Official Title:	ATTAMAGE-A1.: Phase I/II Study of Autologous CD8+ and CD4+ Transgenic T Cells Expressing High Affinity MAGE-A1-Specific T-Cell Receptor (TCR) Combined With Atezolizumab in Patients With Metastatic MAGE-A1 Expressing Cancer
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Fred Hutchinson Cancer Research Center
The University of Washington School of Medicine
Seattle Cancer Care Alliance

Consent to receive treatment as part of a research study:

ATTAMAGE-A1: Phase I/II study of Autologous CD8+ and CD4+ Transgenic T cells expressing high affinity MAGE-A1-specific T-Cell Receptor (TCR) combined with Atezolizumab in patients with metastatic MAGE-A1 expressing cancer

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Important things to know about this study.

You are invited to participate in a research study because you have advanced triple negative breast cancer (TNBC), urothelial carcinoma, or non-small cell lung cancer (NSCLC) that has recurred or not responded to prior conventional chemotherapy and may express a protein called MAGE-A1 . The purpose of this research is to see if we can take immune T cells from your blood, modify them in the laboratory so they specifically kill cancer cells and safely give them back to you after lymphodepleting chemotherapy.

If you agree to join the study you will be asked to participate in pre-treatment procedures, collection of T cells, chemotherapy, T cell infusion and follow-up. You will be actively participating in the study for approximately 15 months. The total time includes the time for the T cells to be made, the T cell infusion, and for approximately 12 months after the T cell infusion is given.

We do not know if treatment with genetically modified T cells will help your MAGE-A1 expressing cancer, and this treatment could even make your condition/disease worse. Genetically modified T cells could cause side effects such as high fevers, low blood pressure, or neurotoxicity, as described below in this form.

You do not have to join this study. You can choose to receive standard methods to treat your triple negative breast cancer (TNBC), urothelial carcinoma, or non-small cell lung cancer (NSCLC) cancer instead of participating in this study. We will give you details about the purposes, procedures, risks and possible benefits related to this study. We will explain other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

We would like you to join this research study.

Protocol 10420 is a research study to find out if we can take immune T cells from your blood, modify them in the laboratory by adding new genes to make them kill cancer cells, and safely give them back to you after chemotherapy. T cells that have genes added in the laboratory are called ‘genetically modified’ T cells. In this case, the added gene encodes a so-called T-cell receptor (TCR) that helps the T cells find and kill cancer cells.

To determine the safest dose for T cell infusions, we will first treat patients one at a time starting at a low dose. At each cell dose level, one patient will be treated without lymphodepleting chemotherapy and, if considered safe, the next three patients will receive lymphodepleting chemotherapy. The purpose of this chemotherapy is to cause a low lymphocyte (white blood cell) count in your blood (termed lymphodepletion), which has been found to help the infused T cells survive and expand. The first four patients will be treated at a low dose during their first and second infusion approximately 6-12 weeks later.

Once a group of patients has been treated at a certain dose cohort, we will look at the safety of that dose and decide if we should enroll an additional cohort of patients who will receive the addition of a PD1-axis therapy called atezolizumab. Atezolizumab is a human antibody that blocks a marker called PD-L1. PD-L1 can be found on cells in a tumor and can interfere with the function of T cells. The antibody has been used to improve the anti-tumor activity of T cells in many cancers. This cohort of patients will receive a dose of atezolizumab approximately every 3 weeks following T cell infusion

Up to 18 patients with either triple negative breast cancer (TNBC), urothelial carcinoma, or non-small cell lung cancer (NSCLC) that expresses MAGE-A1will be treated on this trial.

The information we get from this study may shed light on the future potential for genetically modified T cells to be used to treat MAGE-A1 expressing cancers.

You do not have to be in this study. You are free to say yes or no, or to drop out after joining. There is no penalty or loss of benefits if you say no. Whatever you decide, your regular medical care will not change.

What research tests, procedures and infusions are part of this study?

If you decide to join this study, we will do research tests and procedures, which are performed in addition to your usual care. This will include routine blood tests, including testing for viruses like hepatitis and HIV. Where possible we will try and schedule the times and locations of research tests to coincide with the tests done as part of your usual care.

Procedures are outlined according to study periods: pre-treatment, leukapheresis, T-cell manufacturing process, chemotherapy, T-cell infusion, and long-term follow-up.

