THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Cryoablation Challenge EvaluateD in Adaptive-Immune Resistance (CEDAR)
2019-0502

Study Chair: Alda Tam

_____ _____
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 study the effectiveness of adding cryoablation treatment in patients who are receiving standard of care immunotherapy to treat cancer that is metastatic (has spread to other parts of the body). Cryoablation uses a probe that freezes the tissue around the tumor to try to kill the cancer cells. Researchers will collect biopsies to compare the ablated and non-ablated lesion during the cryoablation session. Only the non-ablated lesion will be biopsied after the cryoablation procedure. The safety of this procedure will also be studied.

This is an investigational study. The cryoablation procedure in this study is delivered using an FDA approved cryoablation needles and system. Using a cryoablation system to improve the effectiveness of immunotherapy treatment is investigational.

Using cryoablation to treat cancerous lesions may help to kill the cancer cells. Future patients may benefit from what is learned on this study. 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 are found eligible and take part in this study, you may experience side effects. Taking part in this study means you may not be able to receive other types of treatment or take part in other clinical trials.

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

Your active participation in this study will be over about 3 months after the ablation procedure. The study staff will also review any standard imaging scans collected up to 12 months after the cryoablation procedure.

The biopsies and cryoablation procedure (including the use of the cryoablation and biopsy needles) will be provided at no cost to you while you are on study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other procedures or treatment options. The study doctor will discuss these options 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

Up to 25 patients will be enrolled in the study. All will take part at MD Anderson.

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 within 14 days before the cryoablation procedure to help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 2 tablespoons) will be drawn for routine tests, including tests of your blood sugar, cholesterol (fats in your blood), blood-clotting function, immune system, and liver and kidney function. If you can become pregnant, this will include a pregnancy test. To take part in this study, you must not be pregnant.
- A stool sample will be collected for microbiome testing. Microbiome testing is a type of testing that checks for certain bacteria and microorganisms in the stool.
- You will have a CT scan or MRI of your chest, abdomen, and pelvis.

You are already enrolled or will be enrolling on a different research study at MD Anderson (Protocol 2014-0938: Longitudinal Biospecimen Acquisition for All Tumor Types And At-Risk Tissue). As part of this study, your leftover tumor tissue from an earlier surgery will be collected and used for research testing as described in 2014-0938 (this includes being sent to the researchers listed in that consent form). The

researcher will discuss this with you, including the type of testing that will be performed.
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 Treatment
If you are found to be eligible to take part in this study, on Day 1 of therapy, you will have the cryoablation procedure performed 1 week (+/- 3 business days) before your next scheduled standard of care immunotherapy treatment.

Your standard imaging scans (CT or MRI) that were collected earlier will be reviewed by the study team to check the position of the lesions.

You will have core needle biopsies performed on both the lesion that will receive the ablation procedure and a metastatic lesion that will not be ablated. To perform a core biopsy, local anesthesia is used and then a sample of tissue is removed using a hollow core needle that has a cutting edge. Researchers will use these tissue samples to compare the effects of ablation on lesions being treated with immunotherapy.

At the same visit when the biopsies are collected, at least 1 cryoprobe (a needle that is used to deliver the cryoablation treatment) will be inserted into the lesion. The cryoablation device uses pressurized gasses to cause the cryoprobe to become very cold. This will freeze the nearby tumor cells and the tissue surrounding the tumor, causing the cells to die. Anesthesia may be given for this procedure. Before starting the cryoablation treatment, the study doctor will discuss this with you.

Follow-up Testing

You will have **physical exams** on or around Days 7, 19, 31, 43, 55, 67, 79, and 91.

Blood (up to 2 tablespoons at each visit) will be drawn on or around Days 7, 19, 31, and 43 for routine tests (including some or all of the blood tests described above).

You will have **core needle tumor biopsies** collected on Day 31. These biopsies will be taken from the same non-ablated lesion as before.

You will have **imaging scans** (CT, MRI, or PET/CT scans) repeated on Day 55 (+/- 10 days). These scans will be repeated later as part of your routine care.

After your cryoablation procedure and at Month 6 after the procedure, stool samples will be collected for microbiome testing.

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 the procedure, 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 procedure.

Cryoablation may cause pain, bleeding, infection, damage to nearby tissues or structures, damage to skin/muscle/nerve (including change in feeling or movement). It may cause skin irritation or frostbite symptoms at the ablation site.

A condition called post-ablation syndrome may occur within the first 24-48 hours after the procedure and can last up to 3-10 days. Symptoms may include low grade fever, pain to the area ablated, nausea, vomiting, and fatigue. You may experience a low white blood cell count. 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. If your liver tissue is ablated, it may cause bleeding in a bile duct in your liver (which can result in blood loss requiring a transfusion or possible surgery). If your lung tissue is ablated, it may cause collapsed lung (possible difficulty breathing).

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. Depending on where the biopsy is performed, additional risks may occur:

- If you have biopsies of the lung, mediastinum, liver, kidney, pancreas, or spleen, rarely (in fewer than 3% of patients), major bleeding may occur.
- If you have a lung and mediastinum biopsy, 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.
- If you have a biopsy of the pancreas, it may cause inflammation of the pancreas, which may result in abdominal pain.

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.

Providing a **stool sample** may make you feel uncomfortable or embarrassed.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss**

of confidentiality. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study.

This study may involve unpredictable risks to the participants.

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 BTG (the company providing the cryoablation equipment) 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. Alda Tam, at 713-563-7920) 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, 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.

Future Research

Data

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

Samples

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

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

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.

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
Research samples collected from you as part of this study may 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.

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
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   BTG (the company providing the cryoablation equipment) will receive some deidentified study information (such as side effect data) but will not receive any participant's PHI.

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

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

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

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

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

CONSENT/AUTHORIZATION

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

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2019-0502.

_____ _____
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.

_____
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