THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

**Informed Consent**

# INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

## An Open-label, Single-center, Phase 1b/2 Study to Evaluate the Safety of Plinabulin in Combination with Radiation/Immunotherapy in Patients with Select Advanced Malignancies after progression on PD-1 or PD-L1 Targeted Antibodies
## 2020-0296

**Subtitle:** Phase 1b and Phase 2

Study Chair: Siqing Fu

_____ _____
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**

There are 2 parts to this study: Phase 1b and Phase 2. This consent form is for both Phases.

The goal of Phase 1b of this clinical research study is to find the highest tolerable dose of plinabulin that can be given in combination with radiation therapy and immunotherapy to patients with advanced solid tumors.

In this study, immunotherapy includes atezolizumab, pembrolizumab, avelumab, durvalumab, and nivolumab.

**This is an investigational study.** Plinabulin is not FDA approved or commercially available. Plinabulin is currently being used for research purposes only. The immunotherapy regimens are FDA approved and commercially available for the treatment of various cancers. Radiation therapy is delivered using FDA-approved and commercially available methods. The combination of these therapies with plinabulin to treat advanced cancer is considered investigational.

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 there are other standard options.

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

You may continue the study treatment until disease progression or development of unacceptable toxicity.

Plinabulin will be provided at no cost to you. You and/or your insurance provider will be responsible for the cost of the radiation and immunotherapy treatment regimen.

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 therapy. The doctor will discuss the risks and benefits of these therapies with you. 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. You will have screening tests within 28 days before your first dose of study drug to help the doctor decide if you are eligible:

- You will have a physical exam.
- You will have an EKG to check your heart function.
- Your vital signs (temperature, blood pressure, heart rate, and breathing rate) and weight will be recorded.
- Blood will be drawn for routine and research tests. If blood is not drawn for research tests at screening, it may be done within the 2 weeks before your first dose of study drug or on the first day you receive the study drug. In this study, research tests include immune system testing, biomarker testing, and genetic testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs. Genetic testing is done to help researchers learn if your DNA (genetic information) affects the way you respond to the study drugs. This also includes looking for genetic mutations (changes).
- Urine will be collected for routine tests.
- You will have an image-guided, core-needle tumor biopsy for research tests. If this is not done at screening, it may be done just before or on the day of your first dose of study drug. This will be discussed with you. To perform an image-guided biopsy, a needle is inserted into the affected area using imaging such as CT, ultrasound, or MRI to collect cells or tissue from an organ, lymph node,

or suspected tumor mass. The doctor will use the imaging to guide the needle into the area, and a small piece of tissue will be collected.
- If you have not had one in the last 28 days, you will have an MRI or CT scan to check the status of the disease.
- If you can become pregnant, urine will be collected for a pregnancy test. To take part in this study, you must not be pregnant. If the test is positive, blood (about 1 teaspoon) will be drawn to confirm you are pregnant.

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 options will be discussed with you.

**Radiation Simulation**

If you are found to be eligible to take part in this study, you will be scheduled for a radiation planning session (also called a simulation) before your treatments begin.

This session is called a “simulation” because the radiation treatment is planned and the radiation machine is moved into position but no actual radiation treatment is given during this visit. However, completing the radiation planning session will help the radiation treatment sessions go more smoothly in the future.

At the beginning of your planning session, your doctor will:
- explain the pros and cons of radiation, the planning and treatment process, and answer any questions or concerns you may have
- review the consent form and have you sign it
- introduce you to the treatment team

During the radiation planning session, a radiation oncologist (cancer doctor) will map out the area that needs treatment. To do this, you may have a 4-dimension CT (4DCT) scan of your chest to check the status of the disease and to help the doctors decide what dose of radiation you will receive. A 4DCT is a type of CT scan that looks at how the tumor may move when you are breathing. You may be asked to hold your breath for short periods of time during this test.

They will then use a special X-ray machine called a simulator to plan the angles and direction of radiation so that the dose of radiation is properly given to the tumor area. The position of your body is very important during radiation therapy, because you need to stay in the same position for each radiation treatment, in order to make sure the radiation is delivered properly. To stabilize your position, you will probably be asked to lie in a special "immobilization device" on the treatment table.

There are different kinds of immobilization devices. Some look like a cradle; others look like a foam box that is shaped to your form. You will not be trapped or closed in. You may be asked to lie down in a custom-shaped mold that just touches your back and sides; or your treatment center may use a "breast board" that places your head, arm, and hand in a fixed position. Unfortunately, no padding can be used on the treatment table or positioning devices because that makes your treatment position less precise.