Pre-treatment

Restaging of your disease may include the following tests:

Tumor imaging studies. You should have CT (Computed Tomography) scans with or without PET (Positron Emission Tomography) scans to determine the amount of disease you have prior to starting chemotherapy.

Tumor Biopsy If you did not require a tumor biopsy during screening, a tumor biopsy may be obtained. There are two reasons you may undergo a tumor biopsy:

- **Clinical biopsy**: A tumor biopsy may be necessary for your clinical care, if obtained, a research sample will be sent to the research lab.
- **Research tumor biopsies:** If you have a tumor that your doctor thinks can be safely biopsied, we would like to perform a biopsy procedure to get some tumor for research. Similarly, should your doctor determine that a biopsy cannot be performed safely for clinical reasons, biopsies may be cancelled or rescheduled. Your doctor will explain the process and risks to you and tell you which tumor they feel is best to biopsy. We would like to collect research biopsies prior to your first T cell infusion,

1-4 weeks after each infusion and, should you relapse, a tumor biopsy may be requested at that time.

The study team may also request some tissue from a previously collected biopsy for research.

Blood tests: If there is a delay between your initial screening tests and your leukapheresis or blood draw for T cell collection, we may need to repeat the screening blood tests, which is a 30 ml sample (6 teaspoons), closer to the time of T cell collection to help us plan the procedure.

Other routine medical tests will be done to evaluate your heart, lungs and other organs to make sure it is safe to give you chemotherapy and T cell infusions. These may include a physical exam, electrocardiogram (EKG), echocardiogram (ECHO) or a multi-gated acquisition (MUGA) and laboratory blood tests.

If it is determined that we can likely make genetically modified T cells for you then we would like to proceed with the collection of your T cells.

Leukapheresis - Collection of T cells

T cells will be collected from your blood by a procedure called leukapheresis, a standard medical procedure in which needles are inserted into both arms and your blood is circulated through a machine before being returned to you. You will be hooked up to the machine for 1-4 hours. While you are on it, some white blood cells will be removed from your blood and collected in a sterile bag. You will be monitored carefully during the procedure.

If you are not able to undergo leukapheresis because of poor venous access you may have a percutaneous central venous catheter inserted to support this collection.

After T cells have been collected from your blood, they will be taken to our laboratory where we will insert a new gene into their DNA to make them kill cancer cells. These genetically modified T cells (called FH-MagIC TCR-T) will then be grown in the laboratory. This process may take several weeks and may be difficult or impossible depending on how much prior chemotherapy you had. If the genetically modified T cells can be made and grown in sufficient numbers, then we will schedule the T cell infusion to take place when clinically appropriate.

Should a technical issue arise during the leukapheresis procedure or in the processing of the product, or if manufactured FH-MagIC TCR-T cells are insufficient for the prescribed FH-MagIC TCR-T cell dose, a second leukapheresis procedure may need to be performed.

Blood samples (also known as: PBMC) not required for cell selections may be archived for research.

Chemotherapy

The purpose of this chemotherapy is to cause a low lymphocyte (white blood cell) count in your blood (termed lymphodepletion), which has been found to help the infused T cells

survive and expand. We will use a chemotherapy regimen including cyclophosphamide and fludarabine because we have found in other studies using this regimen provides the best lymphodepletion and T cell growth.

Chemotherapy will be administered either at the Seattle Cancer Care Alliance (SCCA) or in the inpatient unit at the University of Washington Medical Center (UWMC) prior to each FH-MagIC TCR-T infusion. Risks associated with this chemotherapy are outlined in the 'Risks' section of this consent form and will also be addressed by the treating physician.

T cell infusion

We will assess your health 36-96 hours after the chemotherapy to make sure you are well enough to receive a T cell infusion.

Before you receive the T cell infusion, a blood test for research will be collected (60 ml, almost four tablespoons).

The T cell infusion will be given into a vein. If you have a central venous access device (Port-a-cath) or other similar device to access your veins, we will try to use that to give the T cells.

T-cell infusions and chemotherapies will be given at the Seattle Cancer Care Alliance or at the University of Washington Medical Center. All patients will be observed for 2 hours post infusion. If there is a need for hospitalization following the infusion, patients will be admitted to UWMC.

Atezolizumab - a PD-L1 axis inhibitor:

For a separate cohort of patients, you may receive an IV infusion of atezolizumab approximately every 3 weeks after your T-cell infusion. If an alternative FDA approved PD1-axis inhibitor is available for a patient, it may be substituted.

