THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Phase II Study of AK104 (Cadonilimab) for Recurrent Small Cell Neuroendocrine Carcinomas of the Cervix
2021-0585

Study Chair: Amir Jazaeri, MD

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to learn if AK104 (cadonilimab) can help to control neuroendocrine cervical cancer that is recurrent (has come back after treatment) or metastatic (has spread).

This is an investigational study. Cadonilimab is not FDA approved or commercially available. It is currently being used for research purposes only. The study doctor can explain how cadonilimab is designed to work.

The study drug may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment.

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

You will receive the study drug for up to 2 years.

Cadonilimab will be provided at no cost to you while you are in the study. You and/or your insurance provider will be responsible for the costs of the drug administration.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other standard of care treatments. The doctor will discuss these treatments with you, including their risks and benefits. 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. Most of the tests will be performed within 28 days before your first dose of the study drug:

- You will have a physical exam.
- You will have an EKG to check your heart function.
- You will have an MRI or CT scan to check the status of the disease.
- Blood (about 6 tablespoons) will be drawn for routine tests. If you can become pregnant, this blood will also be used for a pregnancy test. To take part in this study, you cannot be pregnant.
- Urine will be collected for routine tests.
- The results of prior PD-L testing that was performed as part of your standard of care will be collected. This testing checks for proteins that may be targeted by the study drug.

The study doctor will discuss the screening tests 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 18 participants will be enrolled for this study. All will take part at MD Anderson.

Study Drug Administration

If you are found to be eligible to take part in this study, you will be given AK104 by vein over about 60 minutes every two weeks during each 28-day study cycle.

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

Your participation in 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 6 tablespoons) will be drawn for routine and biomarker testing, including genetic biomarkers. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug. If you can become pregnant, this blood will also be used for a pregnancy test.
- Urine will be collected for routine tests.

On **Day 15 of each cycle**:

- You will have a physical exam.
- Blood (about 4 tablespoons) will be drawn for routine and biomarker testing.

End-of-Treatment Visit

- You will have a physical exam.
- You will repeat the questionnaires that you did at screening.
- Blood (about 6 tablespoons) will be drawn for routine and biomarker testing, including biomarker testing. If you can become pregnant, this blood will also be used for a pregnancy test.
- Urine will be collected for routine tests.

Follow-Up Visit

You will have follow-up visits 30 and 90 days after your end-of-treatment visit:

- You will have a physical exam.
- Blood (about 6 tablespoons) will be drawn for routine and biomarker testing, including biomarker testing.
- Urine will be collected for routine tests.

Other Instructions

You will be instructed not to take any medications, including over-the-counter products, without first consulting with the study doctor. You should not receive any of the following during the study:

- Live or attenuated vaccines.
- Probiotics, dietary supplements, and/or medications not approved by the study doctor.

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.

AK104 Side Effects

This is an early study of AK104, so the side effects are not well known. Based on early results of studies in humans, AK104 may cause the following side effects.

• heart inflammation • fast heartbeat • low blood pressure (possible dizziness/fainting) • high blood pressure • flushing • headache • brain inflammation (possible paralysis and/or coma) • fever • fatigue • weakness • chills	• dizziness • lightheadedness • skin reactions (such as rash, itching, and/or sweating) • hormone problems • underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • inflammation of the intestines • nausea • vomiting • diarrhea	• abnormal liver test (possible liver damage) • liver damage • muscle pain • kidney inflammation • difficulty breathing (possibly due to narrowing of the airways) • lung inflammation (possible difficulty breathing) • infusion reaction (possible chills and/or hives)

AK104 may cause low blood cell counts (red blood cells, platelets, 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.

AK104 works by boosting the immune system. This may result in side effects that have not been seen yet, such as inflammation and inflammation-related side effects in any organ or tissue.

Based on similar drugs, AK104 may also cause:

• patches of skin color loss • abdominal pain	• change in hormonal glands function (which may change the way hormones	• abnormal digestive blood test (possible inflammation of the pancreas)

	are released in your body)	

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

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

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish. The MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

CT scans send x-rays through the body at many different angles. You will be exposed to a small dose of radiation. All radiation adds up over a lifetime and may increase the risk of new cancer forming. Some people may feel “closed in” while lying in the scanner. However, the scanner is open at both ends, and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or radiology technicians will give comfort, or the scanning will be stopped. Solution may also be given by vein to make the x-ray pictures more accurate. This may cause an uncomfortable feeling of warmth, nausea, and/or severe allergic reactions. The solution injection may also cause pain, bleeding, bruising, hives, and/or itching.

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

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets during the study and will continue to be stored securely after the

study. Only authorized people who are working on this study will have access to study data.

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 or breastfeed a baby while on this study. If you are sexually active, you must use at least 1 of the highly effective forms of birth control listed below from the time of screening throughout the total duration of the drug treatment and the drug washout period (90 days after the last dose of study drug).

Birth Control Specifications: Acceptable forms of birth control include:

- surgical sterilization (having your "tubes tied"),
- having a vasectomized partner,
- barrier methods (such as cervical cap, sponge, diaphragm, or condom along with spermicide),
- intrauterine device (IUD), OR
- hormonal birth control that contains estrogen and/or progestin (such as birth control pills, patch, shot, or implant).

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 will result in your removal from this study.

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 Akeso Biopharma 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. Amir Jazaeri, at 713-745-1613) 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. It may be dangerous to suddenly stop. The study staff may ask if they can continue collecting the results of routine care from your medical record. If you withdraw from this study, you can still choose to be treated at MD Anderson. If you withdraw from the study before surgery, you will receive standard of care chemotherapy.

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

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data

MD Anderson IRB Approved 09/03/2024

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and Akeso Biopharma, and/or shared with other researchers and/or institutions for use in future research.

Samples
Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research. Leftover samples stored by Akeso Biopharma may be used in future research.

If you do not want your samples or data to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

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

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).

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

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

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

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

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

   If information from this study is published or presented at scientific meetings, participant data will only be shared in group form. None of your PHI will be included, and you will not be identifiable.

   Study data will be stored in REDCap, a protected institutional online database, during the study and for 5 years after the results have been published. Only the research team will have access to the information stored in REDCap.

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. If you withdraw from the study, the study staff may ask if they can continue collecting the results of routine care from your medical record.

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

CONSENT/AUTHORIZATION

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

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under 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

MD Anderson IRB Approved 09/03/2024