THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Phase II Trial of Ixazomib combined with Gemcitabine and Doxorubicin in Patients With Renal Medullary Carcinoma
2018-0065

Study Chair: Pavlos Msaouel

_____ _____
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).

If you are reading and signing this form on behalf of a potential participant, please note: Any time the words "you," "your," "I," or "me" appear, it is meant to apply to the potential participant.

STUDY SUMMARY

If you are reading and signing this form on behalf of a potential participant, please note: Any time the words "you," "your," "I," or "me" appear, it is meant to apply to the potential participant.

The goal of this clinical research study is to learn if the combination of ixazomib, gemcitabine, and doxorubicin can help to control renal medullary carcinoma (RMC).

This is an investigational study. Ixazomib is FDA approved and commercially available for the treatment of multiple myeloma. Gemcitabine and doxorubicin are FDA approved and commercially available for several other types of cancer such as urothelial or bladder cancer. It is considered investigational to use ixazomib, gemcitabine, and doxorubicin to treat RMC.

The study doctor can explain 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 (low white blood cell count from doxorubicin; fever, skin rash, nausea/omitting blood in the urine, possible liver damage/yellowing of the skin/eyes for gemcitabine; swelling, constipation, nausea/vomiting, diarrhea, numbness, eye disease for ixazomib), potential expenses, and time commitment.

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

You may receive the study drugs for up to 2 years, as long as the study doctor thinks it is in your best interest.

Ixazomib will be provided at no cost to you. You and/or your insurance provider will be responsible for the cost of gemcitabine and doxorubicin.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive chemotherapy, surgery, radiation therapy, or immunotherapy. 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 the following screening tests to help the doctor decide if you are eligible.

Within **28 days** before your first dose of study drugs:

- You will have a physical exam.
- You will have an EKG to check your heart function.
- You will have an echocardiogram (ECHO) to check your heart function. If you have already had this test performed as part of your standard care during this time, the results of that ECHO will be collected instead.
- You will have a bone scan to check the status of the disease. If the doctor thinks it is needed, you may also have a skeletal survey (a series of x-rays of your whole body), MRI, CT scan, and/or x-ray. You may also have a follow-up bone scan, if needed.
- If you have never had it done before, blood (about ½ teaspoon) will be drawn for hemoglobin electrophoresis testing. This testing is related to the type of

disease you have and may help researchers learn if you have a high amount of hemoglobin (a type of protein found in the blood).

Within **14 days** before your first dose of study drugs:

- You will have a physical exam
- Blood (about 2-3 tablespoons) will be drawn for routine tests, test to check for tuberculosis (TB), and tests to check for hepatitis B and C. This blood will also be used to see how well your blood clots and to check your glucose (sugar) levels. You must fast (have nothing to eat or drink except water) for 8 hours before this blood draw.
- Urine will be collected for routine tests.

Within 24 hours before your first dose of study drugs, blood (about 2 teaspoons) or urine will be collected for a pregnancy test. To take part in this study, you must not be 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 treatment options will be discussed with you.

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

Study Drug Administration

Each cycle is 14 days. Treatment will be given in 2 phases: Induction (Cycles 1-13) and Maintenance (Cycles 14 and beyond).

On Day 1 of each cycle during Induction, you will take ixazomib 1 time by mouth, receive gemcitabine by vein over about 90 minutes, and receive doxorubicin by vein over 15-30 minutes.

On Day 1 of each cycle during Maintenance, you will take ixazomib 1 time by mouth and receive gemcitabine by vein over about 90 minutes. You will not receive doxorubicin.

Gemcitabine and doxorubicin may be given through a catheter. A catheter is a sterile flexible tube that will be placed into a large vein while you are under anesthesia. Your doctor will explain this procedure to you in more detail, and you will be required to sign a separate consent form.

You should shallow capsules whole, with water, and not chew, break, or open the capsules of ixazomib. Ixazomib should be taken on an empty stomach (no food or drink) at least 1 hour before or at least 2 hours after food. Each capsule should be swallowed separately with about 8 ounces (1 cup) of water.

After 13 cycles, if the tumor in your kidney is still present and the doctor thinks it is safe to do so, you will have surgery to remove as much of the tumor as possible. You

will sign a separate consent form for this surgery which describes the procedure and risks in more detail.

