Informed Consent Form	
Title	Phase I Clinical Trial of Adoptive Transfer of Autologous Folate Receptor–alpha Redirected T Cells for Recurrent High Grade Serous Ovarian, Fallopian Tube, or Primary Peritoneal Cancer
NCT	NCT03585764
Date	09-Feb-2023

University of Pennsylvania
Research Participant
Informed Consent Form and HIPAA Authorization

Protocol Title:	**Phase I Clinical Trial of Adoptive Transfer of Autologous Folate Receptor–alpha Redirected T Cells for Recurrent High Grade Serous Ovarian, Fallopian Tube, or Primary Peritoneal Cancer**
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Emergency Contact:	**Ask for Oncologist on Call** [redacted]

Research Study Summary for Potential Participants

You are invited to participate in a research study. Your participation is voluntary. You should only participate if you completely understand what the study requires and what the risks of participation are. You should ask questions of your study team before agreeing to participate. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at (215) 898-2614 for assistance.

This research study is being conducted to evaluate an experimental drug called MOv19-BBz CAR T cells in patients with ovarian, fallopian tube, or primary peritoneal cancer.

If you agree to join the study, you will be asked to come in to see your study doctor more often than you normally do. You will also be asked to undergo additional tests/procedures to monitor you for side effects, including frequent blood draws and radiology tests at certain intervals. Your participation in this study will last for up to 15 years. Researchers will continue to have access to your study data and any research samples collected as part of this study after your participation has ended.

You may not benefit directly from your participation in this study. The most common risks of participation in this study may include cytokine release syndrome (a severe flu-like syndrome which can be mild or severe and has resulted in death), low blood cell counts, and effects on your central nervous system. This research may also involve risks that are not known at this time. These risks will be explained in more detail later in the "What are the possible risks or discomforts?" section of this consent form.

Your alternative is not to participate in this study. You should discuss alternative treatment options with your study doctor.

Please note that there are other factors to consider before agreeing to participate such as additional medical procedures, use of your personal information, costs, and other possible risks not discussed here. If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop your participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?

You are being invited to participate in a research study because you have ovarian, fallopian tube, or primary peritoneal cancer that continues to grow and spread (metastatic) after standard treatment with at least two prior chemotherapies. Your cancer is also positive for a protein called aFR (alpha folate receptor). Your participation is voluntary which means you can choose whether or not you want to participate.

Before agreeing to participate in this research study, it is important that you read the following explanation of the proposed procedures and how long you will be in the study. This document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time.

We are asking that you participate in a research study. When you take part in a research study, you and the study doctor must follow a set plan called the "study protocol." This is different from receiving care outside of the research study. When you receive medical care from your own doctor, he or she develops a plan of care just for you and your individual needs. When participating in the research study, the study doctor usually cannot adjust the plan for you as he or she needs to follow the study protocol. However, this research plan includes steps to follow if you are not doing well. It's important to understand that a clinical trial is an experiment. By its nature, that means the answer to the research question is still unknown.

Please take time to read the following information carefully. You may wish to discuss it with your family, friends, and your personal doctor (i.e., your family doctor or primary care doctor). If you have any questions, you may ask your study doctor and/or the research team for more information. Take time to decide whether or not you wish to take part. If you decide to participate, you will be asked to sign this form. If you decide to participate, you can change your mind at any time and withdraw from the study without giving a reason.

What is the purpose of this research study?

This research study will take some of your own white blood cells, called T cells, and modify them by introducing a receptor (chimeric antigen receptor, CAR) that recognizes aFR protein, so that they can identify and possibly kill cancerous cells expressing aFR protein. The T cells also will include a receptor that may help them kill cancer cells better. The modification is a genetic change, or gene transfer, to your normal T cells. These modified cells are called MOv19-BBz CAR T cells.

The use of MOv19-BBz CAR T cells is experimental and has not been approved by the Food and Drug Administration (FDA). This is the first time MOv19-BBz CAR T cells are being tested in humans. The MOv19-BBz CAR T cells will be administered directly into your abdominal cavity via intraperitoneal infusion. This type of administration is also considered experimental.

At this time, we do not know the best and safest dose of MOv19-BBz CAR T cells. The goal of this research study is to identify a safe dose of the MOv19-BBz CAR T cells in people with ovarian cancer. This will be done by using three different planned doses of the MOv19-BBz CAR T cells in small groups of participants in this research study. These small groups of participants are called cohorts. Some cohorts of participants will receive chemotherapy also, and other cohorts will not. Therefore, this study will involve up to 4 cohorts and 3 different dose levels of MOv19-BBz CART cells. If the lowest dose of MOv19-BBz CAR T cells are determined to be safe, higher dose levels will be evaluated.

When your own blood cells are taken, there may not be enough cells to make the planned study dose of the modified cells. If this occurs, and if the study physicians feel it is safe and poses no additional risk to you, they may recommend giving you a lower T-cell dose. If you decide not to receive this lower T-cell dose, you will no longer be able to participate in this research study. If you *do* receive a T-cell dose that is lower than the planned study dose, you will undergo the same schedule of visits and procedures as participants who receive the planned study dose.

In addition, subjects in certain cohorts will also receive chemotherapy a few days prior to their MOv19-BBz CAR T cell infusion. The chemotherapy drugs being used as part of this study are cyclophosphamide and fludarabine, which are approved by the FDA for treatment of certain types of cancers, but have not been approved for use in ovarian cancer. You will receive cyclophosphamide and fludarabine through an IV (intravenously through a vein) over 3 days. The purpose of this chemotherapy is to help the CAR T cells grow and survive in your body. Therefore, the use of chemotherapy as part of this study is considered investigational.

Subjects will be assigned to cohorts based on when they enroll on the study and available safety experience. Cohort 3 evaluated the highest dose of MOv19-BBz CAR T cells following chemotherapy, and was prematurely closed in January 2023 due to severe toxicity, including side effects that possibly contributed to the death of a study participant. You are being asked to participate in Cohort 2, which uses a lower dose of MOv19-BBz CAR T cells following chemotherapy.

How long will I be in the study?

If you choose to participate, the main portion of the study will take up to 2 years from the infusion of the MOv19-BBz CAR T cells to complete. You will be asked to come to the Hospital of the University of Pennsylvania 2-3 times during the screening process in order to make sure you are eligible to receive the MOv19-BBz CAR T cells, and to prepare you for the experimental treatment. Treatment itself may involve chemotherapy given over the course of three days, and

a one-time infusion of the cells. Once you receive the MOv19-BBz CAR T cells, you will be monitored very closely by your doctors and study team as either an outpatient or inpatient depending on your clinical condition. Each of these visits should take about 1 to 4 hours.

After you complete the main portion of the study, you will continue to be followed in long-term follow-up. During the long-term follow-up portion of the study, you will be followed for up to 15 years after you receive your MOv19-BBz CAR T cells, or until you withdraw from the study for any reason.

How many other people will be in the study?

It is expected that up to 18 adults will receive MOv19-BBz CAR T cells as part of this research study at the Hospital of the University of Pennsylvania.

What am I being asked to do?

Please note that a list of terms that are used throughout this consent form is provided at the end of this consent with explanations.

Procedures

Prior to taking part in this study, you and your doctor should discuss the current standard treatments for your cancer. The study doctor will ask you to read and sign this Informed Consent Form after all of your questions have been satisfactorily answered.