Pictures will be taken of the area that needs to be treated. Those images are sent to the radiation planning computer, which will help set up the general treatment fields (the areas that get the radiation).

Once the treatment fields are set, the radiation oncologist will mark the corners of the fields with small tattoos or a special pen (markings are usually no bigger than the head of a pin or a freckle). The marking is a guide to help the technician line up the radiation treatment fields the same way each time you receive treatment.

The radiation planning session may last up to an hour total.

## Study Groups

Depending on when you enroll in this study, you will be assigned take part in either Phase 1b or Phase 2.

### Phase 1b

Participants in **Phase 1b** will receive 1 of 2 dose levels of plinabulin that are being tested. The first group of Phase 1b participants will receive the higher dose level. If intolerable dose levels are seen, another group of participants will be enrolled to receive a lower dose. One of these 2 doses will be selected as the highest tolerable dose of plinabulin.

You will also receive radiation therapy and immunotherapy during this phase. The dose schedule for radiation therapy is described below. The study doctor will decide which immunotherapy drug(s) you will receive based on the type of cancer you have.

### Phase 2 (open-label)

Participants in **Phase 2** will be randomly assigned (like the flip of a coin) to 1 of 2 treatment arms. You have an equal chance of being assigned to either arm. This is done because no one knows if one study group is better, the same, or worse than the other group. Both you and your study team will know what treatment you are receiving:

- **Arm A:** Radiation Therapy + Immunotherapy + Plinabulin (the experimental arm)
- **Arm B:** Radiation Therapy + Immunotherapy (the standard or “control” arm)

The immunotherapy drugs being given in this study are:

- Atezolizumab by vein over about 1 hour
- Pembrolizumab by vein over about 30 minutes
- Avelumab by vein over about 1 hour
- Durvalumab by vein over about 1 hour
- Nivolumab by vein over about 30-60 minutes

Up to 194 participants will take part in this study. All will be enrolled at MD Anderson.

## Study Drug Administration

You will receive the study drugs in cycles. Your study cycles will be either 21 days (3 weeks) or 28 days (4 weeks) long, depending on the immunotherapy treatment you are assigned (described below).

**Radiation Therapy**
You will receive Radiation Therapy (RT) administered with one of three regimens: 8 Gy x 3 fractions, 12.5 Gy x 4 fractions, and/or 4 Gy x 5 fractions from Days 1 to 3 (3 fractions), Days 1 to 4 (4 fractions), or Days 1 to 5 (5 fractions) in Cycle 1. The choice of Radiation Therapy regimens for tumors and lesions is at the discretion of the treating radiation oncologist. The doctor may decide to give you additional radiation therapy, if it is needed. Optional sequential Radiation Therapy in Cycle 2 is at the discretion of the treating doctor to target other untreated lesions with same regimens for the study. You will have a visit with the treating radiation oncologist at the end of every cycle of your radiation therapy to check on how you are doing.

**Immunotherapy**
Depending on which therapy the study doctor thinks is in your best interest, you will receive one of the following immunotherapy treatment schedules:

- On Day 1 of each 21-day cycle:
    - Atezolizumab by vein over about 1 hour, OR
    - Pembrolizumab by vein over about 30 minutes
- On Days 1 and 15 of each 28-day treatment cycle, you will receive 1 of the following during the study:
    - Avelumab by vein over about 1 hour
    - Durvalumab by vein over about 1 hour
    - Nivolumab by vein over about 30-60 minutes

**Plinabulin**
If you are assigned to receive **plinabulin,** it will be given by vein over 30-60 minutes on:

- Days 1 and 4 of Cycle 1
- Days 1 and 4 of Cycle 2 (if you receive radiation therapy in Cycle 2)
- Any day you receive immunotherapy (Days 1 and/or 15 of each cycle)

On days when you receive radiation therapy and immunotherapy (with or without plinabulin), you will have radiation therapy, and then about 3-12 hours later, you will have immunotherapy. If you are in Arm A, you will also have plinabulin about 1- 2 hours after completing your immunotherapy infusion.

You will no longer be able to receive the study treatment if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

While on study, you cannot also receive other anti-tumor therapies (such as chemotherapy, hormone therapy, immunotherapy, or radiation to lower side effects). If you need these treatments, you will be taken off study in order to receive them. You may be able to receive a type of supportive drug called a growth factor, but only after you have completed Cycle 2. You can discuss this with your doctor.

## Study Visits

Your study visit schedule will depend on whether you are following a 21- or 28-day cycle. The study staff will discuss your schedule in more detail with you.

