviewing your medical charts annually for up to 3 years after participation in this study.

Scans While You are in the Study

While you are in the study, you will have Computed tomography (CT) scans done to measure the disease in your body. A Magnetic Resonance Imaging (MRI) may be done if a CT is unable to be done or your doctor feels that is indicated. You will have a CT/MRI scan with contrast. An IV (needle in your vein) will be used to give you the contrast. This contrast is used to help organs, blood vessels and other area show up more clearly on the scan.

At screening you will have a CT or MRI of your body to measure your disease before you take the study drugs. You will also have a bone scan to check for disease in your bones.

While you are taking the study drug, you will have a CT or MRI of your body every 3 cycles to measure your disease. You may need to have a bone scan of your body if the scan at screening showed that you have disease in your bones.

What happens during a CT Scan:

The CT scan will take a few minutes. You will be asked to lie on a narrow table. The table slides into the center of the CT scanner. You will be asked to lie very still during the scan. You may be asked to hold your breath for short periods of time.

What happens during an MRI Scan:

The MRI scan will take a few hours. An MRI scan is taken in a large machine that is shaped like a tunnel. This scan does not use x-rays. Instead, they use a strong magnet and radio waves, like those used in an AM/FM radio to make pictures of your body.

You may not be able to have this scan if you have a device in your body such as aneurysm clips in the brain, heart pacemakers or defibrillators, and cochlear implants. Also, you may not be able to have this scan if you have an iron-based tattoo, pieces of metal (bullet, BB, shrapnel) close to or in an important organ (such as the eye).

Certain metal objects like watches, credit cards, hairpins, writing pens, etc. may be damaged by the machine or may be pulled away from the body when you are getting the scan. Also, metal can sometimes cause poor pictures if it is close to the part of the body being scanned. For these reasons, you will be asked to remove these objects before going into the room for the scan.

You will hear "hammering", clicking, or squealing noises during the scan. You can ask the staff whether earplugs are available to reduce the noise.

During the scan, the MRI staff is able to hear and talk to you. You will also be able to hear the staff. They will be talking to you during your scan and may ask you to hold your breath, not move, or other simple tasks. You may be asked to lie very still throughout the scan.

What happens during a Bone Scan:
The bone scan may take a few hours. You will be given an injection of a radioactive material. This is called a tracer. The tracer sends out a type of radiation called a gamma ray. A special camera then makes pictures from these gamma rays.

A few hours after the injection you will be asked to lie still on a table while a machine with an arm-like device with the special camera passes over your body.

After the scan, the tracer in your body does not stay radioactive for long. You will be asked to drink extra water after the scan. This will help remove any unabsorbed radioactive material from your system. After two days all of the tracer should be out of your system.

3. Costs to you if you take part in this study:

If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. Genentech will provide the study drug free of charge for your use in this study.

However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

http://www.cancer.gov/clinicaltrials/learning/insurance-coverage

4. Biospecimens for Research

Your biospecimens (tissue and blood samples) are being used for this research study. As part of the study, we may perform the following research studies on them. In addition, we will ask your permission in the next section for the use of any leftover biospecimens (that is, samples remaining or “leftover” after the research for this study is completed) to be used for future research and the option to contact you in the future. In order to perform additional research, some of your blood and tissue samples may be sent to Genentech for future product development.

We may use genetic analysis in some of the research we do on your samples. Researchers can learn a lot by studying genes. Genes are pieces of DNA that give instructions for building the proteins that make our bodies work. DNA stores these instructions in the form of a code. This is the code that you inherit from your parents and that you pass on to your children.

One of the methods we might use to study your samples is called whole genome sequencing. This allows us to look at some or all of your genetic code. Researchers may also use other methods as they are developed. Studying genes along with your health information will help us to better understand what causes certain diseases. It may also help us to understand how different patients respond to treatment. This knowledge could help us to develop treatments for everyone.

What we learn about you from your samples will not be put in your health record and will not be shared with you or your doctor. No one else (like a relative, boss, or insurance company) will be given your test results.
Your samples will only be used for research and will not be sold. Health insurance companies and group health plans may not request your genetic information that comes from this research.

We will remove your name and any other information that could directly identify you from your samples and information. We will replace this information with codes. We will keep a master list that links those codes to your materials. Only certain study staff can access this master list. We will keep the samples in locked freezers in locked buildings. We will keep health information and research data on secure computers. These computers have many levels of protection.