Once you decide to participate, you will have to undergo a screening process to determine if you are able to join the study. In order to determine if you are eligible to participate in this study, you will be required to undergo the following tests and evaluations:

Day	Part of Your Standard Medical Care?	Procedures
Screening Phase: Approximately 2 months prior to receiving MOv19-BBz CAR T cells	No	These procedures will check to see if you are eligible to participate in the study and will take approximately 1-2 hours. • Review of list of medications • Blood is drawn for clinical laboratory tests (which includes the HIV, hepatitis B and hepatitis C tests, to see how well your blood clots, blood tests to assess additional chemistry levels, and if you have any active infections). This requires a blood draw of about 2 tablespoons. • Electrocardiogram (EKG) • ECHO/MUGA • Leukapheresis screening to see if the veins in your arms are adequate for the apheresis procedure
	Yes	• Review of your relevant medical history and current medical conditions • Physical Exam including vital signs (temperature, blood pressure, heart rate (pulse), and blood oxygen levels), height and weight • Routine blood tests to assess your blood cell counts (to assess the number of each type of blood cell), blood chemistry levels (to test your organ function and the minerals in your blood). This requires a blood draw of about ½ tablespoon. • A urine sample will be obtained for routine analysis • Urine pregnancy test if you are a female/transgender male of childbearing potential • Disease assessments- CT scan of your chest/abdomen/pelvis. If you have already had these scans recently as part of your routine care, they may not need to be repeated. • Brain MRI only if you have a history of cancer that has spread to your brain

Reporting of a positive HIV, hepatitis B and hepatitis C test: You will be tested for HIV, hepatitis B and hepatitis C as one of the screening requirements prior to participating in this study. If you test positive for HIV, hepatitis B or hepatitis C, by law we have to report the positive test results to the City of Philadelphia Health Department and/or PA Department of Health. Personal identifiers such as name, sex, date of birth, address, and phone number will be reported. For more information about the requirements reporting infectious diseases to the City of Philadelphia Health Department, please visit https://hip.phila.gov/ReportDisease. For

more information about the requirements reporting infectious diseases to the PA Health Department, please visit http://www.health.pa.gov/Your-Department-of-Health/Offices%20and%20Bureaus/epidemiology/Pages/Reportable-Diseases.aspx#.V620aZ3D9eU.

Once you have completed the screening visit, your study doctor will determine whether it is safe for you to continue the study or not.

Day	Part of Your Standard Medical Care?	Procedures
• Make sure you tell the study staff about any medications you are taking during the research study. This includes prescriptions drugs, over-the-counter medicines, natural or herbal medicines, alternative medicines, vitamins, and marijuana or other recreational drugs. This is very important. • Tell your study doctor or study staff if you have any unusual symptoms at any time, even outside the visit period.		
Pre-Treatment Phase		
Apheresis Approximately 4 to 6 weeks prior to receiving MOv19-BBz CAR T cells	No	Removal of T cells from your blood is called apheresis and will take place in the Apheresis Unit and is done to collect the T cells into which the new genetic material will be inserted. An apheresis unit is a place where patients who need specific components of their blood removed from their bodies go to have this procedure performed. The apheresis procedure is like donating blood. This apheresis visit will take ~4 hours in total and the apheresis procedure will take ~ 3 hours to complete. If the veins in your arms are not adequate for the procedure, a special apheresis catheter may be inserted into a large vein in your neck for the collection. A review of your current medical conditions will be performed, and an assessment of any symptoms/side effects. Additional assessments may be performed as part of the apheresis procedure as per apheresis unit standard procedures.

Day	Part of Your Standard Medical Care?	Procedures
		You may not have to undergo this apheresis procedure if you have had T cells collected on another research study or at another facility. We may be able to use your T cells collected from the other study if they are acceptable to make your MOv19-BBz CAR T cells for this study.
Pre-Infusion Safety Visit Approximately 1 to 2 weeks before you receive MOv19-BBz CAR T cells	No	• Review of current medical conditions, list of medications, and symptoms/side effects • Respiratory virus panel (RVP) for the flu and other viral infections will be performed within 10 days prior to infusion of your T cells – this test involves swabbing of your throat and nostrils using a cotton swab. o If your RVP test is positive but you do not have any flu symptoms you will receive an antiviral medication called Tamiflu as standard medical care and your T cell infusion will be delayed until you complete this medication. o If your RVP test is positive and you have flu symptoms you will receive Tamiflu. Your infusion will be delayed for at least 7 days and all clinical symptoms must be resolved before you can receive your T cells. o If your RVP test finds another virus, including the virus that causes COVID-19, your treatment will be delayed for at least 7 days, and until symptoms have resolved. • Blood for clinical lab tests, to assess additional chemistry levels, and for research analysis. This requires a blood draw of up to 2 ½ tablespoons. • A urine sample will be obtained for routine analysis. • Blood pregnancy test if you are a female/transgender male of childbearing potential (about ½ teaspoon) • Tumor biopsy if determined clinically appropriate by your study doctor. The doctor may use ultrasound or CT scan or both, to precisely locate the tumor for biopsy. This tissue will be used for research purposes. If you already

Day	Part of Your Standard Medical Care?	Procedures
		underwent a biopsy at screening in order to evaluate your eligibility to participate in this study, a repeat biopsy pre-infusion is not required. • Disease assessments- CT scan of your chest/abdomen/pelvis if you have not had one within 8 weeks of your CAR T cell infusion.
	Yes	• Physical Exam including an assessment of your vital signs • Routine blood tests to assess your blood cell counts, blood chemistry levels, how fast your blood clots, and to measure biomarkers for your disease. This requires a blood draw of about 1 ½ tablespoons.
Chemotherapy (Cohorts 2 and 3 only) Last day of chemotherapy will end approximately 3 days before your MOv19-BBz CAR T cell infusion	No	If you are participating in cohort 2 or 3, you will receive chemotherapy with cyclophosphamide in combination with another chemotherapy called fludarabine. The purpose of the chemotherapy is to "make room" to help the CAR T cells expand and grow in your body. Chemotherapy is given intravenously (through a vein), and you will also receive nausea medications and intravenous fluids before and after the chemotherapy. Chemotherapy will be given over 3 days. Each visit will last about 4 hours. The following procedures will be done before the first dose of chemotherapy: • Review of your current medical conditions, list of medications, and symptoms/side effects • Blood test for routine lab tests (requires a blood draw of about ½ tablespoon) • A urine sample will be obtained for routine analysis.
	Yes	The following procedures will be done before the first dose of chemotherapy: • Physical examination including an assessment of your vital signs • Routine blood tests to assess your blood cell counts (to assess the number of each type of blood cell), blood chemistry levels (to test your organ function and the

Day	Part of Your Standard Medical Care?	Procedures
		minerals in your blood). This requires a blood draw of about ½ tablespoon.
Treatment and Primary Follow-Up Phase		
Receipt of MOv19-BBz CAR T cells (Day 0)	No	You will receive your modified MOv19-BBz CAR T cells on Day 0. This will occur after the cells have been grown in the lab for about 8-12 days. These MOv19-BBz CAR T cells will be tested to make sure that they are healthy and free from impurities. All participants will receive MOv19-BBz CAR T cells through a single infusion in your abdominal cavity. This infusion method will require an intraperitoneal (IP) catheter to be placed in your abdomen. Placement of the IP catheter will performed by Interventional Radiology physicians and staff and will require moderate sedation. This catheter will be removed following your MOv19-BBz CAR T cell infusion (on the same day). If you received chemotherapy prior to your planned MOv19-BBz CAR T cell infusion, some people can get sick from the chemotherapy side effects, so your doctor will need to examine you and may choose to delay your MOv19-BBz CAR T cell infusion until you feel better. In order to reduce potential side effects of the MOv19-BBz CAR T cells, you may also receive acetaminophen (e.g., Tylenol) and/or diphenhydramine (e.g., Benadryl). You will also undergo the following: • Review of your current medical conditions, list of medications, and symptoms/side effects • Vital signs (temperature, blood pressure, heart rate, respiratory rate and blood oxygen levels) will be taken within 10 minutes before administration of the MOv19-BBz CAR T cells, approximately every 15 minutes for one hour after administration, and then every hour for the

