THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

A Phase I Study of Cabozantinib and Pamiparib to Evaluate Triple Inhibition of PARP, VEGFR and c-MET in Advanced Homologous Recombination Deficient Malignancies
2020-0308

Subtitle: BGB-290-103

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

The goal of this clinical research study is to find the highest tolerable dose of cabozantinib that can be given in combination with pamiparib (BGB-290) to patients with solid tumors that are advanced or metastatic (have spread). Researchers also want to learn if these study drugs can help to control the disease.

This is an investigational study. Pamiparib is not FDA approved or commercially available. Cabozantinib is FDA approved and commercially available for the treatment of renal cell carcinoma and medullary thyroid cancer. The use of pamiparib and cabozantinib in patients with advanced or metastatic solid tumors 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. If you take part in this study, you may experience side effects, some of which may be severe or fatal.
You can read a list of potential side effects below in the Possible Risks section of this consent.

You may continue taking the study drugs for as long as the doctor thinks it is in your best interest.

Pamiparib and cabozantinib will be provided at no cost to you while you are on study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard therapy for the disease. The study doctor will discuss with you the possible risks and benefits of these treatments. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer. The study doctor will discuss these alternative treatments with you, including any potential side effects or risks.

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 be done within 28 days before your first dose of the study drugs to help the doctor decide if you are eligible:

- You will have a physical exam.
- You will have an EKG and either an echocardiogram (ECHO) or MUGA scan to check your heart function.
- You will have CT scans or MRIs to check the status of the disease.
- Blood (about 1 teaspoon) will be drawn for routine tests, tumor marker testing, and to check for hepatitis B and C and HIV (the AIDS virus). Tumor markers may be related to the status of the disease. If you can become pregnant, part of this sample will be used for a pregnancy test. To take part in this study, you must not be pregnant.
- Urine will be collected for routine tests. You will be asked to collect your urine over a 24-hour period. The study team will provide a container and instructions how to collect the urine.
- You will have imaging scans (CT, MRI, and/or PET scans) to check the status of the disease.
- Tumor tissue from an earlier procedure will be collected and used in research testing to learn more about how the disease may or may not respond to the study drugs. If you do not have a leftover tissue sample available and it is not known that you have a certain genetic mutation (change in your DNA), you

will have a tumor biopsy. The type of biopsy you have will depend on the location of the disease. The study doctor will describe this procedure to you in more detail.

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.

Study Groups

If you are found to be eligible to take part in this study, you will be assigned to a study part based on when you join this study.

If you are enrolled in **Part 1 (Dose Escalation)**, the dose levels of the study drugs you receive will depend on when you join this study. Up to 4 dose level groups of up to 6 participants each (up to 24 participants total) will be enrolled. The first group of up to 6 participants will receive the lowest dose level of both drugs. Each new group will receive a higher dose of either pamiparib or cabozantinib than the group before it, if no intolerable side effects were seen. This will continue until the highest tolerable drug combination is found.

After the highest tolerable dose combination is found, up to 20 more participants will be enrolled in **Part 2 (Dose Expansion)**. Participants in Part 2 will receive the drug combination at the recommended dose that was found in Part 1.

Up to 44 total patients will take part in this study. All will be enrolled at MD Anderson.

Study Drug Administration

Each study drug cycle is 28 days.

You will take the study capsules/tablets by mouth with a full glass of water (at least 8 ounces). You should take each drug dose quickly, without long breaks between each capsule/tablet.

You will take **cabozantinib** 1 time a day. You should fast (eat nothing and drink only water) for at least 2 hours before and 1 hour after your dose.

You will take **pamiparib** 2 times a day, about 12 hours apart. Pamiparib can be taken with or without food.

Other drug dosing instructions:

- If you forget to take a dose of cabozantinib, you can take your dose up to 12 hours after the scheduled time. If you forget to take a dose of pamiparib, you may take it up to 2 hours after the scheduled time. If you are outside of these dosing windows, do not make up the missed dose or take an extra dose of study drug to make up for that missed dose. Just take your next scheduled doses as prescribed.

- Do not skip any doses unless your study doctor tells you to skip doses for safety reasons.
- If you vomit after taking the dose, do not take it again or take extra the next day. Just take your next dose as scheduled and tell the study staff that this happened.
- The study drugs must be kept at room temperature (between 59°F to 86°F).
- Bring any unused capsules and/or empty bottle(s) to the clinic at each clinic visit. At the end of the study, you will return any remaining capsules and empty containers to the clinic.
- You may be given a diary to record the doses of study drugs taken each day and when you have taken and/or missed a dose for any reason. If you miss a dose, you should write in the reason you missed the dose, even if it was because the study doctor asked you not to take the study drug. Bring this diary back to the clinic at each study visit.

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

Study Visits – All Participants

Baseline Visit
About 7 days before your first dose of the study drugs, you will have a baseline visit. At this baseline visit:

- You will have a physical exam.
- Blood (about 2 teaspoons) will be drawn for routine tests, tumor marker tests, and tests of your thyroid function. If you can become pregnant, part of this sample will be used for a pregnancy test.
- Urine will be collected for routine tests. You will be asked to collect your urine over a 24-hour period.

During **Cycle 1:**

- On Day 1 only, you will have an EKG to check your heart function.
- Every 2 weeks, you will have a physical exam.
- Every 2 weeks, urine will be collected for routine tests. You will be asked to collect your urine over a 24-hour period.
- Every week, blood (about 2 teaspoons) will be drawn for routine tests. Sometimes, this sample will be used to measure your kidney and liver function.

Within 1 week before Day 1 of Cycle 2, you will have a tumor biopsy to learn about how the disease may or may not respond to the study drugs.

During **Cycle 2:**

- Every 2 weeks, you will have a physical exam.
- Every 2 weeks, blood (about 2 teaspoons) will be drawn for routine tests. On Day 1 only, this sample will also be used for thyroid/liver/kidney function tests,

tumor marker tests, and/or a pregnancy test (if applicable).
- On Day 1 only, urine will be collected for routine tests. You will be asked to collect your urine over a 24-hour period.
- On Day 1 only, you will have an EKG to check your heart function.

During **Cycles 3 and beyond**:
- On Day 1 of each cycle, you will have a physical exam.
- On Day 1 of each cycle, blood (about 2 teaspoons) will be drawn for routine tests. If you can become pregnant, part of this sample will also be used for a pregnancy test. Every 2 cycles, this sample will also be used for tumor marker testing and to check your thyroid function.
- On Day 1 of each cycle, urine will be collected for routine tests. You will be asked to collect your urine over a 24-hour period.
- Every 2 cycles, you will have imaging scans (CT, MRI, and/or PET scans) to check the status of the disease.
- Every 2 cycles, you will have an EKG to check your heart function.

You may have the tests above more often during the study, if the doctor feels it is needed for your safety. Some of the tests may be repeated if your drug dose(s) are changed or if the disease needs to be restaged. You may also have other standard tests, such as EKGs/ECHOs or other imaging scans, if the doctor thinks they are needed. The study staff can explain this in more detail.

Pharmacokinetic (PK) Intensive Testing – Part 2 Only

If you are enrolled in Part 2 (Dose Expansion), you will also take part in a PK study. You will either be enrolled in the cabozantinib PK group or the pamiparib PK group:
- Patients in the cabozantinib PK group will take cabozantinib only (no pamiparib) on Cycle 1 Day 1.
- Patients in the pamiparib PK group will take pamiparib only in the morning on Cycle 1 Day 1 (skipping the evening dose), and then on Day 15 of Cycle 1, they will take pamiparib in the morning only (skipping the evening dose) along with cabozantinib.

All PK study participants will have multiple blood draws (about ½ teaspoon each time) on Days 1 and 15 of Cycle 1. These samples will be drawn before the dose, and then at about 1, 2, 4, 6, 8, and 24 hours after the dose, on each day.

If you are in the cabozantinib PK group, additional blood (about ½ teaspoon each time) will be drawn before your dose on Day 1 of Cycles 2, 3, and 4.

End-of-Treatment Visit and Follow-up

Within 30 days after your last dose of the study drugs, the following tests and procedures will be performed:
- You will have a complete physical exam.

- Blood (about 2 teaspoons) and urine will be collected for routine tests and tumor marker testing. The blood sample will also be used for liver/kidney function tests and a pregnancy test (if applicable).
- You will have imaging scans to check the status of the disease.

You will be called by the study staff about 30 days after your last dose of study drugs and asked about how you are doing. You will then be called every 3 months from that point on. Each call may last about 15-30 minutes.

Female participants who can become pregnant will have pregnancy tests every month until 6 months after their last dose of the study drugs. These can be done in the clinic or at home.

Other Instructions

- Attend all study visits and, if needed, reschedule appointments as soon as possible.
- Tell your other doctors and health care providers that you are taking part in this study.
- Do not take part in any other research study.
- Take the study drugs as directed. Tell your study doctor or study staff if you miss any doses or stop taking the study drugs.
- Keep the study drugs in a safe place, for your use only, and away from children.
- Check with the study doctor before taking any new medicines (including prescription, over-the-counter, vitamins and herbal supplements) or changing the doses of medications that you are already taking.
- Some foods like grapefruit, star fruit, Seville (sour) oranges, and St. John's wort, pomegranate, or products made with these fruits (including juice, jams, or candies) as well as some medications may interfere with the way your body processes pamiparib and cabozantinib. This could cause the amount of either of these drugs in your body to be higher or lower than expected. Taking the study drug with your regular medications or supplements may change how your regular medications or supplements work. Avoid grapefruit, star fruit, Seville (sour) oranges, and St. John's wort, pomegranate, or products made with these fruits (including juice, jams, or candies) and tell the study doctor about all medications or supplements you are taking during the study.
- Because of the risk of fatigue (tiredness), care should be taken when driving or operating heavy machinery.
- You will be provided with an identification card which says that you are taking part in this study. Carry this card with you at all times and show it to any doctors or nurses that are involved in your care.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form,

as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures. If needed for your safety, the study staff may tell you to stop taking the study drugs at any point.

You should stop taking cabozantinib and tell the study staff right away if you experience any of the following side effects:

- high blood pressure, even with medication
- development of holes or abnormal connections between organs or blood vessels
- severe bleeding
- heart attack
- stroke
- decreased kidney function (possible kidney damage)
- destruction of the jaw bone
- brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss)

Pamiparib and cabozantinib may each cause low blood cell counts (red blood cells, platelets, and white blood cells):

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

Pamiparib (BGB-290) Side Effects

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

• fatigue • seizures • intestinal blockage • nausea/vomiting • diarrhea	• loss of appetite • stomachache • constipation • decreased bone marrow function (possible leukemia)	• low blood cell counts (red, white, platelet) • loss of strength • build-up of fluid around the lungs • infection

Pamiparib may cause you to develop another type of cancer (such as acute myeloid leukemia, a type of blood cancer) or myelodysplastic syndrome (MDS – decreased bone marrow function that may progress to leukemia).

Cabozantinib Side Effects

Common (occurring in more than 20% of patients)

• high blood pressure • fatigue • weakness • changes in hair color • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering) • skin rash • high blood levels of fat (possible heart disease and/or stroke) • high blood sugar (possible diabetes)	• 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) • underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • mouth blisters/sores (possible difficulty swallowing) • mouth pain • abnormal taste	• loss of appetite • weight loss • diarrhea • nausea • abdominal pain • constipation • vomiting • low blood counts (red/white/platelets) • abnormal liver or bone tests (possible liver damage and/or yellowing of the skin and/or eyes) • abnormal kidney test (possible kidney damage)

Occasional (occurring in 3-20% of patients)

• blood clots in a vein (possible pain, swelling, and/or redness) • blood vessel disorder (possible tissue death) • chest pain • low blood pressure	• hair loss (partial or total) • abnormal blood test (possible pancreas damage) • upset stomach • hemorrhoids • hole in the stomach or	• dry mouth • muscle spasms • abnormal sensation (such as pins and needles) • nerve damage (possible numbness, pain, and/or loss of

(possible dizziness/fainting) • headache • dizziness • depression/anxiety • fainting • sores • skin redness/dryness/ thickening • swelling of mucus membranes	intestines (possibly leaking contents into the abdomen) • dehydration • abnormal connections or passageways between organs or vessels (such as between different parts of the digestive system) • difficulty swallowing • pain	motor and/or sensory function) • kidney failure • difficulty breathing • cough • blockage in the lung (possible pain and/or shortness of breath) • voice changes • infection

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

• severe increase in blood pressure (possible stroke) • blood clots in the arteries (possible organ damage, stroke, and/or heart attack) • seizure	• brain damage that may be reversible (possible headache, confusion, seizures, and/or vision loss) • inflammation of the pancreas (possible abdominal pain)	• severe bleeding • inflammation of the bile tract (possible blockage) • bone destruction (jaw bone) • wound healing problems

Study Drug Combination Side Effects

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

MUGA scans may cause allergic reactions to the radioactive tracer, injection site soreness, and/or swelling. They may cause damage to cells or tissue from being exposed to the radiation used in the scan. These side effects may occur in less than 10% of patients.

