THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Enhancing Immunotherapy by Targeting the EGFR Pathway in Inflammatory Breast Cancer: A phase II study of Panitumumab (PmAb) And Pembrolizumab (Pembro) in Combination with Neoadjuvant Chemotherapy (NAC) In Patients with Newly Diagnosed Triple Negative Inflammatory Breast Cancer (TN-IBC)

2020-0715

Study Chair: Azadeh Nasrazadani

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB – a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn if the combination therapy of panitumumab, pembrolizumab, and standard-of-care chemotherapy can help to control inflammatory breast cancer.

This is an investigational study. Panitumumab is FDA approved and commercially available for the treatment of a certain type of colorectal cancer; it is not approved to treat inflammatory breast cancer. Pembrolizumab is FDA and commercially available for the treatment of many different types of cancer, including certain types of breast cancer. The chemotherapy used in this study (paclitaxel, carboplatin, doxorubicin, and cyclophosphamide) are FDA approved and commercially available for the treatment of breast cancer.

It is considered investigational to give panitumumab, pembrolizumab, and chemotherapy together to treat inflammatory breast cancer. The study doctor can describe how the study drugs are designed to work.

The study drugs may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects, some of which may be severe or fatal. You may choose not to take part in this study because of hospitalization, a prolonged stay out of town, and/or because there are other standard options available

You can read a full list of potential side effects below in the Possible Risks section of this consent.

You may receive up to 25 weeks of treatment, depending on what the study doctor thinks is in your best interest. You will no longer be able to take the study drugs if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Panitumumab will be provided at no cost to you during the study. You and/or your insurance provider will be responsible for the cost of pembrolizumab, paclitaxel, carboplatin, cyclophosphamide, and doxorubicin.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard of care including pembrolizumab, paclitaxel, carboplatin, cyclophosphamide, and doxorubicin before surgery without taking part in this study. The study doctor will discuss with you the risks and benefits of these treatments. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam, including a breast and lymph node exam to check the status of the disease.
- Pictures of both breasts will be taken. Your private areas will be covered (as much as possible), and a picture of your face will not be taken unless there are lesions on your face. Pictures of your breasts are taken during the study to help track any changes in your breast tissue.
- You will have an EKG and either a multi-gated acquisition (MUGA) scan or echocardiogram (ECHO) to check your heart function.

- Blood (about 4 tablespoons) will be drawn for routine and research testing, including genetic testing and microbiome testing (a type of testing that checks for certain bacteria and microorganisms in the body). If you can become pregnant, part of this blood draw will be collected for a pregnancy test. To take part in this study, you must not be pregnant. Urine may also be collected for the pregnancy test.
- You will have imaging scans (such as PET/CT scan, CT scan, MRI, mammogram, ultrasound, and/or bone scan) to check the status of the disease. The study doctor will tell you which scans you may have.
- You will have a breast core biopsy to collect tumor samples for biomarker testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug. To perform a core biopsy, a sample of tissue is removed using a hollow core needle that has a cutting edge. A numbing drug will be given through a needle under the skin before the core biopsy.
    - If you are taking part in another MD Anderson study, called the IBC registry study (Protocol 2006-1072), a core biopsy will be performed, and samples will be collected separately for both studies.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Study Groups

If you are found to be eligible to take part in this study, you will be assigned to 1 of 2 study groups based on when you join the study. The first 6 participants enrolled will be enrolled in Group 1. The next 24 participants will be enrolled in Group 2. Both groups will receive the same study drugs on the same schedule, but the group you are assigned to will determine which dose level of the study drugs you receive.

- If you are in **Group 1**, you will receive a starting dose of the study drugs. This is called the “Safety Run-In” part of the study and is done to confirm the dose.
- If you are in **Group 2**, you will receive the dose of study drugs that was confirmed to be safe in Group 1.

Up to 30 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Every study cycle will be 21 days. You will also have an additional cycle called Cycle 0 that is 7 days (about 1 week before Cycle 1).

You will be given medications as standard of care before some of your treatments to help decrease the risk of side effects. You may ask the study staff for information about how the drugs are given and their risks.

During Cycle 0, you will receive pembrolizumab and panitumumab by vein on Day 1. The infusion will take about 30 minutes for pembrolizumab and about 1 hour for panitumumab.

During Cycles 1-4:

- You will receive panitumumab by vein over about 30 minutes on Days 1, 8, and 15 of Cycles 1-3 and Days 1 and 8 of Cycle 4.
- You will receive paclitaxel by vein over about 1-3 hours on Days 1, 8, and 15 of Cycles 1-4.
- You will receive carboplatin by vein over about 30 minutes on Day 1, 8 and 15 of Cycles 1-4.
- You will receive pembrolizumab by vein over about 30 minutes on Day 1 of Cycles 2-4.

During Cycles 5-8, you will receive standard-of-care treatment, including pembrolizumab, doxorubicin and cyclophosphamide by vein over about 2 hours on Day 1 of Cycles 5-8. You may be able to receive this therapy at a local doctor's office instead of MD Anderson (if this is closer to your home), but the first dose (Cycle 5) should be given at MD Anderson. This will be discussed with you.

Your dosing schedule may be changed if the study doctor thinks it is needed.

Surgery
After you have finished receiving pembrolizumab, doxorubicin, and cyclophosphamide, you will have standard-of-care surgery to remove the breast cancer. You will be given a separate consent form explaining the surgery and its risks.

During surgery, breast tissue samples will be collected for routine testing and for biomarker testing.

After you have surgery, the study doctor will discuss next treatment options with you (which may include additional chemotherapy and/or radiation therapy).

Study Visits

You will come to the clinic on **Days 1, 8, and 15 of each cycle, as well as right before your scheduled surgery.** At each visit, you will have some or all of the tests/procedures, depending on the day. The study doctor or study staff will discuss your schedule in more detail with you:

- You will have a physical exam.
- Blood (about 1½-3 tablespoons) will be drawn for routine tests. At certain visits, additional blood (about 2 tablespoons) will be drawn for research testing.
- Before you begin receiving doxorubicin and cyclophosphamide, after the last dose of doxorubicin and cyclophosphamide, and then before surgery, the study doctor will take pictures of both of your breasts.
- Before and after receiving doxorubicin and cyclophosphamide, you will have a mammogram of the involved breast and an ultrasound of the involved breast and lymph nodes if the doctor thinks it is needed.
- Before Day 1 of Cycle 1, you will have a breast core biopsy to collect tumor samples for biomarker testing.
- As part of your standard care when the doctor thinks it is needed:
    - You will have imaging scans to check the status of the disease.

- You will have an EKG and either an ECHO or MUGA scan to check your heart function.

Follow-Up and Long-Term Follow-Up

About 1 month and 3 months after surgery and then every 6 months after that for up to 2 years, you will be asked about your health and any side effects you may have had. You may be asked during a routine clinic visit, or you may be called by a member of the study staff. If you are called, each call should last about 2 minutes.

Your participation in this study will be over after follow-up.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Pembrolizumab, paclitaxel, carboplatin, docetaxel, doxorubicin, and cyclophosphamide each may cause low blood cell counts (red blood cells, platelets, and white blood cells):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.
- A low white blood cell count increases your risk of infection (such as pneumonia, nail infections, and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Panitumumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue • itching • acne-like rash	• skin problems (such as skin rash/dryness/ peeling/cracking/ redness)	• nausea • diarrhea

Panitumumab may commonly cause an increased risk of infection, such as pneumonia. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Occasional (occurring in 3-20% of patients)

• fever • chills • acne • nail changes • blistering skin rash • shedding and scaling of the skin (possible fatal loss of bodily fluids) • skin sores • low blood levels of magnesium (possible weakness and/or seizure)	• mouth blisters/sores (possible difficulty swallowing) • dry mouth • vomiting • dehydration • painful, red, teary, itchy eyes • eyelash growth • eye inflammation (possible sore on the eye)	• cough • lung inflammation (possible difficulty breathing) • infusion reaction (possible chills and/or hives) • nosebleed • immune reaction

Rare but serious (occurring in fewer than 3% of patients)

• tissue swelling • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • death of skin	• kidney failure as a result of severe diarrhea and dehydration • blockage in the lung (possible pain, shortness of breath, and/or failure to breathe) • lung damage and/or inflammation (possible difficulty breathing)	• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • allergic reaction that may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

Call your doctor right away if your skin becomes red, tender, swollen, hot to the touch, blistered, starts peeling, becomes scaly, or is discolored.