After 13 cycles and/or surgery (if you have it), you may continue to receive the study drugs for up to 2 years.

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.

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

Study Visits

On Day 1 of each cycle:

- You will have a physical exam.
- Blood (about 5 teaspoons) will be drawn for routine testing. During Cycles 1 and 2, you will have these blood draws performed 1 time every week.
- You will have an EKG and ECHO (Cycles 6 and 13). This may be repeated if the doctor thinks it is needed.

At **Weeks 6, 12, and then every 8 weeks after that** (Weeks 20, 28, 36 and so on) during Year 1 and then every 12 weeks after that:

- If the doctor thinks it is needed, you will have an MRI, CT scan, skeletal survey, or bone scan to check the status of the disease.
- Blood (about 1 teaspoon) and will be drawn for routine testing.

End-of-Treatment Visit

About 30 and 90 days after your last dose of study drug(s):

- You will have a physical exam.
- You will have CT scan of the chest/abdomen or an MRI of abdomen/ pelvis
- If the doctor thinks it is needed and depending on why you stopped taking the study drug(s), you will have an MRI, CT scan, skeletal survey, or bone scan to check the status of the disease.

Long-Term Follow-Up

You will be called by a member of the study staff every 3 months to ask how you are doing and if you have started any new anti-cancer treatments. This information may be collected from your medical record instead. If called, this phone call should take about 5-10 minutes. These calls will stop if the disease gets worse or you start a new anti-cancer therapy.

Other Testing

The study staff may ask you to take part in other MD Anderson clinical research studies (PA11-1045) for additional testing. The study doctor will discuss this with you and, if you decide to take part, you will sign a separate consent document.

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 drugs/procedures.

Doxorubicin, gemcitabine, and ixazomib 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 and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Doxorubicin Side Effects

Common (occurring in more than 20% of patients)

• low white blood cell counts

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

• swelling • slow/extra/fast/irregular heartbeat • abnormal EKG • heart failure • enlarged heart • heart inflammation • inflammation of the tissue around the heart (possible chest pain) • severe heart problems • fatigue/lack of energy	• hair loss (partial or total) • discoloration of sweat, urine, saliva, and/or tears • stopped menstrual cycle • dehydration • high blood levels of uric acid (possible painful joints and/or kidney failure)	• nausea/vomiting • death of colon tissue • stomach and/or small intestine ulcer • decreased urine output • inability to have children • low blood counts (red/platelets) • enlarged liver • weakness

• skin rash • hives • itching • skin sensitivity to sunlight or lamps	• abdominal pain • loss of appetite • diarrhea • mouth blisters/sores (possible difficulty swallowing)	• difficulty breathing • build-up of fluid around the lung/fluid in the lungs (possible difficulty breathing) • injection site pain and/or inflammation • severe sunburn-like rash at site of previous radiation (called radiation recall)

Serious side effects occurring in fewer than 1% of patients

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

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

<u>Gemcitabine Side Effects</u>

Common (occurring in more than 20% of patients)

• fever • skin rash • nausea/vomiting • low blood cell counts (red, white, platelets)	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes)	• abnormal kidney test (possible kidney damage) • blood in the urine • difficulty breathing

Occasional (occurring in 3-20% of patients)

• swelling (such as arm/leg) • abnormal sensation (such as pins and needles)	• fatigue • hair loss (partial or total) • mouth blisters/sores (possible difficulty swallowing)	• diarrhea • flu-like symptoms • injection site swelling, pain, and/or heat • infection

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

• irregular heartbeat • heart attack • heart failure • multiple blood clots (possible organ dysfunction and/or failure) • blood vessel inflammation (possible bleeding and/or bruising) • high blood pressure • low blood pressure (possible dizziness/fainting) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss) • nerve damage (loss of motor or sensory function)	• stroke • large skin blisters • decay of body tissue • severe sunburn-like rash at site of previous radiation (called radiation recall) • low blood levels of calcium (possible weakness and/or cramping) • high blood sugar (possible diabetes) • destruction of red blood cells (possible kidney damage and/or failure) • leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing)	• liver damage and/or failure (possibly due to blood clots and/or scarring) • kidney failure • lung inflammation/ damage (possible difficulty breathing) • fluid in the lung (possible difficulty breathing) • difficulty breathing due to narrowing of the airways • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Gemcitabine may cause brain injury that may result in headache, confusion, seizures, and/or vision loss. It is not known how often this may occur.

Ixazomib Side Effects

Common (occurring in more than 20% of patients)

• swelling (arms/legs) • nerve damage (possible numbness, pain, and/or loss of motor function)	• constipation • nausea • vomiting • diarrhea	• low blood cell counts (platelets/white) • pain • eye disease

Occasional (occurring in 3-20% of patients)

• skin rash • abnormal liver function (possible liver damage)	• blurry vision • painful red eyes	• dry eyes • infection

Rare but serious (occurring in fewer than 3% of patients) It is not known if ixazomib causes the side effects below, but it may have contributed to them:

• spinal cord inflammation (possible pain, weakness, and/or loss of feeling or movement) • nerve damage (affecting movement) • posterior reversible encephalopathy syndrome (brain injury with possible headache, confusion, seizures, and/or vision loss)	• very severe blistering skin disease (with ulcers of the skin and digestive tract) • skin condition with fever and skin lesions • multiple blood clots (possible organ dysfunction and/or failure)	• inflammation of the bile tract (possible blockage) • liver damage • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage)

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.

An **ECHO** uses ultrasound or high frequency sound waves to look at your heart. A probe called a transducer is placed on your chest to help measure sound waves through the skin and create a picture of the heart. A cold gel will be placed on your chest in order to perform this test. There are no side effects from the scan, although the lubricating gel may feel cold and you may experience some minor discomfort when the electrodes are removed from your skin at the end of the test.

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.

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.

X-rays send a small amount of radiation though the body. All radiation adds up over a lifetime and may increase the risk of a new cancer forming.

A standard **bone scan** exposes you only to the radiation that comes from injecting the standard radioactive imaging solution for bone imaging.

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. You must use birth control during the study and for at least 5 months after your last dose of study drug(s), if you are sexually active.

Birth Control Specifications: You should tell your study doctor right away if there is a change in your method of birth control or if you start any prescription drug or other drug (including over-the-counter drugs and herbal supplements) not prescribed by the study doctor.

Acceptable methods of birth control for males include condom with spermicide. Even if you are surgically sterilized, you must use a condom.

Acceptable methods of birth control for females include the following:

- Hormonal methods of birth control, including birth control pills (combination of estrogen and progesterone), vaginal ring, injections, and implants. If you choose to use a hormonal method, you must also use a condom or occlusive cap.
- Intrauterine device (IUD) or intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion ("tubes tied")
- condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/vaginal suppository

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 doctor will advise you of the possible risks to your unborn child and discuss options for managing the pregnancy with you. 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, miss your period or it is late, or if you have a change in your usual menstrual cycle (such as heavier bleeding during your period or bleeding between periods), you must tell your doctor right away. Study drug will be stopped immediately and the sponsor will ask for information about the pregnancy until conclusion. You should not breastfeed while receiving study drug and up to 18 weeks from your last study drug dose.

Getting pregnant may result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure # 1: If you agree, blood and tumor tissue that is left over from your diagnosis and/or other tests performed outside of this study will be collected and stored in a research tissue bank at MD Anderson for use in future research related to cancer.

Before your samples can be used for research, the people doing the research must get specific approval from the Institutional Review Board (IRB) of MD Anderson. The IRB is a committee made up of doctors, researchers, and members of the community. The IRB is responsible for protecting the participants involved in research studies and making sure all research is done in a safe and ethical manner. All research done at MD Anderson, including research involving your samples from this bank, must first be approved by the IRB. Samples will be stored until they are gone or you withdraw consent to use the samples.

Your samples will be given a code number. No identifying information will be directly linked to your samples. Only the researcher in charge of the bank 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. Other researchers using your samples will not be able to link this data to you.

Optional Procedure # 2: If you agree, you will have up to 3 tumor biopsies for biomarker testing to help researchers understand how the disease is responding to the study drugs. The first biopsy will be done before you start treatment, the second will be done about 12 weeks after you start treatment (around Cycle 7), and the third will happen if the disease gets worse (but before you start a new cancer treatment). The type of biopsy you have will depend on the location of the disease and your doctor's review. If it is not safe, even if you agree, the biopsy will not be collected.

There are no benefits to you for taking part in the optional procedures. 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:
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.

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.

Some of the areas might include lung, mediastinum, liver, kidney, pancreas, or spleen: Rarely (in fewer than 3% of patients), major bleeding may occur. Occasionally (in 8-12% of patients), you may have a collapsed lung and need to have a chest tube surgically placed. In 15-20% of patients, a collapsed lung that does not require placement of a chest tube may occur.

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 allow leftover blood/tissue from tests outside this study to be stored in a research tissue bank at MD Anderson for use in future research related to cancer?

YES NO

Optional Procedure #2: Do you agree to have up to 3 tumor tissue biopsies for biomarker testing related to response or resistance to cancer treatment?

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 Takeda 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. Pavlos Msaouel, 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.

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

Results of your routine labs will be placed in your medical record.

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: Takeda.

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.

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. 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).

As part of the study, genetic testing may be performed. A federal law, called the Genetic Information Nondiscrimination Act (GINA), provides some protection for 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 collected in 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 collected in this research when making decisions about your employment

However, this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Outside Care

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

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

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Takeda, who is a sponsor or supporter 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.

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
(Adult Participants Only)

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

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2018-0065.

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

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

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

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

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

PARENT/GUARDIAN PERMISSION

I have read and understand the description of this research. I have had a chance to discuss the study and ask questions. My questions have been answered. I give permission for my child or ward to take part in this study.

_____ _____
SIGNATURE OF PARENT/GUARDIAN DATE

_____
PRINTED NAME OF PARENT/GUARDIAN

_____ _____
SIGNATURE OF PARENT/GUARDIAN DATE
Signature of Other Parent (Optional, unless required by the IRB.)

_____
PRINTED NAME OF PARENT/GUARDIAN

____The IRB has determined that the signature of both parents is required.

If not obtaining both parental signatures, please indicate reason below:

____Other parent is deceased, unknown, incompetent, or not reasonably available.

____Parent/Guardian signing above has sole legal responsibility for the care and custody of the child.

____The IRB has determined that the signature of both parents is NOT required.

WITNESS TO PARENTAL/GUARDIAN PERMISSION

I was present during the explanation of the research to be performed under Protocol 2018-0065. The child participant was also present. In my opinion, the parent(s)/guardian provided permission for the child to participate in the research.

_____ _____
SIGNATURE OF WITNESS TO THE PARENTAL/GUARDIAN PERMISSION (OTHER THAN PARENT/GUARDIAN OR MEMBER OF THE STUDY TEAM) DATE

_____
PRINTED NAME OF WITNESS TO THE PARENTAL/GUARDIAN PERMISSION

ASSENT OF MINOR

(Entire section must be completed if the participant's intellectual age is at least 7 and less than 18 years. Participants with an intellectual age of 7 - 12 are not required to sign.)

If written assent is not obtained on an age-appropriate participant, check reason why not:

____ 1.) The participant's intellectual age is less than seven.

____ 2.) The participant dissented, but the participant's parent(s)/guardian felt that the intervention(s) or procedure(s) involved in the research hold out the possibility of a direct benefit that is important to the health and/or well being of the participant and is available only in the context of this research study.

____ 3.) Other: _____

I have been told what I will be asked to do in this study.

I have been told that I do not have to be in this study. If I decide not to be in this study, no one will be mad at me. I may quit at any time, but if I do, I may need to take a different treatment.

I have had a chance to talk about the study and ask the study doctor questions. All of my questions have been answered. I agree to be in this study and do what I am asked to do so long as I want to stay in this study. I agree that the study doctor can put me on this study. By signing this paper, I am not giving up any of my legal rights. I have been given a copy of this document.

_____ _____

SIGNATURE OF MINOR (Age 13-17) DATE

_____

PRINTED NAME OF MINOR

WITNESS TO ASSENT

I was present during the explanation of the research to be performed under Protocol 2018-0065. The child participant was also present. In my opinion, the child assented to participate in the research. (Note: If obtaining assent, a witness signature is required.)

_____ _____

SIGNATURE OF WITNESS TO THE ASSENT (OTHER THAN PARENT/GUARDIAN OR MEMBER OF THE STUDY TEAM) DATE

_____

PRINTED NAME OF WITNESS TO THE ASSENT

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