At **every study visit**, you may have your vital signs recorded. If you are receiving study treatment at that visit, they may be measured multiple times that day. You may also be asked about any side effects that you are having, any other medications you are taking, and/or your ability to complete everyday tasks, at any of these visits.

**On Day 1 of every cycle**:

- You will have a physical exam.
- Blood (around 3 tablespoons) will be drawn for routine tests. Starting at Cycle 2 or 3 (depending on which immunotherapy you are receiving), blood will be drawn for research tests.
- You will have an EKG (Cycle 1 only). After Cycle 1, you will have this performed whenever the doctor thinks it is needed.
- If you can become pregnant, urine will be collected for a pregnancy test. If the test is positive, blood (about 1 teaspoon) will be drawn to confirm you are pregnant.

**If you are following a 21-day cycle:**

- On **Day 4 of Cycle 1** (and Cycle 2, if you continue to have radiation treatment), blood (around 3 tablespoons) will be collected for routine and research tests.
- **Within 7 days before Day 1 of Cycle 3**, you will have imaging-guided core-needle tumor biopsy samples collected (with at least 2-4 research cores collected). These will be used for research tests to help understand how plinabulin works and to look for markers that may help doctors predict which patients may respond to the treatment better.

**If you are following a 28-day cycle:**

- On **Day 4 of Cycle 1** (and Cycle 2, if you are assigned to receive Plinabulin), blood (around 3 tablespoons) will be collected for routine and research tests.
- **Within 7 days before Day 1 of Cycle 3**, if you are assigned to receive Plinabulin, you will have imaging-guided core-needle tumor biopsy samples collected (with at least 2-4 research cores collected). These will be used for research tests to help understand how plinabulin works and to look for markers that may help doctors predict which patients may respond to the treatment better.

On **Day 1 of Cycles 3, 6, 9, and 12 and then every 4 cycles after** (Cycles 16, 20, and 24), you will have an MRI or CT scan to check the status of the disease.

**<u>End-of-Study Visits</u>**

Within 30 days after your last dose of study drug:

- Blood (around 3 tablespoons) will be drawn for routine and research tests.
- Urine will be collected for routine tests.
- You will have a CT, MRI, or PET/CT scan to check the status of the disease.

- If you can become pregnant, urine will be collected for a pregnancy test. If the test is positive, blood (about 1 teaspoon) will be drawn to confirm you are pregnant.

**Follow-up Visits**

Every 12 weeks after your last dose of study drugs:

- You will have a physical exam.
- Blood (around 3 tablespoons) will be drawn for routine tests.
- You will have a CT, MRI, or PET/CT scan to check the status of the disease.

If the disease gets worse or if you start a new anti-cancer therapy, you will be required to stop clinic visits. The study staff will continue to follow-up for as long as you are on study and the study is open. The study staff will call you every 12 weeks to ask how you are doing. Each call should take about 5 minutes.

## 2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. You should discuss these with the study doctor. Many side effects go away shortly after the study drug is stopped, but in some cases side effects may be serious, long lasting, or permanent, and may even result in hospitalization and/or death. If you experience any side effects, the study staff may give you medicines to help lessen these effects. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs.

Plinabulin, atezolizumab, avelumab, durvalumab, pembrolizumab, and nivolumab 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 (thrombocytopenia) 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 (neutropenia) increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening.

**Plinabulin Side Effects**

**This is an early study of plinabulin in humans, so the side effects are not well known.** Based on early testing in humans, plinabulin may cause the following side effects:

| | | |
|---|---|---|
| • swelling (face)<br>• abnormal blood test (possible heart problems) | • hot flashes<br>• hives<br>• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, | • painful/frequent urination<br>• painful menstrual cycle<br>• genital redness<br>• blood in the stool |

| | | |
|---|---|---|
| • high blood levels of fat (possible heart disease and/or stroke)<br>• high blood pressure<br>• low blood pressure (possible dizziness/fainting)<br>• fast/irregular/slow heartbeat<br>• extra heartbeat<br>• heart attack<br>• chest pain (possibly due to heart trouble)<br>• enlarged heart<br>• fatigue<br>• headache<br>• fever<br>• difficulty sleeping<br>• confusion<br>• anxiety<br>• mood changes<br>• restlessness<br>• chills/tremors<br>• stroke<br>• decreased blood supply to the brain caused by stroke<br>• fainting<br>• dizziness<br>• numbness<br>• nerve damage (possible numbness, pain, and/or loss of motor function and/or loss of sensory function)<br>• brain injury (possible headache, confusion, seizures, and/or vision loss)<br>• skin rash<br>• red/itchy/dry skin<br>• hair loss (partial or total)<br>• sweating<br>• nail changes/nail discoloration | fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)<br>• abnormal blood test (possible pancreas damage/inflammation)<br>• high blood sugar (possible diabetes)<br>• low blood sugar<br>• abnormal hormone production (possible breast milk production)<br>• diarrhea (including an urgent need to pass stool)<br>• dehydration<br>• nausea/vomiting<br>• loss of appetite<br>• weight loss<br>• abdominal pain/swelling<br>• paralysis of the intestines and/or intestinal blockage<br>• upset stomach<br>• mouth blisters/sores (possible difficulty swallowing)<br>• gas<br>• inflammation of the stomach and/or intestines<br>• burping/hiccups<br>• chronic heartburn and indigestion<br>• dry mouth<br>• difficulty or painful swallowing<br>• voice changes<br>• bleeding from the rectum<br>• death of gastrointestinal tissue | • low blood cell count (red, white, platelets)<br>• blood disorder<br>• increase in infection-fighting cells<br>• liver failure<br>• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes)<br>• pain<br>• muscle spasms<br>• weakness (possible falls)<br>• loss of reflexes<br>• abnormal kidney tests (possible kidney damage)<br>• kidney failure<br>• ringing in the ears<br>• eye disorders<br>• vision blurred<br>• redness of the eye<br>• blockage in the lung (possible pain and/or shortness of breath)<br>• lung inflammation (possible difficulty breathing)<br>• difficulty breathing<br>• difficulty breathing due to narrowing of the airways<br>• low oxygen level in the blood (possible lightheadedness)<br>• cough<br>• runny nose<br>• nosebleed<br>• flu-like illness<br>• infusion or injection reaction (possible chills and/or hives)<br>• allergic reaction<br>• infection, possibly severe and life-threatening infection |

| | | |
|---|---|---|
| • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering)<br>• skin sores<br>• skin color changes<br>• skin odor<br>• flushing | • hole in the intestines (possibly leaking contents into the abdomen)<br>• vomiting blood<br>• hemorrhoids/bleeding from hemorrhoids<br>• taste changes<br>• slow emptying of food from the stomach into the intestines | (possible low blood pressure, kidney failure, and/or heart failure)<br>• wound healing complications<br>• poisoning<br>• tumor pain |

Plinabulin may cause cytokine release syndrome (CRS). This involves a release of a large amount of proteins into the blood stream. This may cause changes in blood pressure and heartbeat, flu-like symptoms (nausea, fever, and chills), and/or affect your lung/liver/kidney function. It may also cause certain brain-related symptoms, such as dizziness, weakness, memory loss, confusion, difficulty speaking or focusing, and/or decreased brain function (possible paralysis and/or coma).

**Atezolizumab Side Effects**

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

| | | |
|---|---|---|
| • fatigue<br>• fever<br>• 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) | • nausea<br>• loss of appetite<br>• constipation<br>• immune reaction that may cause loss of drug function<br>• low blood cell count (red, white) | • abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes)<br>• weakness<br>• cough<br>• difficulty breathing<br>• infection |

**Occasional (occurring in 3-20% of patients)**

| | | |
|---|---|---|
| • low blood pressure (possible dizziness/fainting)<br>• swelling (arm/leg)<br>• chills<br>• skin rash/itching<br>• underactive thyroid gland (possible weight gain, heart failure, and/or constipation) | • low blood levels of sodium (possible headache, confusion, seizures, and/or coma)<br>• difficulty swallowing<br>• vomiting<br>• diarrhea<br>• abdominal pain<br>• inflammation of the intestines | • low oxygen level in the blood (possible lightheadedness)<br>• liver damage<br>• pain<br>• abnormal kidney test (possible kidney damage) |

| | | |
|---|---|---|
| • high blood sugar (possible diabetes)<br>• low blood levels of potassium (possible weakness and/or muscle cramps) | • blood in the urine<br>• low platelet cell count | • lung inflammation (possible difficulty breathing)<br>• stuffy nose<br>• allergic reaction<br>• flu-like symptoms |

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

| | | |
|---|---|---|
| • heart/heart muscle inflammation<br>• inflammation of the membrane around the spinal cord and brain (possible headache and/or coma)<br>• damage to the nervous system (causing numbness and/or paralysis)<br>• pituitary gland inflammation (possible headaches)<br>• abnormal blood test (possible pancreas damage)<br>• abnormal digestive blood test (possible inflammation of the pancreas) | • severe high levels of sugar and acids in the blood or urine<br>• hormonal deficiency that affects the body's ability to control blood pressure and react to stress<br>• inflammation of the pancreas (possible abdominal pain)<br>• inflammation of the thyroid gland (possible tenderness in the neck)<br>• overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating) | • nerve damage causing muscle weakness and/or paralysis<br>• inflammation of the liver<br>• immune response (causing muscle weakness)<br>• kidney inflammation<br>• severe life-threatening infusion reaction (possible low blood pressure and/or narrowing of the airways)<br>• decreased production of adrenal hormones (possible weakness and/or low blood pressure) |