Day	Part of Your Standard Medical Care?	Procedures
		next 2 hours or until satisfactory and stable • Blood tests to assess additional chemistry levels, disease status, and for research analysis collected prior to receiving the MOv19-BBz CAR T cells and ~1 hour after (requires about 4 ¾ tablespoons of blood) • A urine sample will be obtained for routine analysis. You will be allowed to go home 3 hours after your infusion if you feel well and have not experienced unexpected reactions to the infusion.
	Yes	• Physical Exam including an assessment of your vital signs • Routine blood tests to assess your blood cell counts and blood chemistry levels. This requires a blood draw of about ½ tablespoon.
Safety Follow-up Visit 1 day after receiving MOv19-BBz CAR T cells	No	• Review of your current medical conditions, list of medications, and symptoms/side effects • Blood tests to assess additional chemistry levels and for research analysis (including tests for detection of MOv19-BBz CAR T cells) requires a blood draw of about 2 tablespoons.
	Yes	• Physical exam including an assessment of your vital signs • Routine blood tests to assess your blood cell counts and blood chemistry levels. This requires a blood draw of about ½ tablespoon.
Safety Follow-up Visits Days 2, 7, 10, 14, and 21 after receiving MOv19-BBz CAR T cells	No	• Review of your current medical conditions, list of medications, and symptoms/side effects • Blood tests to assess additional chemistry levels, disease status, and for research analysis (including tests for detection of MOv19-BBz CAR T cells). Requires a blood draw of about 2 ¾ tablespoons. • Day 14 Visit: Tumor biopsy if determined clinically appropriate by your study doctor. The doctor may use ultrasound or CT scan or both, to precisely locate the tumor for biopsy. This tissue will be used for research purposes.

Day	Part of Your Standard Medical Care?	Procedures
	Yes	• Physical exam including an assessment of your vital signs • Routine blood tests to assess your blood cell counts and blood chemistry levels. This requires a blood draw of about ½ tablespoon.
Safety Follow-up Visit Day 28	No	• Review of your current medical conditions, list of medications, and symptoms/side effects • Blood tests to assess additional chemistry levels and for research analysis (including tests for detection of MOv19-BBz CAR T cells) 2 tablespoons. • Apheresis (about 4 tablespoons of blood)
	Yes	• Physical exam including an assessment of your vital signs • Routine blood tests to assess your blood cell counts, blood chemistry levels, and to measure biomarkers for your disease. This requires a blood draw of about 1 tablespoon. • Disease assessments- CT scan of your chest/abdomen/pelvis. Additional scans may be performed as determined necessary by your study doctor.
Follow-up Visits Months 2, 3, and 6	No	• Review of your current medical conditions, list of medications, and symptoms/side effects. • Blood tests to assess additional chemistry levels and for research analysis (including tests for detection of MOv19-BBz CAR T cells). This requires a blood draw of about 2 tablespoons.

	Yes	• Physical exam including an assessment of your vital signs
		• Routine blood tests to assess your blood cell counts, and blood chemistry levels. This requires a blood draw of about 2 teaspoons.
		• A urine sample will be obtained for routine analysis.
		• Blood test to measure biomarkers for your disease. This requires a blood draw of about 1 teaspoon.
		• <u>Months 3 + 6 Only</u> – disease assessments
		  ○ CT scan of your chest/abdomen/pelvis
		  ○ Additional scans may be performed as determined necessary by your study doctor.

Day	Part of Your Standard Medical Care?	Procedures
Follow-up Visits Months 9, 12, 15, 18, 21, 24	No	• Review of your current medical conditions, list of medications, and symptoms/side effects • Blood tests to assess additional chemistry levels and for research analysis (including tests for detection of MOv19-BBz CAR T cells). This requires a blood draw of about 2 tablespoons.
	Yes	• Physical exam including an assessment of your vital signs • Routine blood tests to assess your blood cell counts, blood chemistry levels, and to measure biomarkers for your disease. This requires a blood draw of about 1 tablespoon.

Long-term Follow-up

Once you complete primary follow-up outlined in the table above, or you discontinue early for any reason (i.e. worsening of your disease, receipt of alternative treatment, etc.), you will enter into a long-term follow-up phase that will last for up to 15 years after your MOv19-BBz CAR T cell infusion. Visits in long-term follow-up are based on when you enter long-term follow-up and the amount of time that has passed since your MOv19-BBz CAR T cell infusion. For example, if your last visit in primary follow-up (above) is Month 6, your first visit in long-term follow-up would be Month 9.

Long-term Follow-Up Phase (Up to 15 Years Post Infusion)		
Day	**Part of Your Standard Medical Care?**	**Procedures**
Follow-up Visits Months 3, 6, and 9 after entering the long-term follow-up	No	• Review of your current medical conditions, list of medications, and symptoms/side effects • Blood tests to assess additional chemistry levels and for research analysis (including tests for detection of MOv19-BBz CAR T cells). This requires a blood draw of about 2 tablespoons.
	Yes	• Physical exam • Routine blood tests to assess your blood cell counts and

Long-term Follow-Up Phase (Up to 15 Years Post Infusion)		
Day	**Part of Your Standard Medical Care?**	**Procedures**
		blood chemistry levels. This requires a blood draw of about ½ tablespoon.
Follow-up Visits Month 12 after entering the long-term follow-up and then every 6 months for up to 5 years	No	• Review of your current medical conditions, list of medications, and symptoms/side effects • Blood tests to assess additional chemistry levels and for research analysis (including tests for detection of MOv19-BBz CAR T cells). This requires a blood draw of about 2 tablespoons.
	Yes	• Physical exam • Routine blood tests to assess your blood cell counts and blood chemistry levels. This requires a blood draw of about ½ tablespoon.
Yearly visits from years 6 to 15 post-infusion if the MOv19-BBz CAR T cells are still present in your body. You will continue to have yearly visits until the MOv19-BBz CAR T cells are no longer detected in your blood. Subsequent follow-up may be performed via the Penn patient portal called MyPennMedicine (MPM), phone and/or mail/email.	No	• Review of your current medical conditions, list of medications, and symptoms/side effects • Blood tests for additional chemistry levels and for research analysis (including tests for detection of MOv19-BBz CAR T cells). This requires a blood draw of about 2 tablespoons.
	Yes	• Routine blood tests to assess your blood cell counts and blood chemistry levels. This requires a blood draw of about ½ tablespoon.

Long-term Follow-Up Phase (Up to 15 Years Post Infusion)		
Day	**Part of Your Standard Medical Care?**	**Procedures**
Yearly Follow-up from years 6 to 15 post-infusion if the MOv19-BBz CAR T cells are <u>not</u> present in your body. May be performed via the Penn patient ortal called MyPennMedicine (MPM), phone and/or email/mail.	No	• You will be contacted annually to obtain information about your health status, current medical conditions, and list of medications. This follow-up may be performed via the Penn patient portal called MyPennMedicine (MPM), phone and/or email/mail. Please let your study doctor know if you do not wish to be contacted via email as this is not a secure form of communication. If we are unable to contact you, your name and date of birth may be used to search a public federal government database to get information about your survival status.

You will be required to travel to the Hospital at the University of Pennsylvania for each of the study visits. Once you have received your MOv19-BBz CAR T cell infusion, it is very important that the study doctor is able to monitor your health and safety at each visit. In the event you are unable to travel to the Hospital at the University of Pennsylvania for one of these visits, you should contact your study doctor.

In the event that you cannot return to the study site for the above follow-up visits, your primary care physician and/or local oncologist will be asked to provide information from your medical record to the study team at protocol-defined time points (including the results of any routine care examinations and/or laboratory assessments), and assist in the collection of protocol required blood samples (if applicable) which will be sent to the University of Pennsylvania for protocol required analysis. You and/or your local provider will also be contacted via the Penn patient portal called MyPennMedicine (MPM), phone, and/or email/mail by a member of the study team to assess any potential toxicity.

<u>Additional Research Samples</u>: In the event something unexpected occurs during your participation in the protocol (for example a new side effect that has not been experienced by other participants), the research team may request additional blood be collected for research analysis. This is being done with the intention of evaluating the possible effects from the MOv19-BBz CAR T cells you have received. The total amount of extra blood that will be

collected from you will be 3 tablespoons of blood twice in one week, in addition to the protocol-defined time points listed above.

In addition, if you undergo a biopsy as part of your routine treatment while you are on study, a sample of this tumor tissue will be collected for research purposes.