The Genetic Information Nondiscrimination Act (GINA) may help protect you from health insurance or health-related employment discrimination based on genetic information. The law provides that health insurance companies and group health plans

- may not ask for genetic information from this research and
- may not use genetic information when making decision about eligibility or premiums

The law will not stop health insurance companies from using genetic information to decide whether to pay claims. The law does not apply to other types of insurance (such as life, disability or long-term care).

Despite the GINA protections and the best efforts of the research team to protect your information, you may still be at risk if information about you were to become known to people outside of this study.

5. Side effects and risks that you can expect if you take part in this study:

Because of your illness or the treatment, you may get for your illness, you may have complications or side effects from the drugs. These may be serious or could even threaten your life. Complications from your illness may happen whether or not you are in this study. We are not certain if being in this study affects the risks that come with your illness.

Risks of carboplatin

During your participation in this study, you are at risk for the side effects described below. You should discuss these with the study doctor.

Carboplatin as a Single Agent: Side Effects in Clinical Studies

The common side effects listed below were considered to be related to carboplatin:

- Anemia (low levels of red blood cells)
- Decreased blood platelets
- Decreased function of bone marrow

- Decreased neutrophils (a type of white blood cell)
- Bleeding
- Nausea
- Vomiting
- Infection
- Signs and symptoms at injection site
- Feeling weak
- Hair loss
- Low amounts of calcium, magnesium, potassium, and sodium in the blood
- Numbness, tingling, or pain of hands and feet
- Stomach cramps
- Pain

Less frequent side effects that were considered to be related to carboplatin:

- Bronchospasm
- Hives
- Inflammation of skin/reaction caused by an allergy
- Itching
- Hemorrhage
- Rash
- Toxic effect on brain or spinal cord function
- Toxicity to organs of hearing
- Trouble breathing
- Abnormal liver function tests
- Diarrhea
- Constipation
- Vision problems

Rare side effects that were considered to be related to carboplatin:

- Blockage or closing off of blood vessels in the liver
- Life threatening allergic reaction
- Painful, red or swollen mouth
- Poor vision
- High blood pressure
- Loss of appetite

Risks of atezolizumab

During your participation in this study, you are at risk for the side effects described below. You should discuss these with the study doctor.

Very Common (more than 10% chance)

- Joint pain
- Lack of energy
- Vomiting
- Decreased appetite
- Diarrhea
- Cough
- Shortness of breath
- Fatigue
- Generalized pain and back pain
- Itching of the skin
- Nausea
- Fever
- Rash
- Urinary tract infection

Common (between 1-10% chance)

- Chills
- Nasal congestion
- Inflammation of the large intestines (colitis)
- Abdominal pain
- Infusion-related reaction or hypersensitivity (allergic reaction)
- Hepatitis
- Difficulty swallowing
- Elevated liver enzymes, which may indicate inflammation of the liver
- Decreased potassium in the blood
- Decreased sodium in the blood
- Low blood pressure
- Decreased oxygen resulting in shortness of breath
- Influenza-like illness
- Inflammation of the lungs
- Low platelet count, which may make you more likely to bruise or bleed
- Hypothyroidism
- Immune-mediated pneumonitis (inflammation of the lungs)
- Immune-mediated hepatitis (inflammation of the liver)
- Immune-mediated colitis (inflammation of the large intestines)
- Immune-mediated hypothyroidism
- Infusion-related reactions within 24 hours of administration (such as flu-like symptoms, fever, and rash)

Less common but important (less than 1% chance)

- Decreased ability of your adrenal glands to produce hormones
- Elevated blood sugar (diabetes)
- Hyperthyroidism
- Inflammation of the brain and surrounding tissues usually caused by infection
- Inflammation of the pituitary gland or pituitary stalk (symptoms may include severe headaches, nausea and vomiting, producing large amounts of dilute urine and extreme thirst)
- Inflammation of the heart muscle
- Diabetic ketoacidosis (a life-threatening complication of diabetes)
- Guillain-Barre (auto-immune numbness and/or paralysis)
- Increase in amylase and lipase, which may indicate inflammation of the pancreas
- Myasthenia gravis (muscle weakness)
- Immune-mediated Myositis (inflammation of the muscle), which led to death in 4 cases
- Immune-mediated nephritis (inflammation of the kidneys)
- Immune-mediated pancreatitis (inflammation of the pancreas)
- Immune-mediated diabetes (elevated blood sugar)
- Immune-mediated hypothyroidism
- Immune-mediated adrenal insufficiency, (decreased ability of your adrenal glands to produce hormones), which led to death in 1 case
- Immune-mediated hypophysitis (inflammation of the pituitary gland)
- Immune-mediated Guillain-Barre syndrome (auto-immune numbness and/or paralysis), which led to death in 1 case
- Immune-mediated myasthenic syndrome/myasthenia gravis (muscle weakness)
- Immune-mediated meningoencephalitis (inflammation of the brain and surrounding tissues)
- Immune-mediated myocarditis (inflammation of the heart muscle)
- Decreased levels of red blood cells (anemia)
- Low white blood cell count (leukopenia)
- Inflammation of the lining of the bronchial tubes (bronchitis)
- Viral infection of the nerves (shingles)
- Lower respiratory tract infection
- Lung infection (such as pneumonia)
- Increase in creatinine level in blood
- Decrease in neutrophils (a type of white blood cell)(neutropenia)
- Decrease in white blood cell count
- Low level of magnesium in blood (hypomagnesaemia)
- Autoimmune neuropathy
- Dizziness
- Headache
- Weakness, numbness, and pain in the hands or feet (peripheral neuropathy)
- Peripheral sensory neuropathy (impedes ability to feel or sense your feet)
- Fainting (syncope)
- Inflammation of the muscle (myositis)
- Inflammation of the kidneys (nephritis)

Pregnancy Risks
You should not become pregnant or father a baby while in this study because the study drug may affect an unborn baby. Women should not breastfeed a baby while on this study. If you are a woman who can have children, you will have a pregnancy test before you can be in this study. If you are pregnant, you cannot be in this study. Tell one of the study doctors right away if you suspect that you have become pregnant while in the study. Whether you are a man or a woman, you need to use effective methods of birth control (e.g., abstinence, condoms, diaphragm, vasectomy/vasectomized partner, tubal ligation) while in this study and for at least 3 months after your last dose of study drug. Check with your study doctor about the methods of birth control to use and how long to use them.

Risks of Blood Draw
Pain, redness, soreness, bruising, or infection may occur at the needle stick site. Rarely some people faint. The study doctor may put some cream (called EMLA) on your skin to numb the area so you will not feel the needle stick as much. The numbing cream may make your skin or the area have a change in skin color, but this is rare.

Risks of HIV Testing
You will be tested for HIV (AIDS virus) during this study. If test results show that you have the virus that causes AIDS, the study staff will tell you the results and refer you to the health department to confirm the test results and give you someone to talk to about this disease. We will talk with you before and after testing, and your test result will be given to you only in person. You should know that the study staff must give your name to the Tennessee Department of Health if you test positive because this is the law. If others find out you have this virus, it may cause mental stress, unfair treatment from other people, problems with being able to get insurance or find a job, or other unknown problems. It is important to seek medical care if you have HIV.

Risks of Infusion
You may experience symptoms associated with receiving an infusion. Serious infusion-associated events may include:

- Difficulty breathing (Dyspnea)
- Low blood pressure (Hypotension)
- Wheezing
- Tightening of the airways (Bronchospasm)
- Rapid heart rate (Tachycardia)
- Reduced oxygen saturation
- Respiratory distress

Risks of an ECG
The sticky pads used for the ECG may cause skin irritation.

Risks of Tumor Biopsy
Biopsies are normally performed under the guidance of an imaging technique. Each procedure requires a separate consent prior to the biopsy. The risks may include:

- Pain and discomfort. The amount of pain and discomfort will vary, depending on the location of the biopsy site. These risks can be discussed with the study doctor.
- Minor bleeding at the biopsy site.
- Tenderness at the biopsy site.
- Scarring at the biopsy site.
- Rarely, an infection at the biopsy site.

- Lidocaine, a numbing drug, may burn or cause a rash, redness or soreness where you get the shot. There is a small risk that this drug may cause problems with heart rhythm.

Although uncommon, problems from biopsies can be life threatening. Some potentially serious problems from bleeding or organ damage may occur. These might require surgical repair.

Skin or chest biopsy
Likely: local discomfort and minor bleeding
Rare: moderate or major bleeding. Infection and allergic reaction to the numbing medicine also occur rarely.

Lymph node biopsy
Likely: local discomfort and minor bleeding
Rare: moderate or major bleeding, need for blood transfusion, lung collapse, hospitalization due to bleeding or other complications, infection, damage to bowels, damage to nearby organs, allergic reaction to the numbing medicine.