Each time you are due for an atezolizumab infusion we will assess your health to make sure you are well enough to receive the treatment. The atezolizumab infusions will be given into a vein. If you have a Hickman catheter or other similar device to access your veins, we will try to use that.

Follow-up

After treatment you will enter the active follow-up part of the study. In active follow-up, we will do these tests and procedures:

Tumor imaging studies. CT scans with or without PET scans should be performed 1 month after each T cell infusion, and then approximately 3 months, 6 months, 9 months and 12 months after the last T cell infusion. These tests are performed to restage your cancer to determine the effect of the T cell infusions. These tests are considered part of routine clinical care.

Neurological Testing: A neurological evaluation will be done prior to your first infusion of T cells and then approximately weekly for one month. The evaluation, which takes about 10-

15 minutes, is a series of simple questions and tests that provide important information about your nervous system.

Blood tests. After the T cell infusion, we would like to take blood samples to study the T cells. We plan to collect samples at the following approximate times and amounts after your T cell infusion. These samples will be used to monitor the effects of the T cell infusion. We may collect additional samples, up to 40 ml (almost 3 tablespoons), at other times to evaluate your medical condition after the treatment. Some of the samples will be stored for analysis later.

- At enrollment – 80 ml, about 5.5 tablespoons
- The day of the infusion - 40 ml, about 3 tablespoons
- One day – 50 ml, about 3.5 tablespoons
- Three days – 30 ml, about 2.5 tablespoons
- Seven days – 30 ml, about 2.5 tablespoons
- Fourteen days – 80 ml, about 5.5 tablespoons
- Twenty-one days – 40 ml, about 3 tablespoons
- Twenty-eight days – 50 ml, about 3.5 tablespoons
- Fifty-six days – 50 ml, about 3.5 tablespoons
- Eighty-four days –80 ml, about 5.5 tablespoons
- One hundred and eighty days – 80 ml, about 5.5 tablespoons
- Two hundred and seventy days – 80 ml, about 5.5 tablespoons
- Three hundred and sixty-five days - 80 ml, about 5.5 tablespoons

How long will I be in this study?

You will be actively participating in the study for approximately 15 months. The total time includes the time for the T cells to be made, the T cell infusion, and for approximately 12 months after the T cell infusion is given. All patients who receive treatment with FH-MagIC TCR-T cells should be followed for at least 15 years after the final infusion for safety evaluations in the LTFU portion of the study. The anticipated duration of the study, excluding LTFU assessments, is approximately 2 years.

The study doctor or your doctor may take you out of this study at any time, whether you want to leave the study or not. This would happen if:

- They think it is not in your best interest to continue in the study.
- You are unable or unwilling to follow study procedures.
- The Principal Investigator, the National Institutes of Health (NIH) or the Food and Drug Administration (FDA) stops the whole study.

If you are thinking about dropping out of this study, please tell the study doctor. The doctor can tell you about the effects of stopping. You and the doctor can talk about what follow-up care and testing would help you the most.

If you leave the study, your test results and information cannot be removed from the study records.

We would like to do long-term follow-up.

Long-term follow-up means keeping track of your medical condition for the rest of your life. Long-term follow-up is not the same as the one-year period for this research study. It begins when your active participation in this research study ends, one year after you received your T cell infusion.

The FDA requests that we ask people who receive an infusion of genetically modified T cells if they will participate in long-term follow-up for 15 years after they receive the genetically modified T cells.

Although we would like you to do long-term follow-up, you do not have to agree to be in long-term follow-up. You can say yes or no. Either way, you can still join this study. If you drop out of the study, we will ask again if we may contact you once a year.

If you choose not to join long-term follow-up, we will not contact you regularly after the study has finished, but we may still need to contact you for some other reason.

If you agree to do long-term follow-up we will call you or your provider on the telephone or send you or your provider a letter or survey once a year to see how you are doing. We may ask you to see your physician for a complete exam and to have a blood test twice a year for the first 5 years then once a year after that. This will help us learn about the long-term effects of the T cell infusions. It will also help us let you know about health information that is related to this study and might be important to you.

Request for autopsy - If you are a study participant, investigators may ask your family for permission to do an autopsy if you die, even though this may be years after the study. This may help investigators learn about the effects of treatment with genetically modified cells. By signing this consent form, you are not forcing your family to agree to this. You should talk about this request with your family and advise them of your wishes.