The study team may "bank" (store) some of your blood samples collected throughout your participation in this study. These samples will be kept frozen and will not identify you by name. The blood samples will only be used by the study team to go back and do testing on your blood if an unexpected event occurs.

Request for Autopsy:
In order for the study doctors to learn more about your disease and the safety and function of the MOv19-BBz CAR T cells, they may request to perform an autopsy in the event of your death. Your family will make the final decision as to whether or not an autopsy can be performed and will be required to sign forms that will authorize the autopsy. Therefore, please inform your family of your wishes. If an autopsy is performed, samples obtained during this procedure will be used for research purposes.

What are the possible risks or discomforts?

As of December 2022, MOv19-BBz CAR T cells have been given to 9 subjects at the University of Pennsylvania. In addition, over 500 adults and children with leukemia, lymphoma, and multiple myeloma have also received different types of CAR T cells as part of University of Pennsylvania sponsored research studies.

This section describes the most common side effects seen in subjects receiving other CAR T cell therapies at the University of Pennsylvania, as well as the side effects seen in subjects receiving Mov19-BBz cells to date. These side effects can range from mild to severe, and have resulted in death in rare cases. These side effects may occur together as part of a syndrome (a group of symptoms that indicate a specific condition or disorder) or as independent events.

This research may also involve risks that are currently unknown or unexpected. Therefore, it is important that you tell your doctor if you are experiencing any problems. If you see a doctor other than your study doctor, please let them know that you are involved in a research study. It is very important that you contact your study doctor immediately if you develop signs of fever or other new abnormal symptoms. This may require you to go into the hospital so the study team can monitor or help treat these side effects. It is possible that you will have side effects from these study drugs that are difficult or not possible to fully reverse.

In an effort to detect any potential side effects early and avoid any delays in management of these toxicities, participants treated with MOv19-BBz CAR T cells will be asked to stay within a one-hour drive to the Hospital of the University of Pennsylvania following infusion.

Cytokine Release Syndrome (CRS)/Macrophage Activation Syndrome (MAS)

Rapidly growing activated CAR T cells release proteins and chemicals called cytokines. Release of large amounts of certain cytokines can cause a "cytokine release syndrome", which is a severe flu-like syndrome. Macrophage activation syndrome is an activation of your immune system associated with the cytokine release syndrome. Symptoms of these severe flu-like syndromes include high fevers, chills and shaking, muscle aches, joint aches, sweating, nausea, vomiting, loss of appetite, fatigue, headache, fast heart rate, liver problems, and kidney problems that may require dialysis; it can sometimes also increase risk of bleeding. People can also have trouble breathing and dangerously low blood pressure. Some people need to be treated with a ventilator (a breathing machine). Some people need support with special blood products. Many people with cytokine release syndrome have had to be cared for in an intensive care unit at the hospital. Cytokine release syndrome can be mild or severe and has resulted in death.

These side effects may or may not be reversible. Medications are available to potentially reverse or lessen the severity of the CRS and MAS (such as tocilizumab). It is unknown whether these medicines may make your CAR T cells less effective. The best time to administer medications to treat the cytokine release syndrome and macrophage activation syndrome is not currently known. These medications may also have their own side effects, may weaken the immune system and increase the chance of serious infections.

In addition, some participants with cytokine release syndrome have become very confused and disoriented (unaware of who they are and or where they are, not recognizing family and friends, unaware of the date and unaware of their health problems). Some participants have had seizures or have even become unresponsive. We believe these side effects are caused by the cytokine release syndrome and macrophage activation syndrome. In most cases, these problems resolved over time.

Neurological Toxicity

The following events have been seen in patients receiving CAR T cells. Some events are common, and most are rare.

- Headache
- Difficulty speaking (aphasia)
- Delirium, confusion, or decreased alertness - which may be mild to severe
- Hallucinations
- Seizures (uncontrollable shaking/convulsions)
- Tremors
- Dizziness
- Anxiety
- Difficulty sleeping or sleep disorders
- Tingling and/or weakness in hands and feet (peripheral neuropathy)

- Meningitis (Inflammation of the lining around the spinal cord and brain). May result in headaches, nausea, vomiting, vision problems, and increased pressure in your brain. It may also lead to seizures and death.
- Loss of ability to move
- Severe weakness
- Swelling in the brain

Many of these side effects have occurred with or just after cytokine release syndrome/ macrophage activation syndrome (CRS/MAS) as described above. Some patients have also experienced neurological side effects without CRS/MAS. While neurological side effects have improved in most participants, there is a possibility that you could experience side effects that will not improve and may result in death.

Infusion/Allergic Reactions

Infusion-related reactions may occur, as with other cellular products or transfusions. While rare, symptoms of infusion-related reactions can include:

- Fever
- Chills
- Nausea
- Hives or other rashes
- Changes in blood pressure

More commonly, subjects have experienced an unusual taste in their mouth immediately after the infusion. This is caused by one of the ingredients in the product. This may also cause a temporary odor to your breath.

More Common Side Effects (occurring in > 10% of patients):

- Significant decreases in B-cell counts: CAR T cells can kill cancerous B-cells but can also kill normal B-cells. This happens because CAR T cells cannot tell the difference between cancerous B-cells and normal B-cells. Normal B-cells fight viral and bacterial infections by producing antibodies known as immunoglobulins. Decreasing the number of normal B-cells puts you at risk of potentially life-threatening viral and bacterial infections (including but not limited to pneumonia). If your immunoglobulins are too low, your doctor may give you intravenous immunoglobulin (IVIG). It is possible that your B-cells may never return, in which case you may have a life-long risk for viral and bacterial infections and need repeated doses of IVIG.
- Hypogammaglobulinemia: low immunoglobulin levels which may impair your immune system and may increase your risk of infection.

- Significant decreases in blood counts, including neutropenia (low white blood cell count), anemia (low red blood cell count), and thrombocytopenia (low platelet counts) are common. This will be related to the chemotherapy you receive prior to the MOv19-BBz CAR T cell infusion (if given), and may also be related to the MOv19-BBz CAR T cell infusion. These decreases can last weeks or, much more rarely, months. These decreases may result in the need for transfusions (i.e. anemia and thrombocytopenia) and increase the risk of severe infections.
- Fever
- Infections
- Sepsis- a serious infection which may be fatal
- Decreases and increases in your blood pressure
- Shortness of breath or abnormal rapid breathing
- Liver function test abnormalities
- Electrolyte abnormalities (changes in the levels of certain salts in your body, like sodium)
- Acute kidney injury - kidney failure or damage that can happen very quickly.
- Hypoxia - low levels of oxygen in parts of the body
- Pulmonary edema- excess fluid in the lungs that may make it difficult to breathe
- Bleeding
- Increased/abnormal heart rate
- Nausea
- Vomiting
- Diarrhea
- Constipation
- Abdominal pain
- Pain in your extremities (arms and legs)
- Fatigue
- Decreased appetite
- Weight loss
- Muscle and joint aches
- Swelling
- Cough
- Hives or other rashes, which may cause itching

Less Common Side Effects (occurring in ≥ 1% and ≤ 10% of patients):

- Chills
- Back Pain
- Accumulation of fluid in your body (edema) which may cause pain or swelling
- Sinus congestion
- Coagulation (blood clotting) problems- either a decrease in the capacity to produce clots leading to increased risk of bleeding or increase in the clot production leading to a blood clot (thrombosis)
- Tumor Lysis Syndrome: this happens when cells are killed too quickly for the body to get rid of the dead cells. Tumor lysis syndrome can cause kidney damage and increases in blood potassium, uric acid, calcium and phosphorus. Treatment may require hospitalization, including intensive care.
- Heart attack and heart failure
- Multiple critical organ failure or dysfunction (when an organ does not perform as expected)
- Visual impairment or blurry vision

Rare, Unexpected or Potential Side Effects (have not yet occurred or occurring in less than 1% of patients)

- Excessive T cell growth: though it is expected that the CAR T cells will grow in your body, it is possible the T cell growth could be excessive and cause medical problems. In this case, your doctor may recommend treatment to kill them. This can be done by giving drugs called corticosteroids. If the MOv19-BBz CAR T cell growth is not controlled by the corticosteroid treatment, your doctor may recommend a type of chemotherapy.
- Inability to respond to future gene therapies: you may be less likely to respond to similar gene transfer trials in the future because you may develop an immune response to the biological delivery vehicle, called a vector, which is used for the gene transfer in your T cells.
- Autoimmune disease: the use of MOv19-BBz CAR T cells could lead to an autoimmune disease. An autoimmune disease is when your immune system mistakenly attacks your own body. Autoimmune disease can affect many parts of your body, like your nerves, muscles, the endocrine system (system that directs your body's hormones and other chemicals), skin, liver, and digestive system.