Liver biopsy
Likely: local discomfort and minor bleeding
Rare: moderate or major bleeding, need for blood transfusion, lung collapse, hospitalization due to bleeding or other complications, infection, damage to bowels, damage to nearby organs, allergic reaction to the numbing medicine

Bone biopsy
Likely: local discomfort and minor bleeding
Rare: moderate or major bleeding, need for blood transfusion, lung collapse, hospitalization due to bleeding or other complications, infection, damage to bowels, damage to nearby organs, allergic reaction to the numbing medicine

Some biopsy procedures, such as a liver biopsy, may require “intravenous conscious sedation” (IVCS). For IVCS, a very small hollow flexible tube will be placed in your vein. You will get sedatives and painkillers before and during the procedure. You may become sleepy. However, you will be able to breathe on your own and respond to commands. There is a very small risk of having allergic reactions to the medications, pneumonia, a heart attack, irregular heartbeat, low blood oxygen, and death with IVCS. To minimize these risks, your doctor will review your medical history before the procedure. If you have active heart problems (such as chest pains or a recent heart attack), you cannot take part in this procedure. Your doctor or the IVCS personnel may feel that you would be at moderate or high risk of complications with IVCS. If so, you cannot take part in this study if IVCS would be required for the biopsy. You will be carefully watched during and after the procedure.

Some biopsy procedures require imaging studies, such as a CT scan or ultrasound to plan or guide the procedure. These studies would be done even if you were not donating samples for research purposes. However, if the biopsy is done for research, the imaging studies would also be considered research. Your doctor will tell you whether imaging studies are required for your procedure. If you have a CT scan, there is also a small risk of allergic reaction to the dye that may be used during the scan. You could have anxiety or claustrophobia in the scanning machine. Talk to your doctor if you have had problems during a CT scan in the past. There is no radiation from an ultrasound test.

Risks of Radiation
For your first year of participation in this study, you may be asked to undergo certain imaging procedures that are outside of your normal standard of care. These procedures include the use of CT guidance to obtain tumor tissue biopsy samples. In the first year of the study, you will only be asked to have two of the CT guided biopsy procedures.

The above procedure exposes you to radiation that is in addition to your exposure from normal standard of care imaging.

We estimate your research radiation exposure for the first year to be approximately 12% more than that allowed annually for persons who are exposed to radiation as part of their work.

Should you choose to continue in the study, you may have up to one more CT guided biopsy procedure. This additional exposure to radiation increases your overall exposure to approximately twice that allowed annually for radiation workers.

Additionally, to protect your bladder from the effects of the injected radioactive imaging substance, we encourage you to drink plenty of fluids before and after the CT procedures. You should urinate at least every two hours for up to six hours following the procedures.

Risks of MRI

There are no known major risks with an MRI scan. But, it is possible that harmful effects could be found out in the future. Even though the tunnel is open, it may bother you to be placed in a tight space (claustrophobia), and to hear the noise made by the magnet during the scan. You may also feel the table vibrate and/or move slightly during the scan. It may be hard to lie on the table during the scan. If you have any metal pieces in your body, they could move during the scan and damage nearby tissues or organs.

If you use a transdermal patch (medicated patches applied to the skin), you may need to take it off during the MRI scan. Transdermal patches slowly deliver medicines through the skin. Some patches have metal in the layer of the patch that is not in contact with the skin (the backing). You may not be able to see the metal in the backing of these patches. Patches that contain metal can overheat during an MRI scan and cause skin burns in the immediate area of the patch. Tell the study doctor that you are using a patch and why you are using it (such as, for pain, smoking cessation, hormones). Ask your doctor for guidance about removing and disposing of the patch before having an MRI scan and replacing it after the procedure. Tell the MRI facility that you are using a patch. You should do this when making your appointment and during the health history questions you are asked when you arrive for your appointment.

The contrast dye you will receive is the standard dye used in these scans. Getting the dye through the IV does not cause pain, but you may feel discomfort, tingling or warmth in the lips, metal taste in the mouth, tingling in the arm, nausea, or headache. These symptoms occur in less than 1% (less than 1 in 100) of people and go away quickly. Very rarely, there may be an allergic reaction, which may be severe. This may cause you to have a rash, swelling, tightness in the throat, trouble breathing, low blood pressure, and very rarely death. Placing the needle in your vein may also cause minor pain, bruising and/or infection where it goes into your arm. There will be trained health workers and supplies on hand to treat you and keep you safe if you have any of these symptoms. Also, a doctor will be on hand during the scan to provide any needed care if side effects do occur, and to decide when or if we should stop giving you the dye.

Allergic reactions to the radioactive dye are rare. Most of the dye will be eliminated from your body (through your urine or stool) within a day, so be sure to promptly flush the toilet and thoroughly wash your hands with soap and water. The amount of radiation is so small that it is not a risk for the people you come in contact with after the test.