What are the side effects (risks)?

In this part of the consent form, we tell you the side effects we expect from the tests, chemotherapy and infusion of T cells in this study.

The procedures used to get T cells from the blood, to genetically modify them with lentivirus, and to give them to people are experimental. The FDA will only allow these procedures to be used in research studies and they are not part of standard treatment.

With any new treatment or combination of treatments, there may be side effects that we do not know about and cannot predict.

If we learn about other side effects, we will tell you. We carefully watch everyone in the study for side effects. If you want more information about side effects and risks, ask the doctor or nurse.

You should talk to your doctor about any side effects that you have while you are in this study.

If they occur, side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after the T cell infusion stops. However, sometimes side effects can last a long time or never go away. There is a risk of death if unexpectedly severe side effects occur.

Risks of study procedures

Where possible, we will schedule study blood tests and other procedures to take place at the same times as your regular clinical tests to minimize any risks and discomfort. If you have the tests done separately, the extra risks are as follows.

Blood tests

The risks of blood tests depend on whether the blood is taken by needle directly from a vein or from a device, such as a port or central venous access device, that stays in place for blood tests. If blood is taken from a central venous access device, there is usually no pain or bruising.

Likely side effects (≥ 20%) of blood tests are:

- Temporary discomfort if blood is taken straight from a vein.
- A small bruise or redness at the site from which the blood was taken.

Less likely side effects (3-20%) of blood tests are:

- Fainting, sweating or feeling sick in the stomach that gets better when you lie down and rest.
- Bruising larger than a quarter coin.

Rare but serious side effects (< 3%) of blood tests are:

- Infection from the blood test.
- Injury to blood vessels, nerves or other structures near the blood draw site.

Risks of leukapheresis

Likely side effects (≥ 20%) of leukapheresis are:

- Discomfort associated with the needle puncturing the skin and vein
- A small bruise or redness at the needle stick
- Temporary (1-2 days) decrease in your red blood cell count.
- Temporary (up to 4 hours) decrease in the clotting ability of your blood

Less likely side effects (3-20%) of leukapheresis are:

- Fainting, sweating or feeling sick in the stomach that gets better when you lie down and rest.
- Bruising larger than a quarter coin at the needle stick site.
- During the collection, you may experience stiff arms, chilling sensations, faintness, and muscle cramping in the jaw or fingers and/or tingling around the mouth.

Rare but serious side effects (< 3%) of leukapheresis are:

- Infection from the blood collection.
- Blood vessel disturbances from the needle irritating the vein.
- Injury to blood vessels, nerves or other structures near the needle stick site.
- Rarely, the muscle cramping during the collection may be severe.

Symptoms from the procedure can be reduced or eliminated by slowing the procedure or giving a calcium supplement, either by mouth or as an infusion.

If catheters cannot be placed in the blood veins in your arms to perform a leukapheresis, a central venous catheter will be needed. A separate consent form for the placement of that catheter will be required and will include a complete list of risks.

In general, while the central line is in place you have an increased risk of a local infection around the catheter, which sometimes leads to a generalized infection in the blood. If this happens you will be treated with antibiotics. Clotting in the catheter could also occur and may require the catheter to be removed or treatment with medicines that dissolve blood clots.

CT/PET Scans

Some of the tests that you will have in this research study will expose you to radiation. Everyone receives a small amount of radiation every day called “background radiation”. This radiation is natural and comes from space, air, water, soil, and the food you eat. Each year you are exposed to about 3 milliSieverts (mSv) of this background radiation. A milliSievert is a unit of radiation dose. For comparison, the estimated radiation dose from each of these tests is listed below.

- PET/CT: 19 mSv

Tumor Biopsy

Likely side effects (≥ 20%) of tumor biopsy procedures are:

- bruising
- pain or discomfort from where the needle punctures the skin.

Less likely side effects (3-20%) of tumor biopsy procedures are:

- Infection from the biopsy.
- Injury to blood vessels, nerves or other structures.

Rare but serious side effects (< 3%) of tumor biopsy procedures are:

- Serious reaction to the anesthesia drugs.

Chemotherapy

You will receive chemotherapy drugs prior to the T cell infusion with the preferred regimen of cyclophosphamide and fludarabine when possible. Giving chemotherapy before the T cell infusion is important to allow the transferred T cells to survive better in your body. The risks associated with these two drugs are outlined below.