- New occurrence of cancer: there is a chance that the genetic modification made to your T cells could cause other cancers. This could be caused by the virus (called a vector) used to genetically modify your T cells. In a prior gene therapy study for a childhood disease called Severe Combined Immunodeficiency (SCID), a viral vector caused leukemia in a small portion of patients. Some patients who developed the leukemia were successfully treated while others were not. The vector used in the SCID study is different than the vector used in this research study. Other cancers have been observed in patients who have received CAR Therapy. The relationship of these cancers to the CAR therapy is not known at this time. Based on the way the vector used in this study works, we think the risk of the vector causing other cancers is low. While this risk is low, you will be monitored for development of any new cancers throughout the scheduled protocol visits. If a new cancer develops while you are on study, you will be treated by standard of care clinical procedures, and the cancer will be investigated to determine if the lentiviral vector contributed to its development.
- Potential risks associated with a Replication Competent Lentivirus or "RCL": the lentiviral vector that is used to transfer the MOv19-BBz CAR T genetic material into your T cells has been designed so that it does not grow once inside your T cells and remains inactive. However, there is a risk that portions of the vector could mutate (change) in your T cells and allow it become active (i.e. grow and spread to other cells). This would be called a replication competent lentivirus, or "RCL". The specific risks associated with RCL are unknown. In the worst possible case it may make you sicker than you are now. To date, no patient treated at UPenn with other gene modified T cells using lentiviral vector has developed an RCL.
- Positive HIV Test: the lentiviral vector that is used to transfer the MOv19-BBz genetic material to your T cells is made up of parts of the human immunodeficiency virus or HIV. The lentiviral vector does not behave like HIV and it cannot cause the HIV disease. Most of the lentiviral vector is washed away during the manufacturing process of your T cells; however, there is a possibility it may cause a positive test result for HIV. If you test positive for HIV, you can have a more sensitive test done to determine whether or not you are truly HIV positive.
- Antibody formation: Your white blood cells isolated by the apheresis procedure will have further processing that will isolate the T cells (type of white blood cell) needed for your treatment. The separation is accomplished by using a system in which mouse antibodies are used. Residual mouse antibodies, which are proteins that are foreign to your body, can elicit an antibody response in your body. Furthermore, it is also possible that you may develop antibodies to other residual proteins used during the preparation of MOv19-BBz CAR T cells (e.g. VSV-G or HIV proteins that are present on the vector) that may not have been completely removed during the manufacturing process. The result of this is that your body could develop antibodies to the "foreign" proteins, which could lead to an allergic reaction, such as skin rash, itching and fever. More serious allergic reactions that require medical treatment could also occur, such as shortness of breath and drop in your blood pressure. It is possible that you will develop an immune response against the MOv19-BBz CAR T cells, and that this may result in the loss of

MOv19-BBz CAR T cells from your body. Development of anti-mouse antibodies could prevent you from getting other therapies that use mouse derived antibodies in the future.

- Inflammation: Your T cells will be modified to attack a certain protein called aFR which is located on the surface of your cancer cells. aFR is also found at low levels on the normal cells of your body including your kidney and small intestine. It is possible that treatment with these modified T cells may cause inflammation of these linings. The symptoms of this inflammation may include pain, bloating, distended abdomen, shortness of breath, pressure in the chest, fast or irregular heartbeats. Should significant inflammation occur, your doctors will treat you with steroids to decrease the inflammation. The T cells may also affect the salivary glands in your neck, which may cause dry mouth.
- On Target, Off Tumor Effects: As the target of the T cells is also on some of your kidney cells and some of the cells your brain, it is possible that you may experience inflammation in these areas as well.
- Anaphylactic reaction or anaphylactic shock: In a previous study testing patient T cells expressing a CAR that recognized a protein other than aFR, one patient experienced an anaphylactic reaction (or allergic reaction) after receiving multiple doses of the CAR T cells. Parts of this CAR were made using genes and proteins from mice. This anaphylactic reaction was most likely due to repeated exposure to the mouse components of the CAR. In the current study, we are testing a CAR construct that also contains mouse genes, in addition to human genes. Thus there is risk of developing an allergic reaction. However, in this study, you will only receive one dose of CAR T cells, thus the risk for an allergic reaction is lower. If a patient develops an allergic reaction that we could have not predicted, we will provide all necessary care for their allergic reaction which may include giving additional medications, providing life support and CPR and admission to the hospital for further care.

Reproductive Risks

The reproductive risks of MOv19-BBz are not known at this time. It is possible the cells could cause harm to an unborn child or children who are breastfeeding. The cells could also affect male/female fertility. If you have not already spoken to your treating physician about options for fertility preservation (which can include collection of eggs or sperm) you and your study doctor may discuss this in more detail.

If you are capable of becoming pregnant, you will undergo a urine pregnancy test prior to entry into the research study and a serum pregnancy test prior to the MOv19-BBz CAR T cell infusion. If you are found to be pregnant or breastfeeding at that time you will not be allowed to participate in the research study.

All study participants who are capable of becoming pregnant or fathering a child, MUST use at least one method of birth control for at least one year after your CAR T cell infusion.

Examples of medically acceptable birth control methods include any of the following:

- Total abstinence (no sexual relations)
- Female sterilization- surgical removal of both ovaries (female reproductive system that stores and releases eggs for fertilization and produces female sex hormones), or tubal ligation (having your "tubes tied") at least six weeks prior to signing this consent.
- Male sterilization
- Condoms with or without a spermicidal agent
- Diaphragm or cervical cap with spermicide
- A hormonal or non-hormonal intrauterine device (IUD)
- Hormonal based contraception (including the birth control pill, vaginal rings, etc.)

If you do become pregnant or suspect you may be pregnant, you must tell the investigator immediately and consult an obstetrician or maternal-fetal specialist. If you become pregnant while you are on this research study, you will continue to be followed in long-term follow-up. Your study doctor will also follow your pregnancy until outcome to monitor your safety.

If your partner becomes pregnant, you must tell the study doctor as soon as possible.

Pregnancy outcomes will be collected for any children fathered by study participants. Consent to report information regarding these pregnancy outcomes will be requested.

Risks Associated with Cyclophosphamide (Cohorts 2 and 3 only):
Common (over 10%):

- Decrease of white blood counts (which may result in infections)
- Decrease in platelets (cells that help your blood to clot)
- Decrease in red blood cell counts (which can cause anemia)
- Nausea and vomiting
- Temporary hair thinning or hair loss (beginning 3-6 weeks after administration)
- Sterility (inability to have children)
- Acute hemorrhagic cystitis (inflammation of the bladder causing blood in the urine)

Less common (1-10%):

- Facial flushing
- Headache
- Skin rash
- Nasal congestion, runny eyes, runny nose, sinus congestion, and sneezing during or immediately after the infusion

Risks Associated with Fludarabine (Cohorts 2 and 3 only)

Common:

- Decrease of white blood counts (which may result in infections)
- Decrease in platelets (cells that help your blood to clot)
- Decrease in red blood cell counts (which can cause anemia)
- Fever
- Nausea and vomiting
- Skin rashes
- Muscle pain
- Fatigue (tiredness)
- Pneumonia
- Nervous system toxicity such as changes in vision or changes in degree of alertness both of which can be severe or fatal, deterioration of mental status
- Allergic reaction causing breathing difficulty

Rare:

- Thrombotic thrombocytopenic purpura (TTP) - a rare blood disorder where blood clots form in small blood vessels throughout the body.
- Liver failure
- Tumor lysis syndrome - when tumor cells are killed too quickly for the body to get rid of the dead cells. Tumor lysis syndrome can cause kidney damage and increases in blood potassium, uric acid, calcium and phosphorus. Treatment may require hospitalization, including intensive care.
- Opportunistic infections (protozoan, viral, fungal, and bacterial)
- Autoimmune disorders

Risks of fludarabine combined with cyclophosphamide (Cohorts 2 and 3 only)

Common:

- Decrease of white blood counts (which may result in infections)
- Decrease in platelets (cells that help your blood to clot) leading to bleeding or easy bruising
- Decrease in red blood cell counts (which can cause anemia)
- Fatigue
- Nausea and vomiting
- Temporary hair thinning or hair loss
- Skin infection

Less Likely:

- Allergic reaction
- Severe allergic reaction that causes fever, aches and pains in the joints, skin rash, and swollen lymph glands, stuffy or runny nose, sneezing, sore throat, abnormal fast heartbeat, excessive sweating, flushing, itching, rash, swelling of the lips, eyes, tongue, and throat which can be severe, hives, diarrhea, high blood sugar, low blood potassium, dizziness, convulsions or seizures
- Abdominal pain,
- Back, joint, and/or muscle pain
- Headache
- Wheezing
- Cough
- Shortness of breath
- Inflammation (swelling) of the lung which may cause difficulty breathing and difficulty getting oxygen,
- Sterility (inability to have children), irregular menstrual periods
- Increased production of tears,
- Metallic taste, and
- Acute hemorrhagic cystitis (inflammation of the bladder causing blood in the urine)

Rare but Serious:

- Hemolytic anemia
- Changes in vision or changes in degree of alertness both of which can be severe or fatal
- Rash which may become severe
- Separation of your outer and middle skin layers which may be life-threatening
- Difficulty breathing
- Allergic reactions to blood transfusions
- Tumor lysis syndrome that can lead to kidney and heart failure
- Secondary cancers- including myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML)

Apheresis

Side effects that can occur during T-cell collection include nausea, vomiting, fainting or dizziness, seizures, skin rash, hives, flushing (redness and warmness of the skin, usually the face), blood loss, and infection. Tingling of the lips, muscle cramping and, very rarely, changes in the heart rhythm can occur. These can be prevented or made milder by giving calcium supplements, either by mouth or in the vein, also called intravenous (IV). Very rarely, (less than 1 in 1,000 procedures), clotting may occur in the apheresis machine or in a patient and is potentially life-threatening. To reduce the risk of clotting, a drug called ACD (acid-citrate-dextrose) will be used. This drug may increase the risk of bleeding and may cause temporary tingling of the lips and limbs, muscle cramping, seizures, or changes in the heart rhythm. After

the apheresis procedure you may experience temporary discomfort, including irritation, swelling or bruising at the place where the needle was inserted into your vein to collect the blood. Apheresis can also occasionally cause hives, numbness and tingling, or swelling of your feet and ankles.

Tumor Biopsy

A biopsy is an invasive test in which your cells and/or tissue are collected for examination. It involves the surgical removal of a small bit of tissue for examination. Your study doctor will explain this procedure to you in more detail, and you will be given a standard hospital consent form to sign detailing your specific type of biopsy prior to the procedure.

Likely risks:

- Pain
- Discomfort
- Soreness
- Minor bleeding
- Bruising

Less likely risks:

- Redness
- Swelling
- Bleeding

Rare risks:

- Bleeding that is life-threatening
- Possible damage to adjacent organs
- Drainage from the biopsy site
- Abnormal wound healing
- Fever
- Infection
- Allergic reaction to the medication used to numb the skin over the biopsy site

Intravenous Catheter Placement (IV)

Placement of an IV catheter involves putting a small, short plastic tube in your vein. Occasionally the procedure can cause local infections, pain or bleeding from the needle stick, bruising of the skin, inflammation or irritation of the vein (also known as phlebitis).

Radiation Exposure

This research study may involve exposure to radiation from a CT scan if used to direct the biopsy procedure or a MUGA scan used to assess your eligibility to participate in this study. Therefore, you may receive a radiation dose. At doses much higher than you will receive,

radiation is known to increase the risk of developing cancer after many years. At the dose you will receive, it is very likely that you will see no effects at all.

aFR Testing

The test for aFR expression used in the screening procedures for this study has been developed in a laboratory and is not approved by the Food and Drug Administration (FDA). It is possible that the results of the aFR test are incorrect, and that your tumor does not express aFR. The risks associated with a failed aFR test (i.e. "false-positive") would be due to your T cells attacking aFR on normal cells of your body. Therefore, the risk of a failed aFR test are the same as the risks described in the "Inflammation" section above.

Blood Draws

Occasionally there are risks associated with blood draws such as bruising, swelling, black and blue marks, fainting and/or infection at the site. You may also experience a decrease in hemoglobin and hematocrit (red blood cell number, called anemia) from having blood drawn frequently. Approximately 49 tablespoons (about 3 cups) of blood will be drawn for research purposes during this research study over the period of two years, and approximately 39 tablespoons of blood (about 2 ½ cups) during long-term follow-up for up to 15 years.

Intraperitoneal Administration of CAR T Cells

The risk of peritoneal inflammation with IP administration is anticipated to be higher than that of IV administration given the direct administration into the peritoneal cavity.

Intraperitoneal Catheter Placement

Risks associated with the procedure include, but are not limited to, pain or discomfort at the needle insertion site, bleeding at the site, internal bleeding, injury to a blood vessel, organ puncture, and infection which may result in an infection of the blood stream. The development of any infection may result in the need for intravenous antibiotics. X-ray contrast material may be used at the time of catheter insertion. Risks associated with the X-ray contrast material include an allergic reaction. Moderate sedation is used during the catheter placement. The medications used for the moderate sedation are associated with the risks of aspiration (inhaling food or liquid into your lungs) or respiratory depression. In addition to these potential risks associated with the procedure, the X-ray contrast material, and the moderate sedation medications, there may be other unpredictable risks including death.

You will be asked to sign a standard hospital consent form for this procedure. You will be closely monitored during the procedure by the anesthesia team and/or the primary proceduralist's team and subsequently by the research team.

Another risk of intraperitoneal catheter placement is that the study doctor may decide that administration of the CAR T-cell infusion might not be clinically appropriate for you after you've had the IP catheter placed.

Genetic Testing

Additional research performed using your blood and tissue samples may include genetic testing. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

There can be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all of the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded. Research results will not be returned to you or your doctor.

Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. We believe the chance these things will happen is very small, but we cannot make guarantees.

A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.

What if new information becomes available about the study?

During the course of this research study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the research study. We will notify you as soon as possible if such information becomes available. In order to provide this information to you, you must provide your current address and telephone number to the study doctor and must update this information so that the research staff will be able to contact you to give you any new information learned from this research study in the future.

What are the possible benefits of the study?

You may not get any benefit from being in this research study. However, while you may not benefit personally, the knowledge learned from your participation in this research study may benefit other patients in the future. It is possible that your disease and/or health may worsen as a result of participating in this study.

What other choices do I have if I do not participate?

Your other choices may include:

- Getting treatment or care for your cancer without being in a research study

- Taking part in another research study
- Getting no treatment

Will I be paid for being in this research study?

You will not be paid for participating in this research study.

Will I have to pay for anything?

The research study will cover the cost of research related tests, procedures and clinic visits. There is no cost for the investigational T-cell product that you will receive during your participation. For subjects participating in cohorts 2 and 3, there will also be no cost to you for the cyclophosphamide and fludarabine or their administration.

This research study also requires that you receive certain standard medical tests and examinations during the course of the research study. These exams, tests or procedures are part of routine cancer care and may be done even if you were not in this research study. The costs of these standard tests and examinations will be the responsibility of you and/or your health insurance provider. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this research study may or may not cost your insurance company more than the costs of getting regular cancer treatment. You are expected to pay for any costs not paid by your insurance provider (including co-pays and deductibles).