**Exact frequency unknown:**

| | | |
|---|---|---|
| • decreased blood supply to the heart<br>• blood clots in a vein (possible pain, swelling, and/or redness)<br>• confusion<br>• skin blistering and shedding<br>• destruction of red blood cells | • decreased production of adrenal hormones (possible weakness and/or low blood pressure)<br>• intestinal and/or urinary tract blockage<br>• dehydration<br>• eye inflammation (possible vision problems) | • kidney failure<br>• build-up of fluid around the lungs<br>• blockage in the lung (possible pain and/or shortness of breath)<br>• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) |

Based on the risks of similar drugs, atezolizumab may cause pigmented tissue (possible eye pain/swelling, hearing loss, and/or loss of skin color).

Atezolizumab may cause birth defects. It is not known how often this may occur.

In rare situations, when atezolizumab is combined with other drugs, an excessive immune response can occur. This side effect, called systemic immune activation, can result in inflammation, infection, and/or organ failure. Symptoms of systemic immune activation may include low blood pressure, high-grade fever, cough, difficulty breathing, severe dizziness, confusion, weakness, kidney failure, liver failure, very low blood cell counts, and/or bleeding within the organs.

If you experience any of these symptoms, you should notify your doctor right away as you may need drugs or other treatment and possible hospitalization.

Atezolizumab works by boosting the immune system. This may result side effects that have not been seen yet, such as inflammation and inflammation-related side effects in any organ or tissue.

If you need a vaccination, you must receive it at least 4 weeks before receiving atezolizumab. If you know that you will need a vaccination during the study or within 5 months after the last dose of atezolizumab, please tell your doctor.

It is important to tell your doctor the last time you took any drug that stimulates the immune system. It is also important that you do not take any other drugs that may change your immune system (such as interferons or interleukin-2) for 10 weeks after your last dose of atezolizumab.

**Avelumab Side Effects**

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

| | | |
|---|---|---|
| • fatigue<br>• skin rash<br>• nausea<br>• diarrhea | • low blood cell count (red, platelets, white)<br>• abnormal liver tests (possible liver damage) | • muscle/bone pain<br>• infusion reaction (possible chills and/or hives) |

**Occasional (occurring between 3 -20% of patients)**

| | | |
|---|---|---|
| • swelling (arms/legs)<br>• high blood pressure<br>• dizziness<br>• headache<br>• itching | • underactive thyroid gland (which may result in weight gain, heart failure, and/or constipation)<br>• intestinal blockage<br>• abdominal pain<br>• constipation<br>• loss of appetite<br>• vomiting<br>• weight loss | • abnormal digestive blood test (possible inflammation/damage of the pancreas)<br>• abnormal liver tests (possible yellowing of the skin and/or eyes)<br>• weakness<br>• difficulty breathing<br>• kidney failure<br>• cough |

| | | |
|---|---|---|
| | | • development of antibodies (possible loss of drug function) |

**Frequency unknown**

| | |
|---|---|
| • build-up of fluid in the tissue around the heart | • muscle damage and/or breakdown |

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

| | | |
|---|---|---|
| • heart inflammation<br>• immune system damage to the nervous system (causing numbness and/or paralysis)<br>• large skin blisters<br>• allergic skin reaction<br>• shedding and scaling of the skin (possible fatal loss of bodily fluids)<br>• red, dry, scaly patches of thickened skin (psoriasis)<br>• overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating) | • high blood sugar (possible diabetes<br>• inflammation of the thyroid gland (possible tenderness in the neck)<br>• pituitary gland failure (possible hormone imbalance)<br>• decreased production of adrenal hormones (possible weakness and/or low blood pressure)<br>• inflammation of the intestines<br>• liver damage | • kidney inflammation<br>• inflammation inside the eye (possible vision problems)<br>• lung inflammation (possible difficulty breathing)<br>• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) |

Reactions (including allergic reactions) that occur during or following the infusion may include chills or shaking, fever, flushing, back pain, belly pain, shortness of breath, or wheezing, decrease in blood pressure, or hives. These infusion reactions are mostly mild or moderate and generally resolve with a slowdown or discontinuation of the infusion and administration of medications such as anti-allergic and pain-killer drugs. In some cases these reactions may be severe or life-threatening (in less than 1% of patients) and could require intensive medical care.

Avelumab 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.

**<u>Durvalumab Side Effects</u>**

The study drug durvalumab works by boosting the immune system. Side effects as a result of stimulating the immune system have been reported in patients being given

durvalumab. These immune system side effects are included in the risks outlined below. Durvalumab 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.

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

| | | |
|---|---|---|
| • fatigue<br>• constipation | • loss of appetite<br>• pain (such as muscle/joint)<br>• difficulty breathing | • infection (possible upper respiratory infections, pneumonia, influenza, dental/oral infections)<br>• cough |

**Occasional (occurring in 3-20% of patients)**

| | | |
|---|---|---|
| • swelling (arms/legs)<br>• fever<br>• skin rash<br>• dry, itchy skin<br>• abnormal salts, minerals, and/or acids in the blood (which may cause weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure) | • underactive thyroid gland (possible weight gain, heart failure, and/or constipation)<br>• overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating)<br>• inflammation of the intestines/diarrhea<br>• abdominal pain<br>• nausea/vomiting<br>• dehydration | • low blood cell count (red, white)<br>• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes)<br>• kidney inflammation (possible decreased kidney function)<br>• lung inflammation (possible difficulty breathing)<br>• hoarse voice |

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

| | | |
|---|---|---|
| • heart inflammation<br>• inflammation of the brain or membranes around the spinal cord and brain (possible headache and/or coma)<br>• immune system damage to the nervous system (causing weakness, numbness and/or paralysis)<br>• inflammation of blood vessels | • pituitary gland failure/inflammation (possible headaches, thirst, and/or irregular periods in women)<br>• type 1 diabetes which requires insulin<br>• high blood sugar<br>• hole in the intestines (possibly leaking contents into the abdomen)<br>• inflammation of the pancreas (possible abdominal pain) | • immune response (causing joint, tissue, and/or organ damage)<br>• muscle inflammation<br>• inflammation inside/around the eye (possible vision problems)<br>• kidney failure<br>• immune reaction (possible loss of drug function)<br>• infusion reaction (possible chills, fever, difficulty breathing, |

| | | |
|---|---|---|
| • hardening/tightening of the skin and connective tissue<br>• loss of skin color<br>• decreased production of adrenal hormones (possible weakness and/or low blood pressure) | • anemia due to destruction of red blood cells<br>• low platelet count<br>• hepatitis | and/or change in blood pressure)<br>• multi-organ disease causing lesions, most often in the lungs (sarcoidosis)<br>• allergic reaction |

Durvalumab may cause a low platelet count. 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.

Patients with head and neck cancer may have an increased risk of bleeding. Tell the study doctor right away if you experience any bleeding and about any drugs you are taking that may increase your risk of bleeding (such as aspirin, blood thinners, or NSAIDs).

**Nivolumab Side Effects**

**Common (occurring in more than 10%)**

| | | |
|---|---|---|
| • fatigue/lack of energy | • diarrhea<br>• itching | • skin rash |

**Occasional (occurring in 3-10%)**

| | | |
|---|---|---|
| • fever<br>• underactive thyroid gland (possible increased thyroid stimulating hormone lab test result, weight gain, heart failure, and/or constipation) | • abnormal digestive blood test (possible inflammation of the pancreas)<br>• nausea/vomiting<br>• abdominal pain<br>• loss of appetite<br>• low red blood cell count | • abnormal liver test (possible liver damage and/or yellowing of the eyes and/or skin)<br>• pain (including muscle/bone)<br>• lung inflammation (pneumonitis), and/or bronchitis (possible difficulty breathing) |

**Rare (occurring in fewer than 3% of patients)**

| | | |
|---|---|---|
| • fast heartbeat<br>• abnormal EKG<br>• heart inflammation/ inflammation of the tissue around the heart (possible chest pain) | • decreased production of adrenal hormones (possible weakness and/or low blood pressure)<br>• inflammation of the thyroid gland (possible | • abnormal kidney test (possible kidney damage)<br>• kidney failure<br>• breakdown of muscle tissue (possible kidney failure) |

| | | |
|---|---|---|
| • high blood pressure<br>• low blood pressure (possible dizziness and/or fainting)<br>• swelling of the brain (possible headache and/or mental status changes)<br>• inflammation of the brain and spinal cord (possible altered consciousness)<br>• inflammation of the membrane around the spinal cord and brain (possible headache and/or coma)<br>• swelling (face/arms/legs)<br>• chills<br>• headache<br>• difficulty sleeping<br>• dizziness<br>• dry/red skin<br>• hives<br>• skin blisters<br>• very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract)<br>• red, dry, scaly patches of thickened skin (psoriasis)<br>• allergic skin reaction<br>• hair loss (partial or total)<br>• overactive thyroid gland (possible decreased thyroid stimulating hormone lab test result, weight loss, heart rate changes, and/or sweating) | tenderness in the neck)<br>• pituitary gland failure (possible hormone imbalance)<br>• blood vessel inflammation<br>• low blood levels of sodium (possible headache, confusion, seizures, and/or coma)<br>• abnormal blood test (possible pancreas damage)<br>• high blood sugar (possible diabetes)<br>• diabetes<br>• abnormal blood acid/base balance due to uncontrolled diabetes (possible organ damage)<br>• mouth blisters/sores (possible difficulty swallowing)<br>• constipation<br>• dehydration<br>• dry mouth<br>• inflammation of the intestines<br>• hole in the intestines (possibly leaking contents into the abdomen)<br>• liver inflammation<br>• liver failure/damage<br>• low blood cell count (platelets, white)<br>• destruction of red blood cells due to the body attacking itself (called autoimmune hemolytic anemia) | • damage to the nervous system (causing numbness and/or paralysis)<br>• nerve damage (possible numbness, pain, and/or loss of motor function and/or “pins and needles” sensation)<br>• nerve damage (affecting the head and neck)<br>• muscle inflammation<br>• joint pain/stiffness<br>• dry eye<br>• blurry/double vision<br>• difficulty breathing<br>• cough<br>• infusion reaction (possible fever, rash, pain, and/or swelling)<br>• immune response causing the body to attack itself (possibly causing muscle weakness)<br>• immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures)<br>• multi-organ disease causing lesions, most often in the lungs (sarcoidosis)<br>• allergic reaction, possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)<br>• patches of skin color loss |

| | | |
|---|---|---|
| | | • inflammation of multiple areas of the body (see below) |

You may need to take drugs to reduce inflammation while taking nivolumab. Long-term use of these drugs may increase your risk of infection. These infections may occur anywhere and may be fatal. Treatment with antibiotic or antifungal drugs may be required to treat these infections.

The study drug 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.

Nivolumab may cause serious side effects that affect your immune system. Some of these side effects start as inflammation in different areas of the body like the skin, hormone glands, pancreas, eye, kidney, or stomach. Tell the study staff right away if you have diarrhea, nausea, vomiting, blurred vision, dizziness, fainting, or you are feeling cold all the time.

**Frequency Unknown**

| | |
|---|---|
| • graft-versus-host disease (when transplanted donor tissue attacks the tissues of the recipient's body)<br>• Hemophagocytic lymphohistiocytosis (HLH) syndrome (see below) | • Vogt Koyanagi Harada syndrome -- pigmented tissue (possible eye pain/swelling, hearing loss, and/or loss of skin color)<br>• risk of organ transplant rejection |

Nivolumab may cause Hemophagocytic lymphohistiocytosis (HLH) syndrome at an unknown frequency. HLH is a disease that may affect your body's defense system, (your immune system) and certain white blood cells made by your immune system may attack other blood cells. These abnormal blood cells collect in your spleen and liver, causing these organs to enlarge, possibly causing fever, rash, and low blood cell counts

**Pembrolizumab Side Effects**

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

| | | |
|---|---|---|
| • fatigue<br>• fever<br>• skin rash and/or itching<br>• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, | • high blood sugar (possible diabetes)<br>• high blood levels of fat (possible heart disease and/or stroke)<br>• loss of appetite<br>• nausea<br>• constipation | • abnormal liver test (possible liver damage)<br>• pain<br>• abnormal kidney test (possible kidney damage)<br>• cough |

| | | |
|---|---|---|
| heart problems, changes in mental status, and/or seizure) | • low blood cell count (white/red/platelets) | |

**Occasional (occurring in 3-20% of patients)**

| | | |
|---|---|---|
| • swelling (face/arm/leg)<br>• headache<br>• confusion<br>• underactive thyroid gland (possible weight gain, heart failure, and/or constipation)<br>• overactive thyroid gland (possible weight loss, diarrhea, mood swings, difficulty sleeping, heart rate changes, and/or sweating) | • weight loss<br>• diarrhea<br>• abdominal pain<br>• blood in the urine<br>• vomiting<br>• abnormal liver test (possible yellowing of the skin and/or eyes)<br>• weakness | • nerve damage (possible numbness, pain, and/or loss of motor function)<br>• difficulty breathing (possibly due to lung inflammation)<br>• infusion reaction (possible dizziness, low blood pressure, nausea, pain, and/or difficulty breathing |