There are no known risks of having MRI scans without contrast while pregnant. However, there may be risks that are unknown.

Risks of Drug Interaction with Foods and Other Medicines

As with all drugs, there is a chance that some foods or medications can affect how the study drugs work. Medications including some over-the-counter medications and common herbal supplements may cause bad effects, by making the study drug action stronger or weaker. You will be given more information about medicines and products that should be avoided.

For your safety, you must tell the study doctor or nurse about all the drugs you are taking, including over-the-counter drugs and herbals, before you start the study and before taking any new drugs while you are on the study. Your doctor and nurse will make sure that your prescription medications are not going to interfere with the study drugs and vice-versa. If you are visiting any other doctor who prescribes you any medication, it is important that you tell him/her that you are taking part in this study.

6. Risks that are not known:

Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

7. Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt or for the study supporters to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt or for the study supports to give you money for the injury

8. Good effects that might result from this study:

a) The benefits to science and humankind that might result from this study: The information from this study will help doctors learn more about how atezolizumab affects patients' bodies and cancers when combined with carboplatin.

b) The benefits you might get from being in this study: If you decide to take part in this study, there is no guarantee that your health will improve.

9. Other treatments you could get if you decide not to be in this study:

Your other choices may include the following:

- Getting treatment or care for your cancer, such as other chemotherapy regimens or radiation therapy (in a few special circumstances), without being in a study
- Taking part in another study
- Getting no treatment
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

10. Payments for your time spent taking part in this study or expenses:

You will not be paid to take part in this study.

11. Reasons why the study doctor may take you out of this study:

You may be taken out of the study if:

- staying in the study would be harmful to you
- you have side effects that you cannot tolerate
- you need treatment not allowed in the study
- your disease gets worse or progresses
- you fail to follow instructions
- you become pregnant
- the study is cancelled

There may be other reasons to take you out of the study that we do not know at this time. If you are taken out of the study, you will be told the reason why, and your doctor will discuss other treatments with you. You will be followed for 30 days after stopping study drugs. If you stop taking study drugs due to bad side effects from the treatment that you cannot tolerate, you will be followed until these side effects are better or resolved. A medical chart review will be conducted annually for survival purposes.

12. What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way. Being in this study is voluntary. You can change your mind about being in this treatment program at any time. Your decision will not affect your future care. Deciding not to be in this study, or stopping participation in it, will cause no penalty or loss of benefits you otherwise would have. You may seek care from a doctor of your choice at any time. If you decide to no longer take part in the study, the study doctor may ask you to allow him/her to follow you and collect information from your medical records, if you agree. You will also be asked to return to clinic for a last visit to check blood work and your physical well-being.

If you decide to leave the study, please contact Dr. Abramson in writing and let her know that you are leaving. Her mailing address is:

[redacted]

13. Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact [redacted]

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

14. Clinical Trials Registry.

A description of this clinical trial will be available on 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.

15. Confidentiality:

All efforts, within reason, will be made to keep your personal information in your research record confidential but total confidentiality cannot be guaranteed. Your information and samples will be given a code. Dr. Abramson, her staff, and other authorized people will be the only people who know your personal information.

Study data will be recorded in the Vanderbilt ONCORE electronic database which is maintained by the research coordinator and data manager at Vanderbilt. The ONCORE electronic database is password protected in order to protect your identity. Your study records will be locked up in the clinical trials office.

Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Abramson and her staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

16. Authorization to Use/Disclose Protected Health Information

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is, or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Dr. Abramson and her study team may share the results of your study and/or non-study linked physical exams, lab tests, ECG, radiology scans, tumor tissue testing, as well as parts of your medical record, to the groups named below. These groups may include people from the Federal Government Office for Human Research Protections, the Vanderbilt University Institutional Review Board and Scientific Review Committee, National Cancer Institute, Food and Drug Administration, representatives of Genentech and its authorized agents; Johns Hopkins University on behalf of the Translational Breast Cancer Consortium (TBCRC;),and insurance companies for billing purposes. Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Dr. Abramson in writing and let her know that you withdraw your consent. Her mailing address is Vanderbilt-Ingram Cancer Center, Attn: [redacted]. At that time, we will stop getting any more data about you. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

You have the right to see and copy the PHI we gather on you for as long as the study doctor or research site holds this data. To ensure the scientific quality of the research study, you will not be able to review some of your research data until after the research study is finished.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date	Signature of patient/volunteer

Consent obtained by:

Date	Signature
	Printed Name and Title