What happens if I am injured or hurt during the research study?

If you have a medical emergency during your participation on this study, you should go to the nearest emergency room. You should contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or their staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them. There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury.

Financial compensation for such things as traveling, parking, lost wages, disability or discomfort due to injury is not available.

You will not lose any of your legal rights when you sign this form.

When is the research Study over? Can I leave the Research Study before it ends?

This research study is expected to end after all participants have completed all visits, and all information has been collected. Your participation in this research study may also be stopped at any time by your study doctor, study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Principal Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide not to participate, you are free to leave the research study at any time. You may do this by contacting the investigator noted on page one of this consent. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. Only the minimum necessary data will be provided to the people/entities named below and when possible participants will be identified with a unique study identification number. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. This study is being overseen by the Food and Drug Administration (FDA), who may also review your research records.

Electronic Medical Records and Release of Study Related Information

An Electronic Medical Record (EMR) is an electronic version of your medical chart within a health system. An EMR is simply a computerized version of a paper medical record.

What may be placed in the EMR?

Information related to your participation in the research (e.g., laboratory tests, notes from your physician, imaging studies, and clinical procedures, etc.) may be placed in your EMR maintained by Penn Medicine.

Once placed in your EMR, your information may be accessible to appropriate Penn Medicine workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by Penn Medicine to be appropriate to have access to your EMR (e.g., health insurance company, disability provider, etc.).

Penn Medicine also participates in automated information sharing through Health Information Exchanges (HIEs). HIEs securely share parts of your electronic health record, including research information, with other healthcare organizations involved in your care. This information is shared to improve the quality, safety and efficiency of your healthcare. To request that your health information not be shared through HIEs, please call [redacted].

Will I, as a participant, have access to research related information within the EMR?
The 21st Century Cures Act requires healthcare institutions to allow patients increased access to their electronic medical record. As part of your participation in this research, you will have access to research related information within your EMR through Penn Medicine's patient portal – called MyPennMedicine (MPM).

Information that may be placed in the medical record
Your medical record may include information physical examinations, clinical assessments, and medication orders/administration records required as part of your participation in this study. Your medical record will also include results from laboratory tests, imaging studies, and clinical procedures, etc. (or any results that would have been placed in the medical record, regardless of research participation).

Information placed in the medical record is part of the designated record set and you have a right to review this information per HIPAA regulations.

Information that may not be placed in the medical record
Information from the collection and handling of clinical samples for research purposes will not be included in your medical record. This includes the results from biospecimen testing conducted in a laboratory that is not part of the HIPAA covered entity OR results from testing conducted in a non-CLIA certified laboratory (i.e., the results would not have been placed in the medical record as part of clinical care).

Will I receive the results of research testing?
Most tests done in research studies are only for research and have no clear meaning for your routine medical care. Research results will not be returned to you because they would not be relevant to your routine medical care.

Will information about this study be available to the public?
A description of this clinical trial will be available on *http://www.ClinicalTrials.gov* and included on University of Pennsylvania websites. These postings will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What information about me may be collected, used or shared with others?

The following personal health information will be collected, used for research, and may be disclosed during your involvement with this research study:

- Name, address, telephone number, e-mail address, date of birth
- Personal and family medical history, allergies; prior hospital admission/discharge information
- Current and past medications or therapies
- Medical record number
- Sex assigned at birth, gender
- Information from a physical examination that generally also includes blood pressure reading, heart rate, and temperature
- Results of tests and procedures you will undergo during this research study as described in this informed consent form

Why is my information being used?

Your information is used by the research team to contact you during the research study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right
- evaluate and manage research functions.

Where may my information be stored?

Information related to your participation in clinical research will be contained in a clinical trial management system (CTMS). A clinical trial management system (CTMS) is used to register your information as a participant in a study. This allows for your research data to be entered and stored for the purposes of study operational and financial applications and other activities required as part of the conduct of the research. Once placed in the CTMS your information may be accessible to other authorized personnel at Penn Medicine that support research operations. Your information may also be held in other research databases.

Who may use and share information about me?

The following individuals may use or share your information for this research study:

- The Principal Investigator and the study team
- Other authorized personnel at Penn Medicine and the University of Pennsylvania, including offices that support research operations.
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB.

As part of your participation in this study, we may need to contact you via the Penn patient portal called MyPennMedicine (MPM), phone and/or email/mail to facilitate scheduling, send you appointment notes or send you information about your participation in the study. Email communications are often not secure and may be seen by others as a result. By agreeing to participate in this study, you accept this potential risk. If you wish for us to use a different means to communicate with you during the course of the trial, please discuss this with the research team and alternative methods can be arranged.

Who, outside of Penn Medicine, might receive my information?

The following Study Funders:

- OvaCure and their authorized agents
- Alliance for Cancer Gene Therapy and their authorized agents
- Ovarian Cancer Alliance of Greater Cincinnati and their authorized agents
- National Institutes of Health (NIH) and their authorized agents

Regulatory and safety oversight organizations

- The Food and Drug Administration
- The Office of Human Research Protections
- The NIH Office of Biotechnology Activities and their committees overseeing gene therapy research
- The Study Data and Safety Monitoring Board
- Public Health agencies and other governmental agencies (including non-U.S.) as authorized or required by law

Once your personal health information is disclosed to others outside of Penn Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to Penn Medicine procedures developed to protect your privacy.

How long may Penn Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific research study does not expire. Your information may be held in a research database. However, Penn Medicine may not re-use or re-disclose information collected in this research study for a purpose other than this research study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the research study. If you withdraw your permission, you will not be able to stay in this research study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

What may happen to my information and samples collected on this study?

As outlined above, you will have research samples (or specimens) collected as part of your participation in this study. Depending on the type of specimen, these samples may be labeled with identifiable information. It is possible that your specimens may be used to establish products that could be patented, licensed, or sold, which could make money for others. If this happens, there are no plans to tell you or provide financial compensation to you or your family.

Whole genome sequencing will not be conducted on your samples as part of the planned study analysis. However, this may be performed as part of future use of your specimens (described in more detail below). Whole genome sequencing involves analyzing your entire personal genetic code. Please refer to the risks section of the consent for the risks of genetic testing.

Future Use of Data and Specimens

Blood, remaining unmanufactured cells (from your apheresis collections), unused manufactured CAR T cells or other samples obtained from you while you are participating in this study will be stored indefinitely and used for future research. Your study data and samples may be shared with other researchers within Penn, or other research institutions as well as with for-profit pharmaceutical or biotechnology companies. There are no plans to tell you about any of the specific testing that will be done. This future research may include genetic testing and/or whole genome sequencing. Whole genome sequencing involves analyzing your entire personal genetic code. It is possible that you may have chosen not to participate in these future research studies, if you had been approached for participation. Please refer to the risks section of the consent for the risks of genetic testing.

You will not be given the results of any future testing performed on your samples.

You will also not directly benefit from any future research with your specimens. However, it is possible this research may help others by improving our understanding of your disease and possible treatments.

There is also a risk of breach of confidentiality (unintentional release of your information). We will do our best to make sure that this does not happen. However, we cannot guarantee total privacy. We will protect your confidentiality during storage and sharing by using coded specimens. Coded means that all direct identifiers (name, initials, medical record numbers) have been removed. However, your samples will still include your unique subject identification number and may be linked back to information/data that was collected from you as part of this study (i.e., disease response, safety, diagnosis, etc). However, the information shared with other researchers will also be coded. It will not be possible for future researchers to identify you. The future use of your samples only applies to the samples collected on this study.

As part of your consent to participate in this study, you are agreeing to the use of your samples as outlined above. If you have any questions about the storage of your samples, or would like to withdraw your permission to use and store these samples at any time, please contact the study doctor, Dr. Shah at [redacted]. However, any samples that have already been used for research purposes will be retained. After all research analysis on these samples is complete, these samples may be destroyed at any time without notice.