Other drugs similar to panitumumab may cause heart damage. It is unknown if panitumumab may cause heart damage. If you have any symptoms such as fatigue, shortness of breath, weight gain, leg swelling, irregular heartbeat, chest discomfort, or other symptoms that you believe are related to the heart, you should contact your local emergency number and your study doctor right away.

<u>Pembrolizumab Side Effects</u>

Common (occurring in more than 20% of patients)

• fatigue • fever • skin rash and/or itching • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• high blood sugar (possible diabetes) • high blood levels of fat (possible heart disease and/or stroke) • loss of appetite • nausea • constipation • diarrhea • abdominal pain	• low blood cell counts (red, white, platelets) • abnormal liver test (possible liver damage) • pain • abnormal kidney test (possible kidney damage) • cough • difficulty breathing

Occasional (occurring in 3-20% of patients)

• swelling (face/arm/leg) • inflammation of the tissue around the heart (possible chest pain) • irregular heartbeat • headache • confusion • patches of skin color loss • underactive thyroid gland (possible weight gain, heart failure, and/or constipation)	• overactive thyroid gland (possible weight loss, diarrhea, mood swings, difficulty sleeping, heart rate changes, and/or sweating) • low blood sugar • weight loss • fluid in the abdomen • blood in the urine • vomiting • abnormal liver test (possible yellowing of the skin and/or eyes)	• weakness • nerve damage (possible numbness, pain, and/or loss of motor function) • difficulty breathing (possibly due to lung inflammation) • flu-like symptoms • infusion reaction (possible dizziness, low blood pressure, nausea, pain, and/or difficulty breathing)

Frequency Unknown

• heart failure • heart attack • build-up of fluid around the heart (possible heart failure)	• abnormal connections or passageways between organs or vessels • bleeding in the rectum and/or uterus	• blockage in the lung (possible pain and/or shortness of breath) • nosebleed • coughing up blood

Rare but serious (occurring in fewer than 3% of patients)

• low blood pressure (possible dizziness/fainting) • heart inflammation	• hormonal deficiency that affects the body's ability to control blood pressure and react to	• inflammation inside the eye (possible vision problems) • kidney inflammation

• build-up of fluid in the tissue around the heart • blood vessel inflammation (possible bleeding and/or bruising) • seizure • immune system damage to the nervous system (causing muscle weakness, numbness and/or paralysis) • spinal cord inflammation (possible pain, weakness, loss of feeling or movement, and/or paralysis) • brain inflammation (possible paralysis and/or coma) • shedding, scaling and/or inflammation of the skin (possible fatal loss of bodily fluids) • large skin blisters • very severe blistering skin disease (loss of large portion of skin and/or with ulcers of the skin and digestive tract)	stress • pituitary gland inflammation (possible headaches) • inflammation of the thyroid gland (possible tenderness in the neck) • diabetes requiring insulin • severe high blood sugar due to uncontrolled diabetes • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • inflammation of the pancreas (possible abdominal pain) • anemia due to destruction of red blood cells • liver damage (hepatitis) • inflammation/scarring of the bile ducts (tubes that carry digestive fluid that is made in the liver), which may cause liver damage, stomach pain, yellowing of the skin/eyes, fatigue, and/or itching	(possible kidney damage/failure) • kidney failure • build-up of fluid around the lungs • immune response that causes the body to attack itself (possible organ damage) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • immune response (causing muscle weakness) • immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • Vogt Koyanagi Harada syndrome -- pigmented tissue (possible eye pain/swelling and changes in vision, hearing loss, and/or white patches on the skin)

If you have a solid tumor type and you have an organ transplant, pembrolizumab may increase your risk for the transplant to be rejected by your body.

Pembrolizumab works by boosting the immune system. This may cause unknown side effects resulting from your immune system attacking your organs. This may cause inflammation and inflammation-related side effects in any organ or tissue. These side effects can affect more than one of your normal organs and tissues at the same time.