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

| | | |
|---|---|---|
| • heart inflammation<br>• blood vessel inflammation (possible bleeding and/or bruising)<br>• seizure<br>• immune system damage to the nervous system (causing numbness and/or paralysis)<br>• spinal cord inflammation (possible pain, weakness, loss of feeling or movement, and/or paralysis)<br>• brain inflammation (possible paralysis and/or coma)<br>• shedding, scaling and/or inflammation of the skin (possible fatal loss of bodily fluids)<br>• large skin blisters | • hormonal deficiency that affects the body's ability to control blood pressure and react to stress<br>• pituitary gland inflammation (possible headaches)<br>• inflammation of the thyroid gland (possible tenderness in the neck)<br>• diabetes requiring insulin<br>• severe high blood sugar due to uncontrolled diabetes<br>• decreased production of adrenal hormones (possible weakness and/or low blood pressure)<br>• inflammation of the pancreas (possible abdominal pain) | • inflammation inside the eye (possible vision problems)<br>• kidney inflammation (possible kidney damage/failure)<br>• kidney failure<br>• build-up of fluid around the lungs<br>• immune response that causes the body to attack itself (possible organ damage)<br>• multi-organ disease causing lesions, most often in the lungs (sarcoidosis)<br>• immune response (causing muscle weakness)<br>• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) |

| | | |
|---|---|---|
| • very severe blistering skin disease (loss of large portion of skin and/or with ulcers of the skin and digestive tract) | • anemia due to destruction of red blood cells<br>• liver damage (hepatitis) | • 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.

**Radiation Therapy Side Effects**

**It is not known how often the side effects of radiation therapy may occur.**

| | | |
|---|---|---|
| • swelling<br>• swelling of the arms or torso<br>• skin changes (possible dryness, itching, peeling, and/or blistering) | • hair loss at the treatment site<br>• mouth problems<br>• trouble swallowing<br>• nausea<br>• vomiting<br>• diarrhea | • urinary and/or bladder changes<br>• sexual changes<br>• inability to produce children<br>• joint problems<br>• secondary cancers |

Radiation therapy may cause you to develop another type of cancer. Side effects may not occur for up to 6 months after radiation therapy is over. Side effects will vary depending on what part of the body is receiving radiation therapy.

There are no expected risks from **radiation simulation**.

The study doctor will discuss the risks of your individual **immunotherapy** treatment with you.

**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.

**EKGs** may cause discomfort while lying on the exam table, and the tape on the EKG pads may cause skin irritation.

The **ultrasound** involves placing a gel on your skin and rubbing the ultrasound wand over it. There are no known complications from the ultrasound procedure. It is associated with slight discomfort.

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

**CT scans** send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel “closed in” while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

A **PET scan** may cause you to feel “closed in” while lying in the scanner. However, the scanner is open at both ends and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or technicians will give comfort or the scanning will be stopped.

The PET scan exposes your body to radiation. The radioactive solution does not remain in your system for a long period of time. However, you should wait 2 hours before holding an infant or getting close to a pregnant woman to avoid exposing them to radiation. You should drink fluids after the scan to help remove the solution from your system.

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 and will continue to be stored securely after the study.

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 are sexually active, you must use birth control during the study and for 5 months after your last dose of atezolizumab or nivolumab, 4 months after your last dose of pembrolizumab, 3 months after your last dose of durvalumab and avelumab, and 3 months after your last dose of plinabulin (if you receive it).

If you can become pregnant or father a child, you must use 2 methods of birth control. Acceptable methods include:

- IUD or IUS (intrauterine devices or intrauterine system, except IUD progesterone T) in addition to a barrier method with spermicide
- Use of approved hormonal methods such as pills, implants, shots/injections, and patches in addition to a barrier method with spermicide. This must be approved by your study doctor before you begin taking the study drug.
- Acceptable barrier methods include diaphragm, male or female condom, cervical cap, or birth control sponge

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 Beyond Spring Pharmaceuticals 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 will receive no compensation for taking part in this study.

**Additional Information**

4. You may ask the study chair (Dr. Siqing Fu, at 713-563-1930) 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.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Beyond Spring Pharmaceuticals, 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: Beyond Spring Pharmaceuticals.

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 Beyond Spring Pharmaceuticals, 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. Leftover samples will not be stored by Beyond Spring Pharmaceuticals.

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

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

### 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.

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.

**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
   - Beyond Spring Pharmaceuticals, who is a sponsor or supporter of this study, and/or any future sponsors/supporters and/or licensees of the study technology
   - 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.

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 this protocol

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE
A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
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.)