Cyclophosphamide:

Likely side effects (≥ 20%) of cyclophosphamide:

- Nausea, vomiting, diarrhea
- Low white cells, which can increase your risk for infection
- Low red cells (anemia)
- Low platelets, which can increase your risk of bleeding
- Ulcers in the mouth and intestines
- Hair loss
- Disruption of menstrual cycle (women)
- Lower sperm count (men)

Less likely side effects (3-20%) of cyclophosphamide:

- Bladder irritation and bleeding
- Severe infection requiring hospitalization

Rare but serious side effects (< 3%) of cyclophosphamide:

- Heart damage
- Lung damage

- Confusion, coma
- Intestinal bleeding
- Liver damage
- Severe skin reaction
- Blurred vision
- Damage to bone marrow causing permanent inability to make normal blood cells
- Cancer of blood or bladder
- Death

Fludarabine:

Likely side effects (≥ 20%) of fludarabine:

- Low white blood cell count with an increased risk of infection (from bacteria, fungi or viruses)
- Lower platelet count with an increased risk of bleeding
- Anemia
- Nausea (feeling sick to your stomach)
- Vomiting
- Diarrhea (loose stools)

Less likely side effects (3-20%) of fludarabine:

- Fatigue
- Numbness and tingling in hands or feet
- Visual changes

Rare but serious side effects (< 3%) of fludarabine:

- Rash
- Confusion
- Coma (at high-doses)
- Pneumonia

Risks of receiving genetically modified T cells

There are risks associated with genetically modifying cells. There are also risks associated with treatment with T cells.

Risks of genetic modification of cells

The new gene is inserted into the DNA of the T cells using a virus called a lentivirus, which has been made in the laboratory. The lentivirus that we will use to insert the new gene into your T cells is experimental and the risks are not completely known. The FDA requires that the lentivirus be manufactured in highly specific conditions that allow it to be given to people. However, there are some risks associated with using lentiviruses to modify genes in cells.

Development of cancers or other diseases.

Researchers have wondered whether a transferred gene might sometimes land in a place in the DNA of a cell where it can cause harm. This appears to have happened in other studies in which five children who were treated with genetically modified blood stem cells subsequently developed leukemia. These children's stem cells were genetically modified using a virus called a 'retrovirus'. A group of experts found that the retrovirus caused the leukemia. These problems have not been seen in people who received T cells that were genetically modified with lentiviruses, the type of virus that we will use. Research studies suggest that these problems are less likely to occur with lentiviruses, but the exact risks are unknown.

Transfer of the lentivirus and new gene to unintended cells or people.

Lentiviruses used for genetic modification are made in a way that prevents the virus from reproducing. Although it has never been seen in people, it is possible that the lentivirus could change in a way that would allow it to reproduce itself. We do not know what the effects of this might be in people, but it is possible that the new virus could be passed to other cell types in the body, to other people with whom you have contact or to your children if they are conceived or born during or after T cell treatment. We will test for changes in the lentivirus, but the genetically modified T cells will be given to you before the results are available.

Risks of infusion with genetically modified T cells in this study

While T cells are being given it is very common for the recipients to have mild reactions that usually get better within 24 hours after the T cell infusion has finished. However, it is possible that unpredictable and unexpected severe or life-threatening reactions can occur during or after experimental T cell infusions. After T cell infusions patients may develop more serious complications associated with the TCR-T cell growth and possibly tumor killing.

Likely (≥ 20%) side effects of genetically modified T cell infusions include:

- Fevers
- Chills or shakes
- Temporary changes in blood pressure

- Cytokine release syndrome. After being given to patients with cancer, genetically modified T cells become activated, which allows them to kill cancer cells. This usually occurs between one day and three weeks after the T cell infusion, and can be mild, requiring observation in hospital, or severe and life threatening, requiring intensive care treatment. Cytokine release syndrome can cause high fevers, low blood pressure, or abnormal heart, lung, kidney or liver function. In some patients cytokine release syndrome is associated with confusion, seizures or stroke-like symptoms, such as speech impairment, loss of coordination or reduced strength.

  The symptoms of severe cytokine release syndrome may last for weeks, but usually improve when the T cells become less activated. If cytokine release syndrome is very severe, treatments to suppress the genetically modified T cells may be needed. Fatal cytokine release syndrome can occur.

- Neurotoxicity. In some patients neurotoxicity is associated with confusion, seizures or stroke-like symptoms, such as speech impairment, loss of coordination or reduced strength.

Less likely (3-20%) side effects of genetically modified T cell infusions include:

- Nausea or vomiting
- Pain
- Headache

Rare (< 3%) but serious side effects of genetically modified T cell infusions include:

- Risks due to genetic modification of T cells (see RISKS OF GENETIC MODIFICATION OF CELLS, above)
- Infection can be transferred by the T cell infusion. This sometimes causes no symptoms, but it can rarely cause severe and life-threatening problems.
- Severe allergic reactions to the materials used in the manufacture of the T cells rarely happen but can be very serious. Severe allergic reactions may occur during or shortly after the T cell infusion and can lead to breathing and blood pressure problems that might require intensive care treatment and life support.
- Reactions can occur as a result of the T cells rapidly killing the tumor cells and they might be seen close to the time of the T cell infusion or some weeks afterwards. These reactions sometimes cause kidney problems or blood acid disturbances due to toxins being released from the tumor cells.
- T cell infusion is an experimental procedure, and unexpected and unpredictable problems can occur that can be serious and could lead to death or permanent disability.

Macrophage Activation Syndrome

Macrophage activation syndrome (MAS) is a serious disorder potentially associated with uncontrolled stimulation and multiplying of TCR T cells and the subsequent stimulation

of macrophages (a type of white blood cell that consumes and digests cellular remains). Treatment with steroids and anti-cytokine drugs has been shown to improve the symptoms associated with MAS. Macrophage activation syndrome is a theoretical risk but has occurred with other modified T cell therapies.

Risk of damage to normal tissues expressing the MAGE-A1 antigen

The possibility of causing severe or even fatal toxicity from the effects of anti-MAGE-A1 TCR-T cells attacking normal tissues expressing the MAGE-A1 antigen are not known. You will be monitored closely for any side effects and treatment will be given to suppress TCR-T cell proliferation if severe unexpected toxicity is encountered.

Risks of Atezolizumab

You may experience none, some or all of those listed below. The side effects of treatment with atezolizumab may be enhanced by treatment with genetically-modified T cells.

More likely side effects (>10%):

Headache

Vomiting

Infections (generally mild), including skin infection, Upper respiratory tract infection (cold), pneumonia, and bone and joint infections)

Injection site reaction

Fever

Chills

Rigors

Less likely side effects (1% to 10%):

Nausea

Diarrhea

Decreased white blood cell count

Decrease or increase in platelet count

Rare side effects (<1%)

Hepatitis (noninfectious)

Hypersensitivity reaction (including anaphylaxis, angioedema, pruritus, skin rash, urticaria)

cancer

Side effects of unknown frequency:

Skin rash

High cholesterol level

Reproductive risks

You should not be in this study if you are planning a pregnancy soon. Because this is experimental research, we do not know what the risks due to infusion with genetically modified T cells might be in pregnant women. It is possible that unpredictable problems could occur in a pregnancy or baby that is conceived or born during or after you receive the T cell infusion.

For women:

- You should not become pregnant or nurse a baby while you are in this study and for 2 months after the infusion of genetically modified T cells.

For women and men:

- If you are having sex that could lead to pregnancy, you should use birth control while you are in this study and for 2 months after the infusion of genetically modified T cells.

Check with your doctor about birth control methods and how long to use them. Some common methods might not be appropriate while you are in this study.

- If you are planning a future pregnancy, discuss the options for storage of eggs or sperm before you begin this study. Loss of fertility can occur after chemotherapy. The additional effects of genetically modified T cell infusions on fertility are unknown.
- If you or your partner becomes pregnant while on this study you should notify the study doctors immediately.

Non-physical risks

This study involves growing T cells in a laboratory. Sometimes T cells do not grow well, which could mean that you might not be able to receive the T cell infusion even if you received the lymphodepleting chemotherapy. Your regular medical care would not be affected.

What are the benefits of participating in the study?

We hope this study will help participants by providing them with T cells that target and kill advanced triple negative breast cancer (TNBC), urothelial carcinoma, or non-small cell lung cancer (NSCLC), but we do not know if it will. Infusion with genetically modified T cells is experimental, and we are testing it to find the highest safe dose. We hope the information from this study will help us find out if genetically modified T cells can help patients with MAGE-AI specific cancers in the future.

You have other choices besides this study.

You do not have to join this study. You are free to say yes or no. Your regular medical care will not change.

If you do not join this study, you have other choices for treatment. Each of these choices has risks and benefits. Talk to your doctor about your choices.

Your other choices may include:

- Additional conventional chemotherapy, biologic therapies or hormonal therapy.
- Supportive care
- A different research study

Protecting your privacy as an individual and the confidentiality of your personal information

Some people or organizations may need to look at your research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- SignalOne Bio, Inc., the study financial supporter, and their agents.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Research Center IRB. An IRB is a group that reviews the study to protect your rights as a research participant.
- Fred Hutchinson Cancer Research Center, University of Washington, and Seattle Cancer Care Alliance.
- Office for Human Research Protections, Food and Drug Administration, and other agencies as legally required.

We will do our best to keep your personal information confidential. but we cannot guarantee total confidentiality. Your personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use your personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

In some cases, government agencies and medical journals may require us to make information about this study available to researchers outside of Fred Hutchin order to use or publish the results of this study. In that case, we will remove your Personal Information before making the study information available.

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.

If you join this study, information about your participation in this study such as the title of the study and the names of the researchers involved in the study will be made a part of your permanent medical record. This information would include a copy of this consent form. If an

insurance company, employer, or anyone else were authorized to see your medical record, they would see a copy of this consent form.

How is my genetic information protected?

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect your genetic information.

GINA restricts access to your genetic information so that it cannot be used for health insurance coverage decisions. GINA won't allow health insurance companies or group health plans to:

- ask for your genetic information you have provided in research studies.
- use your genetic information when making decisions regarding your eligibility or premiums.

GINA ***does not*** help or protect you against genetic discrimination by companies that sell life, disability or long-term care insurance.

Will you pay me to be in this study?

There is no payment for being in this study.

However, you or your caregiver are eligible for reimbursement of up to $3500.00 for travel expenses (i.e. airfare, mileage, parking and overnight accommodations) related to your participation in this study from the time of your consent to 30 days post your immunotherapy infusion.

SignalOne Bio, Inc. also has no plans to share with you any profits or other compensation that come from any of its research related to this study.

How much will this study cost me?

You or your insurer will have to pay for the routine costs of treating your cancer in this study. Check with your insurer before you join this study as some insurers will not pay for research. Taking part in the study may lead to extra costs for you or your insurance company because of the possibility of additional hospitalizations, procedures and blood tests.

The collection, production and infusion of the investigational T cells are paid for by SignalOne Bio, Inc.

Medical and psychological resources of the SCCA and UWMC will be available as standard care.

Should you choose to undergo research biopsy procedures, they will be conducted at no cost to you.

If you have any questions concerning your costs, financial responsibilities, and or medical insurance coverage for this activity, please contact the SCCA Patient Financial Services Department at (206) 606-6226.

What if I get sick or hurt in this study?

If you get sick or hurt in this study, tell the study doctor in person or call the SCCA Immunotherapy Clinic at (206) 606-6000.

Emergency medical treatment is available at the usual charge. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You will not lose your legal right to seek payment for treatment if you sign this form.

Financial interests of the center and certain center employees

Fred Hutchinson Cancer Research Center ("Fred Hutch") has filed a patent on the genetically modified T cells used in this study, and will receive royalty and other milestone payments from SignalOne Bio, Inc., the study financial sponsor. Fred Hutch will pay the scientists at Fred Hutch who were involved in the development of this process a share of payments received by Fred Hutch. These payments are required by Fred Hutch's Patents and Inventions Policy.

Fred Hutch also owns stock in (in other words, are part owners of) SignalOne Bio, Inc. which is the company that has licensed the rights to develop the genetically engineered T cells and is providing financial support for this study. Employees of Fred Hutch may also own stock in SignalOne Bio, Inc.

Certain employees of Fred Hutch provide consulting services to SignalOne Bio, Inc. and receive outside income for this work that is more than $10,000 per year. Other employees of Fred Hutch may in the future provide similar consulting services.

No individual Fred Hutch employee that has any of the interests described in this Section is or will be, allowed to be directly involved in the conduct or oversight of this study. It is possible that some Fred Hutch employees with interests described in this section will provide expert clinical or scientific advice to the study team if requested.

What will my information and/or tissue samples be used for?

Your information and tissue samples (such as blood and tumor cells) will be used for the purposes of this study.

Your tissue samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your tissue samples.

During this study, if the researchers learn new information that may be important to your general health or to your disease or condition, they will share that information with you.

In addition, be aware that by agreeing to participate in this study, your information or tissue samples and FH-MagIC TCR-T cell product made from your T cells but not used in the study, could be used for future research studies or sent to other investigators for future research studies without additional consent from you. These future research studies will be reviewed by an oversight group known as an institutional review board if required by law. The information that identifies you will first be removed from your information or tissue samples. If you do not want your information or tissue samples to be used for future research studies without your consent, you should not participate in this study.

Samples may be sent to SignalOne Bio, Inc. or other institutions for research testing, analysis, and other immunotherapy research related to this study and for product development related to the FH-MagIC TCR-T cells and similar products. Prior to sending any of these samples, personal information that could easily identify you, such as your name, age, date of birth and medical record number will be removed. These samples will be identified to the recipient by your study identification code. There will be no cost to you for any of the independent testing and analysis of these samples. Data from this testing and analysis will not be part of your medical record and will not be provided to you.

Your rights

- You do not have to join this study. You are free to say yes or no. Your regular medical care will not change.
- If you join this study, you do not have to stay in it. You may stop at any time (even before you start). There is no penalty for stopping. Your regular medical care will not change.
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.
- During the study, we may learn new information you need to know. For example, some information may affect your health or well-being. Other information may make you change your mind about being in this study. If we learn these kinds of information, we will tell you.

For more information

If you have questions or concerns about this study, you may talk to your doctor anytime. Other people you can talk to are listed here.

If you have questions about:	**Call:**
This study (including complaints and requests for information)	206-667-3403 (Monica Dherin, CRC)
If you get sick or hurt in this study	206-606-6000 (SCCA Immunotherapy Clinic)
Your rights as a research participant	206-667-4867 (Director of Institutional Review Office, Fred Hutchinson Cancer Research Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	206-606-6226 (SCCA Patient Financial Services)

Emergency number (24 hours): 206-598-8902

We would like you to donate some of your tissue samples for other future research.

During the study, samples of blood, bone marrow, tumor biopsies you agree to provide, other tissue, and T cells may be collected from you, and FH-MagIC TCR-T cells may be made from your T cells, as described above. We refer to these materials as "samples." After we do tests on your samples in this study, some samples may be left over. We would like you to donate these leftover samples for future research. This may include genetic research.

You do not have to donate your tissue for research. You are free to say yes or no. Your regular medical care will not change. If we want to use your tissue for other research or share it with other scientists for research, an ethics review committee (IRB) will review the request. The IRB will decide if we need to ask for your consent to do the research.

Your donated tissue will be stored in a secure location. and will be used for research and for other studies that might help to develop new treatments. These future research and drug development studies may be done by us at FHCRC or by for-profit companies including SignalOne Bio, Inc. which funded this study, and its collaborators. Researchers will not report their results to you or your doctor. The research results will not appear in your health record. They will not affect your care.

Research on your tissue may help develop new products. If these products make money, there is no plan to share the money with you.

If you donate your tissue for research, you can change your mind anytime. Just call Dr. Michael Schweizer at 206-606-6252 and tell us you do not want us to use your tissue. There is no penalty for changing your mind. Your regular medical care will not change. However, if you do change your mind, we cannot return donated tissue. We may be able to destroy tissue we know is yours. But if it is stored or shared anonymously (without any label saying who it belongs to), we cannot destroy it. In this case it would still be used for research, but no one would know it was yours

Read each question and think about your choice. When you decide on each question, please circle **YES** or **NO**.

Do you agree to donate your samples to study cancer and related diseases? (circle and initial one) **YES** **NO**

Do you agree to donate your samples to study other health problems, such as diabetes, Alzheimer's disease, or heart disease? (circle and initial one) **YES** **NO**

Is it OK if someone contacts you in the future to ask you to donate more samples for research? (circle and initial one) **YES** **NO**

Read the statements below and initial next to the one that applies to you:

_____ I AGREE to have a tumor biopsy to provide tumor for research.
_____ I DECLINE to have a tumor biopsy to provide tumor for research.

Signature

If you have read this form (or had it read to you), asked any questions, and agree to participate, please sign:

Participant printed name (18 years or older) Date

Participant signature

If you served as an interpreter or witness during the consent process, sign below to indicate you attest to the accuracy of the presentation to the participant and the apparent understanding of the research by the participant.

Witness or Interpreter / Printed Name, Signature, and Date

Researcher's statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Person obtaining consent printed name Date

Person obtaining consent signature