Paclitaxel Side Effects

Common (occurring in more than 20% of patients)

• abnormal EKG • swelling • flushing • hair loss (partial or total) • mouth blisters/sores (possible difficulty swallowing)	• nausea/vomiting • diarrhea • low blood cell counts (red/platelets/white) • abnormal liver tests (possible liver damage) • pain (muscle/joint) • weakness	• nerve damage (possible numbness, pain, and/or loss of motor function) • abnormal kidney test (possible kidney damage) • wheezing/shortness of breath • allergic reaction • infection

Occasional (occurring in 3-20% of patients)

• low blood pressure (possible dizziness/ fainting) • slow heartbeat • fever • blood clots in a vein (possible pain, swelling, and/or redness)	• skin rash • abdominal pain • abnormal liver tests (possible yellowing of the skin and/or eyes)	• lung damage (possible shortness of breath) • injection site reaction (possible redness, swelling, skin discoloration)

Rare but serious (occurring in fewer than 3% of patients)

• fast/irregular heartbeat • heart failure • heart attack • decreased blood supply to the heart • high blood pressure • fainting • decreased brain function (possible paralysis and/or coma) • decreased brain function due to liver damage • seizure • severe sunburn-like rash at site of previous radiation (called radiation recall) • death of skin • worsening of existing scleroderma (severe hardened skin, which	• inflammation at the site of previous tissue death • very severe blistering skin disease (with ulcers of the skin and digestive tract) • very severe blistering skin disease (loss of large portion of skin) • inflammation of the pancreas (possible abdominal pain) • inflammation of the intestines • dehydration • hole in the intestines (possible leaking contents into the abdomen) • decreased blood flow to part of the bowel	• intestinal blockage • difficulty walking • liver damage and/or failure • hearing loss • decreased kidney function • blockage in the lung (possible pain and/or shortness of breath) • lung inflammation (possible difficulty breathing) • blood clots in the lung (possible failure to breathe) • difficulty breathing • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

can cause difficult movement)	(possibly causing death of tissue) • paralysis of the intestines	• tissue death at the injection site caused by drug leakage

Carboplatin Side Effects

Common (occurring in more than 20% of patients)

• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• vomiting • low blood counts (red/white/platelets) • pain	• abnormal liver tests (possible liver damage) • abnormal kidney test (possible kidney damage)

Occasional (occurring in 3-20% of patients)

• nerve damage (possible numbness, pain, and/or loss of motor function) • hair loss (partial or total)	• abdominal pain • nausea • constipation • diarrhea	• weakness • abnormal liver tests (possible yellowing of the skin and/or eyes) • allergic reaction • infection

Rare but serious (occurring in fewer than 3% of patients)

• high blood pressure • low blood pressure (possible dizziness/fainting) • heart failure • stroke • dehydration • blood vessel blockage	• destruction of red blood cells (possible anemia, kidney damage, and/or failure) • reduced blood supply to the arms and legs • blindness • hearing loss	• difficulty breathing due to narrowing of the airways • tissue death at the injection site caused by drug leakage • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

It is not known how often the following side effects may occur:

• decreased bone marrow function

Doxorubicin Side Effects

Common (occurring in more than 20% of patients)

• low white blood cell counts

It is not well known how often the following side effects of doxorubicin may occur:

• swelling • slow/extra/fast/irregular heartbeat • abnormal EKG • heart failure • enlarged heart • heart inflammation • inflammation of the tissue around the heart (possible chest pain) • severe heart problems • fatigue/lack of energy • skin rash • hives • itching • skin sensitivity to sunlight or lamps • hair loss (partial or total)	• discoloration of sweat, urine, saliva, and/or tears • stopped menstrual cycle • dehydration • high blood levels of uric acid (possible painful joints and/or kidney failure) • abdominal pain • loss of appetite • diarrhea • mouth blisters/sores (possible difficulty swallowing) • nausea/vomiting • death of colon tissue • stomach and/or small intestine ulcer	• decreased urine output • inability to have children • low blood counts (red/platelets) • enlarged liver • weakness • difficulty breathing • build-up of fluid around the lung/fluid in the lungs (possible difficulty breathing) • injection site pain and/or inflammation • severe sunburn-like rash at site of previous radiation (called radiation recall)

Serious side effects occurring in fewer than 1% of patients

• fever • coma • seizure • shock • very severe blistering skin disease (loss of large portion of skin) • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• low sperm count • liver damage • abnormal liver tests (possible yellowing of the skin and/or eyes) • stunted growth in children • nerve damage (possible numbness, pain, and/or loss of motor function) • lung inflammation (possible difficulty breathing)	• allergic reaction, possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure and/or heart failure)

Doxorubicin may cause you to develop another type of cancer (such as cancer of the bone marrow, and/or secondary acute myelogenous leukemia, a type of blood cancer).