Genomic Data Sharing

Genomic studies examine genetic differences in the entire human genome (the complete set of human genes called whole genome sequencing or WGS) to determine changes and mutations in DNA, and the association between these genetic differences and health conditions. The significance of these results may not be well-defined. Not all genetic variations affect one's health. As this is an NIH-funded study, we are required to send this data to a NIH designated data repository that includes all kinds of genomic data from studies funded by the NIH.

The aim of collecting this information is to look for genetic connections that may:

- Increase the likelihood of getting a certain disease (such as asthma, cancer, diabetes, heart disease or mental illness) or a condition (such as high blood pressure or obesity)
- Affect the progress of a certain disease or condition
- Affect treatments (medicines, etc.) that work for certain diseases in some people, but not others

The data that is shared will not include any direct identifiers (such as your name) and will be coded. The key to this code, which links your data back to your identifiers, will not be shared. The repository is a controlled-access repository. Controlled-access data is only available to researchers and companies who apply to the NIH. The NIH will review data requests for scientific merit and for methods to protect data and methods to ensure data will be used for the approved purpose. We will not know what types of health-related research will be done with the data that are sent to the repository.

There may be risks to your privacy and the privacy of your relatives from storing your information in the repository. Although the NIH takes measures to protect privacy, we do not

know how likely it is that your identity could be re-connected with your genetic and health information. If your genetic information were re-identified, personal information about you, your health and your disease could become known to others. This could present unknown risks. Current federal law will help protect you from genetic discrimination in health insurance and employment. Please also refer to the risks of the consent for the risks of genetic testing for additional information.

There is no direct benefit to you from placing your genetic information in this database. However, allowing researchers to study your genetic information may lead to a better understanding of how genes affect health, therefore may help other people in the future.

Who can I call with questions, complaints or if I'm concerned about my rights as a research participant?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research participant, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached, or you want to talk to someone other than those working on the research study, you may contact the Office of Regulatory Affairs with any concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

Financial Conflict of Interest

The University of Pennsylvania (the Sponsor of this study) and Dr. Daniel Powell (a scientific advisor for this study) have significant financial interest in the study drug being evaluated in this research protocol. It is possible this technology will be licensed to an outside company in the future. If this occurs and the study drug proves to be effective, it is possible that both the University and Dr. Powell will receive significant financial benefit.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form and your questions have been answered. Your signature also means that you are permitting Penn Medicine and the University of Pennsylvania to use your protected personal health information collected about you for research purposes within our institution. You are also allowing Penn Medicine and the University of Pennsylvania to disclose that protected personal health information to outside organizations or people involved with the operations of this research study.

A copy of this consent form and Research Participant HIPAA Authorization describing your confidentiality and privacy rights for this research study **will be given to you.** By signing this document you are permitting the Penn Medicine and the University of Pennsylvania to use and disclose personal health information collected about you for research purposes as described above.

Name of Participant	Signature of Participant*	Date

Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date

* ☐ **N/A- Non-English Speaker**

The below section should only be used when consenting a non-English speaker. In this instance, only the participant's name will be printed above and the Interpreter/Witness will sign this consent below attesting to the following information.

Interpreter/Witness:

By signing this form, you are indicating that:

- The information in the Informed Consent Form/HIPAA Authorization, as well as any additional information conveyed by the person obtaining consent, was presented to the participant in a language preferred by and understandable to the participant; and
- The participant's questions were interpreted and the responses of the person obtaining consent were presented in a language preferred by and understandable to the participant.
- At the conclusion of the consent conference, the participant was asked in a language preferred by and understandable to the participant if s/he understood the information in the Informed Consent Form/HIPAA Authorization as well as any additional information conveyed by the person obtaining consent (including responses to the participant's questions) and responded affirmatively.

Name of Interpreter	Signature of Interpreter	Date

Name of Witness*	Signature of Witness	Date

***If different than Interpreter; otherwise this may be left blank.**

List of Terms Used in the Consent:

Autoimmune disease - When the body's immune system attacks and damages its own normal organs or tissues.

Biopsy - A tumor biopsy is a common and routine procedure, however the tumor biopsies performed as part of this study will be done for research purposes only. The type of biopsy you undergo depends on your disease. These biopsies will be done by a qualified physician. The doctor will numb the biopsy area with a medicine used to minimize unnecessary pain or discomfort (such as lidocaine), which is similar to that which you may get when you go to the dentist. The doctor may use ultrasound or CT scan or both, to precisely locate the tumor for biopsy. One or two needles, about the size of IV needles, will be inserted through the skin into the site where your cancer is present, and the appropriate samples will be removed. In some case, tumor cells may be obtained simply from a blood sample or some other body fluid which may have tumor cells in it. Your study doctor will explain this procedure to you in more detail. You will be asked to sign a separate hospital consent form further describing the biopsy procedure.

Blood draw – When blood is taken from a vein using a needle, in order to monitor your health and for research.

CT-Scan – The CAT (Computerized Axial Tomography) scan, also known as the CT (computed tomography) scan, is an x-ray technique that produces a film representing a detailed cross section of body tissues and structures. The standard CT scan procedure is painless, noninvasive, and requires no special preparation.

In this test, a computerized axial tomography (CAT or CT) scanner is used to produce a series of cross-sectional x-ray pictures of a selected part of the body. A computer operates the scanner, and the resulting picture represents a slice of the body. Areas above and below the chosen slice do not appear on the image. Information from several slices can be combined to create a view across the body from any angle, and it produces pictures with 10 to 20 times the detail of regular x-rays.

ECHO/MUGA – Both an echo (or echocardiogram) and a MUGA are test that are used to find out if the heart is functioning normally. An echo uses sound waves produce pictures of the heart. A MUGA uses a special camera that follows the radioactive substance that is given in your vein to produce images of your heart.

Electrocardiogram - An electrocardiogram (EKG or ECG) is a test that checks for problems with the electrical activity of your heart. An EKG translates the heart's electrical activity into line tracings on paper. The spikes and dips in the line tracings are called waves. During an EKG, several electrodes are attached to the skin on each arm and leg and on your chest. These are hooked to a machine that traces your heart activity onto a paper. If an older machine is used, the electrodes may be moved at different times during the test to measure your heart's electrical activity from different locations on your chest.

Immune System - The body's defense system against infections and diseases like cancer.

Immunity - protection against a foreign invader (like cancer or a germ).

Infectious disease testing - Blood tests to check for any sign of previous viral infection such as HIV (which causes AIDS), hepatitis B and C.

Intraperitoneal – means within or administered through the peritoneum. The peritoneum is a thin, transparent membrane that lines the walls of the abdominal (peritoneal) cavity and contains/encloses the abdominal organs such as the stomach and intestines.

Lentivirus – a virus-like particle that is made from the human immunodeficiency virus (HIV) virus but cannot cause HIV infection or disease. It is used to deliver or transfer the new genetic material into the T cells.

Medical History – the doctor or study nurse will ask you about all previous medical conditions, past and current medications you may have taken, and participation in any prior clinical trials.

Physical Examination – A doctor or nurse will examine you and ask you how you are feeling and may include obtaining your height and weight and vital signs (temperature, blood pressure, heart rate, or blood oxygen levels).

Previous viral infections tests - Blood tests to check for any sign of previous viral infection such as HIV (which causes AIDS), hepatitis B, hepatitis C and Cytomegalovirus (CMV).

Redirected or "gene-modified" T cells – T cells that contain a new gene or new genetic material that may result in the ability of the T cells to recognize and attack cancer cells that they could not identify before.

Retrovirus - A type of virus that is made up of RNA. After the virus enters the cell, it uses an enzyme (called reverse transcriptase) which transforms the RNA into DNA. The virus DNA is then inserted into the infected cell's DNA. A lentivirus is a type of retrovirus that can insert itself in both dividing and non-dividing cells while a retrovirus can only insert itself in dividing cells.

T cells – Type of white blood cell that helps fight against infection and cancer; also known as T-lymphocytes.

Transfusion - A procedure for giving a blood cell product to a patient through the vein or through a catheter ("tube") which is inserted into a vein.