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 or for at least 180 days after your last dose of the study drugs. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you can become pregnant or father a child, you must use birth control while you are on study and for at least 180 days after the last dose of study drugs. Please discuss your chosen methods of birth control with the study doctor.

Acceptable methods of birth control include:

- Intrauterine devices or systems (IUD/IUS)
- Having a surgically sterilized partner ("tubes tied" or a confirmed vasectomy)
- Hormonal birth control pills (with 2 hormones), injections, patches, or implants, when combined with a barrier method of birth control (such as a condom).

If you are in an exclusive same-sex relationship and are not engaged in attempts to become pregnant, are not planning to donate eggs, and are not breastfeeding, it is not necessary to use birth control. However, if you are a female, you will still have to have pregnancy tests according to the study plan.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy. If your partner/spouse becomes pregnant while you are on this study, the sponsor would like to collect information about the pregnancy. The study sponsor's contact information will be made available so that, if you and your partner wish to, you can share information about the outcome of the pregnancy with the sponsor. If you and/or your partner choose not to share this information, it will not result in any penalty or loss of benefits to which you are otherwise entitled.

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. The sponsor will ask for information about the pregnancy.

Getting pregnant may result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: You will be asked to have 3 additional tumor biopsies while you are on study to learn more about how the disease may or may not respond to the study drugs. These biopsies will be collected before you start taking the study drugs, on Day 15 of Cycle 1, and at the End-of-Treatment visit (if the disease got worse while you were on study).

Optional Procedure #2: You will be asked to allow blood (about 2 teaspoons each time) to be drawn for pharmacodynamic (PD) testing at different time points during the study. PD testing measures how the level of study drug in your body may affect the disease. These PD samples will be collected before you start taking the study drugs, on Day 15 of Cycle 1, on Day 1 of Cycle 2, any time the disease is restaged (if appropriate) and at the End-of-Treatment visit (if available).

Optional Procedure #3: You will be asked to complete a questionnaire about your symptoms and side effects every week during Cycles 1 and 2, and then 1 time a cycle after that.

You do not have to agree to the optional procedures in order to take part in this study. There are no benefits to you for taking part in the optional procedure~~s~~. 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 procedure~~s~~.

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.

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.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the study chair.

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 additional tumor biopsies to learn more about how the disease may or may not respond to the study drugs?

YES NO

Optional Procedure #2: Do you agree to allow blood samples to be collected throughout the study for PD testing?

YES **NO**

Optional Procedure #3: Do you agree to complete questionnaires about your symptoms and side effects?

YES **NO**

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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 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.

If you become injured or ill as a direct result of the study drug or study procedures, the sponsor may pay for the treatment of the injury or illness. MD Anderson cannot determine at this time what you may be reimbursed for. A financial counselor will be made available to you after the injury or illness is reported.

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.

   Please inform your doctor or study staff if you decide to interrupt or stop taking the study drug early. You will be asked to return to the study site for a visit with the study doctor. Your study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study procedures, or the study is stopped by the sponsor or regulatory agency, even if you want to continue. If you are removed from the study, your doctor will explain the reason for this.

   If you decide to stop the treatment, or if your study doctor stops you from taking part, your doctor will ask you to return for study visits and tests after stopping study treatment.

   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, BeiGene USA, Inc., Exelixis, 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.

   Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will not contact you to let you know what they have found.

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: BeiGene USA, Inc. and Exelixis.

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 BeiGene USA, Inc. and Exelixis 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.

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

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. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

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

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

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

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
   - BeiGene USA, Inc., and Exelixis who are the sponsor or supporters of this study, and/or any future sponsors/supporters of the study
   - regulatory bodies in other countries where the study is being conducted and affiliated companies and/or representatives of BeiGene USA, Inc. and Exelixis
   - 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.

You will be assigned a unique study identification code that will not include any personal identifiers, such as name, medical record number, date of birth, zip code, or telephone number. The assigned study identification code and/or your initials will be the only identification used on all research records and study specimens. The study doctor will keep a list that matches the study identification codes to participant names, but the study doctor will not send that list to the sponsor. However, since the study forms will contain other information about you, such as your age, sex and medical history, it is possible that this other information could be used to identify you even though your name does not appear. Your coded study information and study specimens will be used by the sponsor for the purpose of the research study and research in cancer.

Blood and tissue samples may be stored for up to 2 years after the end of the study and used for the tests described in this consent form. PK testing samples may be sent to contracted laboratories for testing, but any samples left after that testing will be destroyed.

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

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

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

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

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

E. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONSENT/AUTHORIZATION

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

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2020-0308.

_____ _____
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