THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

A Phase 2 Clinical Trial of Axitinib and Avelumab in Patients with Recurrent/Metastatic Adenoid Cystic Carcinoma (ACC)
2019-0107

Study Chair: Renata Ferrarotto

_____ _____
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.

STUDY SUMMARY

The goal of this clinical research is to learn if treatment with axitinib and avelumab will help control adenoid cystic carcinoma (ACC). The safety of the treatment combination will also be studied.

This is an investigational study. Axitinib and avelumab are FDA approved for the treatment of kidney cancer, but their use in ACC is considered investigational. At this time, the combination is being used in patients with ACC for research only. The study doctor can explain how the study drugs are designed to work.

The study drug combination may help 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 serious 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.

Axitinib and avelumab will be provided at no cost 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 other investigational therapy, if available. You may choose to receive comfort care to relieve your symptoms. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms.

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 performed to help the doctor decide if you are eligible:

- You will have physical exam.
- Blood (about 4 tablespoons) will be drawn for routine tests and biomarker testing. Biomarkers are found in the blood and may be related to your reaction to the study drugs.
- Urine will be collected for routine tests.
- If you can become pregnant, blood (about ½ teaspoons) or urine will be collected for a pregnancy test. To take part in this study, you must not be pregnant.
- You will have MRI scans and either CT or PET scans to check the status of the disease.
- You will have an echocardiogram (ECHO) and electrocardiogram (EKG) to check your heart function.
- Leftover tumor tissue from a previous procedure will be collected for biomarker testing. If no leftover tissue is not available, you will have a tumor biopsy. The type of biopsy you will have will depend on where the tumor is. The study doctor will tell you what type of biopsy you will have and its risks.

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.

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

Study Drug Administration
If you are found to be eligible, you will begin treatment on Day 1 of Cycle 1. Each study cycle is 28 days.

Axitinib

You will take **axitinib** tablets by mouth 2 times a day (morning and evening), at about the same time every day. Each dose should be taken about 12 hours apart, with a full glass of water. Axitinib can be taken with or without food. If you vomit or miss a dose, an additional dose should not be taken. The next dose should be taken at the next scheduled time.

You will be given a pill diary to complete. In the diary, you should write down when you take each axitinib dose, and when/if you missed or vomited any doses. If needed, the study staff can show you how to fill out the diary. You should bring this diary with you each study visit.

Avelumab
You will receive avelumab by vein over 1 hour every 2 weeks, on Days 1 and 15 of each study cycle. You will be watched for side effects in the clinic for about 30 minutes after each dose.

Other Medications
You will also be given standard drugs to help decrease the risk of an allergic reaction, pain, and/or fever. You may ask the study staff for information about how the drugs are given and their risks.

You may continue to take the study drugs if your disease gets worse and the study doctor thinks this is in your best interest. You will no longer be able to take the study drugs if intolerable side effects occur, if the doctor does not think it is in your best interest to continue, or if you are unable to follow study directions.

Study Visits
On **Day 1 of each cycle** (+/- 7days):

- You will have a physical exam
- Blood (about 2 tablespoons) will be drawn for routine tests before you receive avelumab.
- If you can become pregnant, blood (about ½ teaspoon) or urine will be collected for a pregnancy test.
- If your doctor thinks it is needed, you will have an ECHO to check your heart function.

On **Day 15 of each cycle**, blood (about 2 tablespoons) will be drawn for routine tests before you receive avelumab. During Cycle 1 only, blood (about 2 tablespoons) will also be drawn for biomarker testing.

Every 8 weeks (+/- 7 days), you will have imaging scans (CT, PET, and/or MRI) to check the status of the disease.

Before **Day 1 of Cycle 3**, blood (2 tablespoons) will be drawn for biomarker testing.

If your doctor thinks it is needed, you will have an ECHO to check your heart function.

Whenever the doctor thinks it is needed, you may also have urine collected for routine tests.

Follow-up
About 30 days (+/- 7 days) after your last dose of study drug, you will have a physical exam, and blood (about 2 tablespoons) will be drawn for routine tests.

If you continue to have side effects after your last dose of study treatment, you will receive follow-up phone calls from the study staff for up to 90 days after your last dose of avelumab. Each call lasts about 10 minutes.

Long Term Follow-up
Every 6 months, you will be asked to come back to the clinic for follow-up visits. At these visits, you will have imaging scans to check the status of the disease. You will also be asked about your medical history and any new therapies you may be receiving.

If you cannot return to the clinic for these visits, the study staff will call you to ask about your health status. Each call should last about 10 minutes.

Additional Instructions
You should not consume grapefruit or products containing grapefruit juice while taking axitinib.

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.

Axitinib and avelumab 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.

Axitinib Side Effects

Common (occurring in more than 20% of patients)

• high blood pressure • fatigue • hand-foot syndrome (palms of hands/soles of feet having pain, swelling, and blistering) • 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)	• high blood sugar (possible diabetes) • nausea/vomiting • diarrhea • weight loss • loss of appetite • abnormal digestive blood test (possible pancreas damage and/or inflammation of the pancreas) • low blood count (red, white)	• weakness • abnormal liver tests (possible liver damage) • abnormal kidney test (possible kidney damage) • voice changes

Occasional (occurring in 3-20% of patients)

• headache • dizziness • blood clots in a vein (possible pain, swelling, and/or redness) • underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • low blood sugar • skin rash	• dry skin and/or itching • hair loss (partial or total) • dehydration • mouth blisters/sores (possible difficulty swallowing) • abnormal taste • abdominal pain • upset stomach • constipation • hemorrhoids	• low platelet count • increased levels of hemoglobin in the red blood cells • blood in the urine • pain • ringing in the ears • nosebleed • cough • difficulty breathing

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

• severe increase in blood pressure (possible stroke) • blood clots in an artery (possible organ damage such as stroke and/or heart attack) • heart failure • brain damage that may be reversible (possible headache, confusion, seizures, and/or vision loss)	• bleeding in the brain • temporary stroke symptoms • stroke • fever • overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating) • hole in the intestines (possibly leaking contents into the abdomen)	• bleeding or blood in the stool • abnormal connections or passageways between organs or vessels • high red blood cell count (possible headache, dizziness, and/or stoke) • blood clot inside the eye (possible blindness) • blockage in the lung (possible pain and/or shortness of breath) • coughing up blood

Avelumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue • skin rash • nausea • diarrhea	• low blood cell count (red, platelets, white) • abnormal liver test results (possible liver damage	• pain • infusion reaction (possible chills and/or hives)

Occasional (occurring between 3 -20% of patients)

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

Frequency unknown

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

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

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

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

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

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 blood cell count), which may create a need for blood transfusion.

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.

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 6 months after your last dose of the study drugs, if you are sexually active.

Birth Control Specifications: Female participants must use highly-effective birth control (for example, hormonal birth control (such as injections, pills, patches, and/or implants), intrauterine devices or systems (IUDs/IUSs), or having a vasectomized male partner, starting at least 2 weeks before the first dose of the study drugs. Male partners of female participants must use a male condom during sex.

Male participants who can father children must use condoms during sexual intercourse. In addition, female partners of male study participants must use hormonal birth control (such as birth control pills), IUDs/IUSs, or barrier methods of birth control (for example, condom plus spermicide, a diaphragm or cervical vault/cap) while the male participant is receiving treatment, until at least 30 days after the last dose of study treatment. You must not donate sperm nor father a child for 6 months after completion of the last dose of study medications.

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

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant may result in your removal from this study.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, blood (about 2 tablespoons) will be drawn on Day 7 of Cycle 1 for biomarker testing.

Optional Procedure #2: If you agree, blood (about 2 tablespoons) will be drawn for biomarker testing if the disease gets worse.

Optional Procedure 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.

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 blood (about 2 tablespoons) to be drawn on Day 7 of Cycle 1 for biomarker testing?

YES **NO**

Optional Procedure #2: Do you agree to allow blood to be drawn for biomarker testing if the disease gets worse?

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 or Pfizer 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. Renata Ferrarotto, at 713-792-6363) 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, Pfizer, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

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

9. This study is sponsored and/or supported by: Pfizer.

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.

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
   - Pfizer, 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.

   The research/biomarker samples will be stored in a research laboratory at MD Anderson.

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

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 2019-0107.

_____ _____
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

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