Informed Consent/Authorization for Participation in Research

TITLE: Phase 2 Study of Combination Tivozanib and Nivolumab in Advanced Non-Clear Cell Renal Cell Carcinoma (FORTUNE)

PROTOCOL NO.: 2022-0485

SUPPORTER: Aveo Oncology

INVESTIGATOR: Eric Jonasch, MD

STUDY-RELATED PHONE NUMBER(S): 713-745-5659
713-792-2121 (24 hours)

_____ _____
Participant's Name Medical Record Number

Key Information

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?

You are invited to take part in a research study because you have an advanced form of non-clear cell renal cell carcinoma (nccRCC).

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The goal of this clinical research study is to learn if giving tivozanib in combination with nivolumab can help to control advanced nccRCC.

This is an investigational study. Tivozanib is FDA approved and commercially available for the treatment of certain types of RCC, but not for the treatment of advanced nccRCC. Nivolumab is FDA approved and commercially available for the treatment of advanced nccRCC. It is considered investigational to give tivozanib and nivolumab together.

The study doctor can explain how the study drugs are designed to work.

How long will the research last and what will I need to do?

You may receive tivozanib and nivolumab for as long as the study doctor thinks it is in your best interest.

You will have study visits in which various tests and procedures will be performed to check your health and for research purposes.

More detailed information about the study procedures can be found under ***"What happens if I agree to be in this research?"***

Is there any way being in this study could be bad for me?

If you take part in this study, you may experience high blood pressure, fatigue, fever, pain, headache, itching, skin rash, nausea, diarrhea, loss of appetite, constipation, low red blood cell count, and/or abnormal liver and/or kidney function tests. You should be aware that on the days of certain research blood tests, imaging studies, and the biopsy described below, you will need to be in Houston for 1-3 days at a time.

More detailed information about the risks of this study can be found under ***"Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

It cannot be promised that there will be any benefits to you or others from your taking part in this research. However, 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.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate, not participate, or discontinue participation at any time without penalty or loss of your regular benefits.

Instead of being in this research study, your choices may include standard of care treatment. These alternative treatments have risks and benefits that may be the same or different than those in this research study. The study doctor can discuss these alternative treatments, including their risks and benefits with you.

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.

If you decide that you don't want any more active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually this care can be provided at home.

If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

Detailed Information

The following is more detailed information about this study in addition to the information listed above.

Who can I talk to if I have questions or concerns?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the study doctor, Dr. Eric Jonasch, at 713-792-2830 or 713-792-7090.

This research has been reviewed and approved by an Institutional Review Board (IRB – an ethics committee that reviews research studies). You may talk to them at (713) 792-6477 or IRB_Help@mdanderson.org if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be in this study?

About 48 people will be enrolled in the entire study at all locations.

What happens if I agree to be in this research?

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

- You will have a physical exam.
- Blood (about 7-8 teaspoons) will be drawn for routine tests, standard-of-care tumor genetic testing, circulating tumor DNA (ctDNA) testing, and for use in future research testing. ctDNA is genetic material from tumor cells that can be found and measured in the blood.
- You will have an EKG to check your heart function.
- You will have imaging scans, including CT scans and/or MRIs, to check the status of the disease.
- Tumor tissue left over from a previous procedure, if available, will be collected for standard-of-care tumor genetic testing, biomarker testing (including genetic markers), and to be compared to later biopsies to learn how the study drugs have affected the disease. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drugs. If tumor tissue is not available, you will have a tissue biopsy. The study doctor will tell you what kind of biopsy you will have.

- If you can become pregnant, 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.

Study Drug Administration
Each study cycle is 28 days.

If you are found to be eligible to take part in this study, you will receive:
- Nivolumab by vein over about 60 minutes every 4 weeks (Day 1 of each cycle).
- Tivozanib tablets by mouth 1 time every day for 21 days (Days 1-21 of each cycle), and then no tablets on Days 22-28 of each cycle.

Nivolumab may be given through a port instead of by vein. If you prefer this method and the study doctor agrees it is appropriate, you will have a port placed. Before the port is placed, you will be given a separate consent form that will explain this procedure and its risks. This will be discussed with you in detail, including where the port will be placed.

Tivozanib should be swallowed whole with a full glass of water (about 8 ounces). If you forget to take a dose or if you vomit a dose of tivozanib, do not take another dose. Wait and take the next dose as scheduled and contact the study doctor to tell them you missed a dose. You will also be given a dosing diary to write down when you take each dose of tivozanib and if you forget or vomit a dose. Bring this diary with you to 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

On **Day 1 of all cycles:**
- You will have a physical exam.
- Blood (about 2 ½ teaspoons) and urine will be collected for routine testing. At Cycle 2, additional blood (about 2 teaspoons) will be drawn and stored for future research.

At **Week 1 of Cycle 2**, blood (about 7-8 teaspoons) will be drawn for standard-of-care tumor genetic testing.

If it is safe to do so, at **Week 1 of Cycle 4** you will have a tissue biopsy. The tissue will be compared to the tissue collected at screening to learn how the study drugs have affected the disease.

Every 2 cycles for 6 cycles, then every 3 cycles after that, you will have CT scans or MRIs to check the status of the disease.

End-of-Treatment Visit

After you stop both nivolumab and tivozanib:

- You will have a physical exam.
- Blood (about 3 teaspoons) and urine will be collected for routine testing.
- Blood (about 7-8 teaspoons) will be drawn for standard-of-care tumor genetic testing and future research testing.

Safety and Long-Term Follow-Up

About 7 days after the End-of-Treatment visit and then every 180 days (+/- 30 days) after that, you will be asked how you are doing and if you have started any new anticancer therapies or had any side effects. This may be asked during a routine clinic visit or you may be called. The calls should last about 10-20 minutes.

If you stopped study therapy and the disease has not gotten worse, you will continue having CT scans or MRIs every 12 weeks as part of your standard of care. This will be both during follow-up and long-term follow-up.

If the safety or effectiveness of the drug needs to be studied further, the study doctor may try to collect study-related information about your health from you or from other sources, including your regular care doctor and public sources such as national patient registries (such as cancer registries). This may also include contacting you again by phone or letter.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for the following:

- Tell the study doctor about all medications you are taking, including prescriptions, herbal supplements, and over-the-counter medications.
- Tell the study doctor about any medical treatments that you plan to receive during the study (such as surgery or radiation).
- Tell the study doctor if you want to start taking any new medications or supplements (prescription or over-the-counter).
- Foods and medications known to significantly change levels of an enzyme called CYP3A4 (such as grapefruit, ketoconazole) should not be eaten/taken if possible. Your study doctor will explain what these medications are. If you need treatment with any medications that are not allowed during your participation in this study, you must tell the study doctor or the study staff. If this happens, you may need to stop taking the study drug(s). This is for your safety, since some medications may not work well with the study treatment, and side effects may occur.
- Bring back empty study medication packages and all unused study medication to each study visit.
- Tell your study doctor or staff if you change your address, phone number, or other contact information.

What happens if I say yes, but I change my mind later?

You can leave the research at any time; it will not be held against you.

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. It may be dangerous to suddenly stop taking the study drug(s). If you withdraw from this study, you can still choose to be treated at MD Anderson.

If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Is there any way being in this study could be bad for me? (Detailed 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.

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

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

<u>Nivolumab Side Effects</u>

Common (occurring in more than 10%)

• fatigue/lack of energy

• diarrhea • itching • skin rash

Occasional (occurring in 3-10%)

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

Rare (occurring in fewer than 3% of patients)

• fast heartbeat • abnormal EKG • heart inflammation/ inflammation of the tissue around the heart (possible chest pain) • high blood pressure • low blood pressure (possible dizziness and/or fainting) • swelling of the brain (possible headache and/or mental status changes) • inflammation of the brain and spinal cord (possible altered consciousness) • inflammation of the membrane around the spinal cord and brain	• decreased production of adrenal hormones (possible weakness and/or low blood pressure) • inflammation of the thyroid gland (possible tenderness in the neck) • pituitary gland failure (possible hormone imbalance) • blood vessel inflammation • low blood levels of sodium (possible headache, confusion, seizures, and/or coma) • abnormal blood test (possible pancreas damage) • high blood sugar (possible diabetes)	• nerve damage (affecting the head and neck) • muscle inflammation • joint pain/stiffness • dry eye • blurry/double vision • lung infiltrates (possible infection or inflammation) • difficulty breathing which can lead to respiratory failure • cough • infusion reaction (possible fever, rash, pain, and/or swelling) • immune response causing the body to attack itself (possibly causing muscle weakness)

(possible headache and/or coma) • swelling (face/arms/legs) • chills • difficulty sleeping • dizziness • dry/red skin • hives • skin blisters • very severe blistering skin disease (loss of large portion of skin and/or ulcers of the skin and digestive tract) • red, dry, scaly patches of thickened skin (psoriasis) • allergic skin reaction • hair loss (partial or total)	• abnormal blood acid/base balance due to uncontrolled diabetes (possible organ damage) • mouth blisters/sores (possible difficulty swallowing) • constipation • dehydration • dry mouth • inflammation of the intestines • hole in the intestines or stomach (possibly leaking contents into the abdomen) • liver inflammation • liver failure/damage • low blood cell count (platelets, white) • viral/bacterial infection that affects nose, throat and airways (upper respiratory tract infection) • destruction of red blood cells due to the body attacking itself (called autoimmune hemolytic anemia) • abnormal kidney test (possible kidney damage) • kidney failure • breakdown of muscle tissue (possible kidney failure) • damage to the nervous system (causing numbness and/or paralysis) (Guillain-Barre syndrome) • nerve damage (possible numbness, pain, and/or loss of motor function	• neuromuscular disease (possible weakness of eye, face, breathing and swallowing muscles) (myasthenic syndrome, myasthenia gravis) • immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures) • multi-organ disease causing lesions, most often in the lungs (sarcoidosis) • allergic reaction, possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure) • abnormally excessive sweating involving the arms, legs, hands and feet, underarms, and face, usually unrelated to body temperature or exercise • flu-like symptoms (which may include fever, chills, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches, feeling tired) • patches of skin color loss • inflammation of multiple areas of the body (see below) • Hemophagocytic lymphohistiocytosis (HLH) syndrome (see below)

	and/or “pins and needles” sensation)	

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

At this time, it is not known whether taking a COVID-19 vaccine may affect the way that the study drug works in your body or if the study drug may affect the way the vaccine works in your body. No information is known about the interaction between a COVID-19 vaccine and nivolumab.

The study drug works by boosting the immune system. This may cause unknown side effects resulting from your immune system attacking your organs. This may cause inflammation and inflammation-related side effects in any organ or tissue.

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

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

Frequency Unknown

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

<u>Tivozanib Side Effects</u>

Common (occurring in more than 10% of patients)

• high blood pressure • fatigue/weakness • hand-foot (syndrome (palms of hand/soles of	• nausea/vomiting • mouth blisters/sores (possible difficulty swallowing) • diarrhea	• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood

feet having pain, swelling, and blistering) • skin rash	• loss of appetite • low blood cell count (red, white, and/or platelet) • underactive thyroid gland (possible weight gain, heart failure, and/or constipation)	pressure, organ failure, heart problems, changes in mental status, and/or seizure) • high blood sugar (possible diabetes) • hoarseness/voice disorder • abnormal liver test (possible liver damage) • back pain • abnormal kidney test (possible kidney damage) • cough • difficulty breathing

Rare but serious (occurring in fewer than 4% of patients)

• blood clots in a vein, usually in the leg or that travels from a vein to the lung (possible pain, swelling, and/or redness) • blood clots in an artery (possible organ damage such as stroke and/or heart attack)	• heart failure • heart attack	• overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating)

Based on similar drugs, tivozanib may also cause a hole in the intestines (possibly leaking contents into the abdomen) or abnormal liver tests (possible liver 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.

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. Rarely (in fewer than 3% of patients), major bleeding may occur.

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. When a CT scan of the abdominal area is taken, material may be inserted into the rectum to better define the bowel. You will usually drink liquid to help define various abdominal organs. This may cause nausea and/or vomiting. 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.

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**.

Pregnancy Related Risks

Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. If you are sexually active, you must use acceptable birth control during the study and for up to 120 days after the last study drug dose.

Acceptable methods of birth control include the following:

- Hormonal methods of birth control, including birth control pills, injections, patches, vaginal rings, or implants
- Intrauterine device (IUD) or intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion (having your “tubes tied”) or hysterectomy
- Vasectomy or vasectomized partner
- Condoms plus spermicide.

You should contact 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.

Males: You must tell your female partners who can become pregnant about the birth control requirements. Tell the doctor right away if your partner becomes pregnant or suspects 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: You should not breastfeed while taking the study drug or for up to 5 months after the last dose of study drug. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant may result in your removal from this study.

Will it cost anything to be in this study? Will I be paid to be in this study?

Tivozanib will be provided at no cost to you during the study. You and/or your insurance provider will be responsible for the costs of nivolumab.

You and/or your insurance provider will not have to pay for certain research exams and procedures done that are covered by the study. These include: blood tests to check your thyroid function, urine pregnancy tests (if applicable), tumor biopsies, and the collection of leftover tumor tissue.

You and/or your insurance provider will be responsible for the costs of routine clinical services (such as diagnostic/therapeutic procedures, drugs, devices, laboratory assays, and other services that would ordinarily be ordered for medical care, regardless of whether or not you are participating in a study). There may be extra costs that are not covered by your medical plan that you will have to pay yourself. These include: MRI and CT scans.

Taking part in this study may result in added costs to you (such as transportation, parking, meals, or unpaid leave from work). You may have to pay for medication

prescribed to treat or prevent side effects, and you may have to visit the clinic/hospital more often than if you were not participating in this study.

If you have insurance, talk to your insurance provider and make sure that you understand what your insurance pays for and what it does not pay for if you take part in this study. Also, find out if you need approval from your plan before you can take part in the study.

You may ask that a financial counselor be made available to you to talk about the costs of this study.

You will not receive any compensation for taking part in this study.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who need to review this information. Complete secrecy cannot be promised. The IRB and other representatives of the IRB may inspect and copy your information.

Any personal information that could identify you will be removed or changed before data are shared with other researchers or results are made public.

The sponsor, monitors, auditors, the IRB, and the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. The results of this research may be published. However, your name and other identifying information will be kept confidential.

Federal law provides additional protections of your medical records and related health information. These are described below.

Will my data or samples be used for 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 and Aveo Oncology, or shared with other researchers and/or institutions for use in future research.

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

If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or shared with another researcher for future research studies without your additional informed consent.

Can I be removed from the research study without my permission?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include the disease getting worse, intolerable side effects, or inability to follow the study directions.

What happens if I get hurt from being in this study?

If you get sick or hurt and it is related to your participation in this study, you will be given care at MD Anderson (if you are at the clinic when you are sick or hurt). If you get hurt or sick and you are not at the clinic (for example, you are at home or at another doctor's office):

- call your personal doctor right away (or in an emergency, call 911).
- tell your personal doctor or ER staff that you are in this study (try to give them a copy of this consent form or show them your participant card).
- call the study doctor (Dr. Eric Jonasch, at 713-792-2830 or 713-792-7090) or 713-792-2121 (24-hours) with any questions you may have.

You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. Costs of treatment received because you were hurt or sick will be billed to you or your insurance company. No other form of payment is available.

You may also contact the MD Anderson 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.

What else do I need to know?

This research is being supported by Aveo Oncology.

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

Your information and samples (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

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.

This research study involves genetic testing. The Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Please contact the study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

Genetic testing 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.

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
   - Aveo Oncology, who is a supporter of this study
   - Any future sponsors/supporters of the study
   - Labs performing research testing and designees of the sponsor
   - 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.

   An outside laboratory chosen by the sponsor may receive blood samples for biomarker testing.

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, and it may be re-disclosed.

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

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 this protocol.

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

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

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

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT