THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Randomized Phase II Study of Olaparib Maintenance Following Cabazitaxel-Carboplatin Induction Chemotherapy in Men with Aggressive Variant Prostate Cancer (AVPC)
2017-0133

Study Chair: Ana M. Aparicio

_____ _____
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 olaparib, when given after treatment with cabazitaxel, carboplatin, and prednisone, can help to control aggressive variant prostate cancer (AVPC). The safety of these drugs will also be studied.

This is an investigational study. Cabazitaxel and carboplatin are FDA approved and commercially available for the treatment of certain types of prostate cancer. Prednisone is FDA-approved and commercially available as a corticosteroid. Olaparib is FDA approved and commercially available for the treatment of certain types of ovarian cancer. The combination of cabazitaxel and carboplatin followed by olaparib in this study is investigational. 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. You may not want to take part in this study due to the potential for side effects like cytokine release syndrome (described later) and the need for hospitalization.

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

You will receive carboplatin and cabazitaxel for up to 6 cycles. If you are in Group 1 (described below), you may continue receiving olaparib for as long as the doctor thinks it is in your best interest.

Olaparib will be provided at no cost to you while you are on this study. You and/or your insurance provider will be responsible for the cost of cabazitaxel, carboplatin, and prednisone.

You may choose not to take part in this study. You may choose to have cabazitaxel and or carboplatin without taking part in this study. 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:

Within 28 days before you can receive the study drugs:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests, to check your prostate specific antigen (PSA) levels, and for tumor marker testing. Tumor markers may be related to the status of the disease. You must fast (eat or drink nothing except water) for about 9-12 hours before this blood draw.
- Blood (about 2 teaspoons) will be drawn to check for circulating tumor cells (CTCs). This is a test of how many tumor cells are in the blood.
- Blood (about 2 tablespoons) will be drawn for biomarker testing. Biomarkers are found in the blood and tissue and may be related to your reaction to the study drug.
- Urine will be collected for routine tests and tumor marker testing.
- You will have a bone scan and either an MRI or a CT scan of the chest, abdomen, and pelvis to check the status of the disease.
- You will have an EKG to check your heart function.
- You will have a tumor biopsy for biomarker testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug. The type of

biopsy you have will depend on where the disease has spread and/or what the doctor thinks is in your best interest. The doctor will discuss with you the type of biopsy you will have.

Within 7 days before you can receive the study drugs, blood (about 2 teaspoons) will be drawn for routine tests, to check your PSA levels, and for tumor marker testing. You must fast for about 9-12 hours before this blood draw.

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 randomly assigned (as in a roll of dice) to 1 of 2 study groups. This is done because no one knows if one study group is better, the same, or worse than the other group. You will have a 2 in 3 chance of being assigned to Group 1 and a 1 in 3 chance of being assigned to Group 2:

- If you are in **Group 1**, you will receive olaparib.
- If you are in Group 2, you will not receive olaparib.

All participants will receive cabazitaxel and carboplatin.

You and the study staff will know to which group you have been assigned.

Up to 96 participants will be enrolled on this study. All will take part at MD Anderson.

Study Drug Administration

Each study cycle is 21 days.

You will receive cabazitaxel by vein over 60 minutes on Day 1 of Cycles 1-6. You will then receive carboplatin by vein over 60 minutes on Day 1 of Cycles 1-6.

You will take 1 tablet of prednisone by mouth 2 times each day of Cycles 1-6.

You will be given standard drugs to help decrease the risk of side effects (for example, filgrastim-sndz) before and/or after each dose of cabazitaxel and continuing through several days. Your doctor will describe these drugs to you in more detail, including how they are given and any side affects you may expect.

If you are in Group 1, you will take tablets of olaparib 2 times by mouth each day starting on Day 1 of Cycle 7. Swallow the whole tablet or tablets. Do not chew, crush, divide, or dissolve the tablets. If you vomit shortly after taking your olaparib tablet you can retake a new dose as long as you can see that the tablet came out whole. You should take the doses at the same time each day (or within 2 hours of the scheduled times). Do not take the dose if you forget and it is more than 2 hours since your scheduled time. Take olaparib at least 1 hour after and 2 hours before eating.

If you are in Group 2, you will receive standard of care treatment and follow-up after Cycle 6. The study doctor will tell you more about what this may mean for you.

You may 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.

Your participation on the study will be over after the follow-up visits.

Study Visits

On **Day 1 of Cycles 1-6**:

- You will have a physical exam.
- Blood (up to 5 tablespoons) will be drawn for routine tests, biomarker testing, tumor marker testing, and to measure your PSA level. At some of these visits, this sample will also be used for CTC testing. You must fast for up to 12 hours before the Cycle 4 visit.
- At Cycle 4 only, you will have a bone scan and either MRIs or CT scans to check the status of the disease.

After Cycle 6, you will have a second tumor biopsy for biomarker testing to compare to the one taken at screening. The type of biopsy you have will depend on where the disease has spread and/or what the doctor thinks is in your best interest. The doctor will discuss with you the type of biopsy you will have.

On **Day 1 of Cycles 7-10**:

- You will have a physical exam.
- Blood (up to 5 tablespoons) will be drawn for routine tests, tumor marker testing, biomarker testing, and to measure your PSA level. At some of these visits, this sample will also be used for CTC testing. On Cycle 7 only, part of this sample will also be used to check your testosterone levels.
- Urine will be collected for tumor marker testing.
- In Cycle 7 only:
    - You will have an EKG.
    - You will have a bone scan and either MRIs or CT scans.

After Cycle 10, you will only have study visits every 3 cycles. Beginning on **Day 1 of Cycle 13, every 3 cycles (Cycles 13, 16, 19, and so on)**:

- You will have a physical exam.
- Blood (up to 5 tablespoons) will be drawn for routine tests, tumor marker testing, biomarker testing, and to measure your PSA level. At some of these visits, this sample will also be used for CTC testing. You must fast for up to 12 hours before the visits at Cycle 10 and every 3 cycles after that.
- You will have a bone scan and either MRIs or CT scans to check the status of the disease.
- You will have an EKG.

If you have severe side effects, you may return to the clinic more often so the study doctor can check on your health.

End of Study Visit

When you leave the study, the following tests and procedures will be performed:

- You will have a physical exam.
- You will have a bone scan and either MRIs or CT scans to check the status of the disease.
- You will have an EKG.
- Blood (about 3 tablespoons) will be drawn for routine tests, tumor marker testing, and to measure your PSA level. You must fast for up to 12 hours before this visit.
- Urine will be collected for tumor marker testing.

30 Day Post-Study Visit

When you leave the study, the following tests and procedures will be performed:

- You will have a physical exam.
- You will have a bone scan and either MRIs or CT scans to check the status of the disease.
- You will have an EKG.
- Blood (about 3 tablespoons) will be drawn for routine tests, tumor marker testing, and to measure your PSA level. You must fast for up to 12 hours before this visit.

Follow-Up

About every 6 months after the end-of-study visit, the study staff will check your health. This will be done either by a chart review or a phone call. If you are called, this call will last about 5 minutes. These calls will stop if you withdraw from the study.

Other Testing

The study staff will ask you to take part in other MD Anderson research study (PA13-0247 and LAB02-152) for additional testing. The study doctor will discuss this with you and you will sign a separate consent document.

Other Instructions

You should avoid eating or drinking grapefruit and Seville oranges and their juices while you are receiving the study treatment because they can affect the amount of study drug in your blood.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. 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.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drug/procedures.

Cabazitaxel, carboplatin, olaparib, and filgrastim-sndz each may cause low blood cell counts (red blood cells, platelets, and/or 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, severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Cabazitaxel Side Effects

Common (occurring in more than 20% of patients)

• fatigue • diarrhea	• vomiting • nausea	• low blood cell counts (red, platelets, white)

Occasional (occurring in 3-20% of patients)

• swelling (arm/leg) • irregular heartbeat • low blood pressure (possible dizziness/fainting) • fever • dizziness • headache • abdominal pain • loss of appetite • abnormal taste	• hair loss (partial or total) • dehydration • constipation • upset stomach • abdominal pain • weight loss • mouth sores and/or blisters (possible difficulty swallowing) • difficult and/or painful urination	• blood in the urine • urinary tract infection • nerve damage (possible numbness, pain, and/or loss of motor function) • pain (back/joint) • muscle spasm • weakness • difficulty breathing • cough

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

• changes in body salts such as sodium, potassium, and/or magnesium (possible fatigue and/or weakness) • digestive system bleeding	• paralysis of the intestines • intestinal blockage • hole in the intestines (possibly leaking contents into the abdomen) • abnormal liver test (possible liver damage and/or yellowing of the skin and/or eyes) • kidney failure	• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • severe allergic reaction (such as skin rash, skin redness, low blood pressure, and/or difficulty breathing due to a narrowing of the airways)

Receiving the study drug by vein may cause temporary irritation and/or bruising at the site of the infusion. It may also cause an allergic reaction.

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

<u>Olaparib Side Effects</u>

Common (occurring in more than 20% of patients)

• fatigue • headache • skin rash • nausea • abdominal pain • vomiting • diarrhea	• upset stomach • loss of appetite • abnormal taste • enlarged red blood cells • low blood counts (red, platelet, white) • weakness	• pain (muscle/bone/ • back) • abnormal kidney test (possible kidney damage) • cough • infection

Occasional (occurring in 3-20% of patients)

• swelling (arm/leg)	• dizziness • constipation	• difficulty breathing

Frequency unknown but occurring in 1-10% of patients

• high blood pressure • blood clots in a vein (possible pain, swelling, and/or redness) • fever • anxiety • depression • difficulty sleeping • dry skin/itching • eczema (skin inflammation)	• hot flashes • high blood sugar (possible diabetes) • low blood levels of magnesium (possible weakness, muscle cramps, and/or irregular heartbeat) • mouth blisters/sores (possible difficulty swallowing)	• difficult and/or painful urination • loss of bladder control • disease of the female genitals and vagina • nerve damage (possible numbness, pain, and/or loss of motor function) • blockage in the lung (possible pain and/or shortness of breath)

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

• lung inflammation (possible difficulty breathing)

Olaparib may rarely cause you to develop another type of cancer, such as acute myeloid leukemia (a type of blood cancer) or cancer of the bone marrow (possible low blood cell counts).

Prednisone Side Effects

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

• heart failure • high blood pressure • swelling • headache • increased pressure between the skull and brain (possible swelling of the eye nerve, vision changes, and/or headaches) • mental health disturbances (including euphoria [unusual feelings of happiness or well-being]) • difficulty sleeping • mood swings • personality changes • severe depression • seizure	• failure of hormone-producing organs • decreased ability to process carbohydrates • high level of steroid in the body (possible mood changes and diabetes) • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • diabetes • abnormal blood acid/base balance (possible organ damage) • underactive thyroid	• stomach ulcer (with possible hole and bleeding) • esophagus sore • abnormal liver or bone tests (possible liver damage) • pain or loss of function of the hips and/or shoulders due to bone death • loss of muscle • muscle weakness (possibly caused by muscle damage) • loss of bone strength (possible broken bones) • brittle/broken bones • tendon tear

• fatigue and anxiety • dizziness • bruising • facial skin redness • tiny dots on the skin • thin fragile skin • hives • sweating • wound healing problems • Cushing's syndrome (possible weakness, diabetes, and/or bone weakness)	gland (possible weight gain, heart failure, and/or constipation) • body-wide loss of proteins (possible weakness and/or swelling) • low blood levels of potassium (possible muscle cramps) • high blood levels of sodium (possible weakness and/or swelling) • abdominal swelling • inflammation of the pancreas (possible abdominal pain)	(particularly Achilles tendon) • collapse of bones in the spine • bulging eye • increased pressure in the eye (possible vision loss, pain, and/or blurry vision) • cataracts (clouding of the lens of the eye) • allergic reactions that are possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

Rarely (in fewer than 3% of patients)

• blood clots in a vein (possible pain, swelling, and/or redness)

Prednisone may 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/or difficulty breathing.

Prednisone may cause you to develop another type of cancer (such as Kaposi's sarcoma).

Filgrastim-sndz Side Effects

Common (occurring in more than 20% of patients)

• fever • fatigue	• nausea • enlarged spleen	• low platelet counts • bone pain

Occasional (occurring in 3-20% of patients)

• chest pain • high blood pressure • swelling (arm/leg) • dizziness	• loss of appetite • high blood levels of uric acid(possible painful joints and	• muscle spasm • numbness • lung inflammation • cough

• headache • difficulty sleeping • skin rash • hair loss (partial/total) • abnormal blood test • vomiting	/or kidney failure) • low red blood cell counts • abnormal liver tests (possible liver damage) • pain (muscle/joint/limb) • weakness	• difficulty breathing • nosebleed • allergic reaction • reaction to a blood transfusion • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

The drug may occasionally cause an increased risk of infection, such as pneumonia and/or urinary tract infection. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

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

• low blood pressure (possible dizziness/fainting) • irregular heartbeat • heart attack • fast heartbeat • blood vessel inflammation (possible bleeding and/or bruising) • swelling (face) • bleeding in the brain • skin condition with fever and skin lesions	• painful skin bumps • worsening of existing skin disease (psoriasis) • leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing) • diarrhea • enlarged liver • blood in the urine • sickle cell crisis in patients with sickle cell disease	• ruptured spleen • loss of bone strength (possible broken bones) • decreased kidney function (possible kidney failure) • coughing up blood • bleeding in the lungs and/or airways • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • immune reaction

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.

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

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.

Fasting may cause your blood sugar to drop. You may feel tired, hungry, and/or nauseous. If you have diabetes, it is important to talk to your doctor about managing your blood sugar while fasting.

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. A prostate biopsy may cause you to feel a stinging sensation each time a sample is taken. It may cause infection, soreness, discomfort, bleeding in the urine or rectum, and/or blood-tinged ejaculate (the fluid released by the prostate during sexual intercourse). It may also result in the temporary inability to urinate.

Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. The researchers with this CoC may not disclose or use information that may identify you in any federal, state, or local civil, criminal, administrative,

legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information protected by this CoC cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below).

The CoC cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation. You should understand that a CoC does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The CoC will not be used to prevent disclosure for any purpose you have consented to.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn baby, so you must use birth control if you are sexually active.

Birth Control Specifications: If your partner can become pregnant, you and your partner must be willing to use 2 methods of birth control from screening until 13 weeks after your last dose of study drug. Check with your study doctor about what kind of birth control methods to use. The 2 methods must consist of:

1. Condom, and
2. The use of another barrier method (such as a diaphragm or cervical/vault caps) with a spermicidal agent, or the use by your female partner of an intrauterine device or system (IUD or IUS) or birth control pills, injections, or implants.

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

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: You may be asked to have a tumor biopsy for biomarker testing if the disease gets worse. The type of biopsy you have will depend on where the disease has spread and/or what the doctor thinks is in your best interest. The doctor will discuss with you the type of biopsy you will have.

Optional Procedure #2: If you agree, leftover tumor tissue from procedures performed on this study or from previously performed procedures will be collected and stored in a research bank at MD Anderson for use in future research related to cancer.

Before your samples can be used for research, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson. The IRB is a committee of doctors, researchers, and community members. The IRB is responsible for protecting study participants and making sure all research is safe and ethical.

Your samples will be given a code number. Only individuals with IRB permission and designated bank staff will have access to the code numbers and be able to link the samples to you. This is to allow medical data related to the samples to be updated as needed. Additionally, if needed for certain types of research in the future and if the IRB approves, the bank staff and approved research staff will be able to link your samples back to you.

There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedures.

Optional Procedure Risks:

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. Prostate biopsy may cause you to feel a stinging sensation each time a sample is taken. It may cause infection, soreness, discomfort, bleeding in the urine or rectum, and/or blood-tinged ejaculate (the fluid released by the prostate during sexual intercourse). It may also result in the temporary inability to urinate.

MD Anderson and others can learn about cancer and other diseases from your **banked samples**. In the future, people who may do research with these samples may need to know more information about your health. This information may be collected from your medical record. MD Anderson will make reasonable efforts to preserve your privacy, but cannot guarantee complete privacy. Sometimes your samples may be used for genetic research about diseases that are passed on in families. The type of **genetic testing** being performed in this study will not provide you or your doctor information about diseases that are passed down in families. It will not tell the study researchers anything that will prevent you from getting health insurance, and it will not tell the study researchers anything about any diseases or conditions you may get in the future.

If you withdraw your consent to the storage of leftover samples in the tissue bank, then they will no longer be collected for storage. Any of your samples that remain in the tissue bank will no longer be used for research and will be destroyed.

However, if any of your de-identified samples were already released for research purposes before you withdrew consent, MD Anderson will not be able to destroy them.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Circle your choice of "yes" or "no" for each of the following optional procedures:

Optional Procedure #1: Do you agree to have an additional tumor biopsy if the disease gets worse?

YES **NO**

Optional Procedure #2: Do you agree to allow leftover tumor tissue to be stored in a research bank at MD Anderson for use in future research related to cancer?

YES **NO**

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 AstraZeneca 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. Ana M. Aparicio, at 713-792-2830) 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, AstraZeneca, Merck & Co., the NCI, 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, 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: AstraZeneca, Merck & Co., and the NCI.

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

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson or shared

with other researchers and/or institutions for use in future research (if you agree to Optional Procedure #2).

Before being shared for future research, every effort will be made to remove your identifying information from any data and/or 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 samples are used for future research. If this 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 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 will 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. 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
   - AstraZeneca and Merck &Co. Inc., who are sponsors or supporters of this study, and/or 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 2017-0315.

_____ _____
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 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