Cyclophosphamide Side Effects

Common (occurring in more than 20% of patients):

• hair loss (partial or total) • mouth blisters/sores (possible difficulty swallowing) • nausea/vomiting • inability to regulate water/salt balance which can cause frequent urination and dehydration	• headache • abdominal pain • loss of appetite • diarrhea • problems with production of sperm and eggs • inability to have children • stopped menstrual cycle • low blood counts (red, platelet, white)	• fever with dangerously low white blood cell count (febrile neutropenia) • bladder inflammation and bleeding (possible pain and/or urge to urinate) • infection

Cyclophosphamide may cause you to develop another type of cancer (such as bladder cancer, acute leukemia [a type of blood cancer], lymphoma [a type of lymph node cancer], thyroid cancer, and/or sarcoma [a type of cancer that can start in the soft tissue, bone, or other tissue].

Rare but serious (occurring in fewer than 3% of patients)

• irregular heartbeat • build-up of fluid around the heart (possible heart failure) • build-up of blood in the sac around the heart (possible impaired heart function) • inflammation of the heart and/or the tissue around the heart (possible chest pain and/or bleeding) • heart damage/failure, death of heart tissue, or other severe heart problems • heart attack, which can be serious and life-threatening • blood clots in a vein (possible pain, swelling, and/or redness)	• wound healing problems • low blood levels of potassium (possible weakness) • low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • hormonal deficiency that affects the body's ability to control blood pressure and react to stress • decreased supply of blood to the abdomen • digestive system bleeding • enlarged bowel (possible abdominal pain) • inflammation of the intestines (possible bleeding)	• hearing loss • breakdown of muscle tissue (possible kidney failure) • death of kidney tissue (possible kidney failure) • difficulty breathing • lung inflammation (possible difficulty breathing) • problems with blood carrying oxygen (possible blue skin) • lung damage due to blood clots • increased blood pressure in the lungs (possible difficulty breathing and/or heart failure) • multiorgan failure • breakdown products of the cancer cells entering

• blood clots in an artery (possible organ damage such as stroke and/or heart attack) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) • dizziness • very severe blistering skin disease (with ulcers of the skin and digestive tract) • severe sunburn-like rash at site of previous radiation (called radiation recall) • very severe blistering skin disease (loss of large portion of skin)	• inflammation of the pancreas (possible abdominal pain) • liver damage (possibly due to blood clots) • jaundice (yellowing of skin and/or eyes) • high blood levels of uric acid (possible painful joints and/or kidney failure) • ovarian scarring • urinary tract or bladder scarring • decreased testicle size and function • blood in the urine • blurry vision	the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

Diagnostic procedures, such as **imaging scans and EKGs, ECHOs, and MUGAs**, are part of your standard of care. You may discuss the risks of these scans with the study staff/study doctor if you have questions about them.

Although every effort will be made to keep **study data** safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets during the study and will continue to be stored securely after the study. Only authorized people who are working on this study will have access to study data.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study.

If you can become pregnant or father a child and you are sexually active, you must use effective methods of birth control during the study and for at least 4 months after the last dose of study drugs. Effective methods of birth control include:

- Hormonal methods (such as birth control pills, shots/injections, implants, or patches)
- Intrauterine device (IUD)
- Double barrier method (each partner uses 1 of the following barrier methods): condom plus diaphragm, cervical cap, or sponge with spermicide.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Amgen for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You may receive some reimbursement for the costs that are a direct result of your participation, such as travel expenses. You may receive up to a maximum of $100 for transportation per visit (up to 10 times), and you may receive up to a maximum of $15 for parking per visit (up to 10 times). The total amount you may be reimbursed for is up to $1,000. You will need to provide receipts for your expenses to be eligible for reimbursement. Please ask the study staff about this possible reimbursement.

Additional Information

4. You may ask the study chair (Dr. Azadeh Nasrazadani, at 713-792-2817) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson. If you withdraw from the study, the study staff may ask if they can continue collecting the results of routine care from your medical record.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Amgen, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, including the results of all of your standard tests performed as part of this research, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: Amgen.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data
Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and Amgen, and/or shared with other researchers and/or institutions for use in future research.

Samples
Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research. Amgen will not store any leftover samples for future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples

Genetic Research
Samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

Outside Care

Part of your care may be provided outside of MD Anderson by your home doctor(s).

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Amgen, who is a supporter of this study
   - Any future sponsors/supporters of the study
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

   The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2020-0715.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION