PHASE 2 STUDY OF AUTOLOGOUS T CELLS ENGINEERED TO EXPRESS AN ANTI-CD19 CHIMERIC ANTIGEN RECEPTOR (CART-19) FOLLOWING FIRST-LINE AUTOLOGOUS STEM CELL TRANSPLANTATION FOR HIGH-RISK MULTIPLE MYELOMA

INFORMED CONSENT FORM AND HIPAA AUTHORIZATION

NCT02794246

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University of Pennsylvania
Research Participant
Informed Consent Form and HIPAA Authorization

Protocol Title:	**Phase 2 Study of Autologous T Cells Engineered to Express an Anti-CD19 Chimeric Antigen Receptor (CART-19) Following First-line Autologous Stem Cell Transplantation for High-risk Multiple Myeloma**
Principal Investigator:	[redacted]
Emergency Contact:	***Ask for Oncologist on Call*** ***215-662-4000***

Why am I being asked to volunteer?

You are being invited to participate in this research study because you have a form of blood cancer called multiple myeloma. This is a cancer of plasma cells in which abnormal plasma cells grow excessively in the bone marrow and occasionally in other parts of the body. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you would otherwise be entitled.

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 inviting you to participate in a research study. 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 is a research study for people who are receiving treatment for multiple myeloma and whose physician has recommended autologous stem cell transplant (ASCT) as the next step in their therapy. Multiple myeloma is a blood cancer caused by the overgrowth of plasma cells, which are a type of white blood cell and are part of your immune system. In an ASCT, a patient's own blood-forming stem cells are collected. He or she is then treated with a high dose of a chemotherapy called melphalan. The high-dose melphalan kills cancer cells, but also eliminates the blood-producing cells that are left in the bone marrow. Afterward, the previously collected stem cells are transplanted back into the patient, allowing the bone marrow to produce new blood cells and recover from the high dose of melphalan. ASCT is a standard therapy for multiple myeloma. ASCT is typically recommended for young and otherwise healthy multiple myeloma patients who have completed several months of first-line therapy.

This research study will take some of your own white blood cells (called T cells) and modify them. The modification is a genetic change, or gene transfer, to your normal T-cells. These modified cells are called CART-19 T-cells. The use of CART-19 T-cells is experimental and has not been approved by the Food and Drug Administration (FDA). On this study, CART-19 T-cells will be given back to you through a single infusion about two months after your ASCT. CART-19 T-cells are designed to identify and kill a type of white blood cell called a "B-cell." In multiple myeloma patients, B-cells may help multiple myeloma plasma cells grow. By eliminating B-cells, CART-19 T-cells may help control your multiple myeloma after ASCT. It is not known, however, whether CART-19 T-cells will eliminate B-cells, and it is not known whether eliminating B cells will help control your multiple myeloma. CART-19 T-cells are not expected to directly kill your multiple myeloma plasma cells.

The main purpose of this study is to evaluate the effect of CART-19 T-cells on your disease and further assess the safety of CART-19 T-cells when given to patients after ASCT.

At this time, we do not know the best and safest CART-19 T-cell dose. A CART-19 T-cell dose has been planned for this research study, but it is possible that a lower dose could be effective. If the full planned study dose cannot be made in your case, the study physicians may recommend that you receive the lower T-cell dose that has been made, if they feel it is safe and poses no additional risk to you. The study doctors will inform you if the full, planned CART-19 T-cell dose could not be made in your case. If you decide not to receive a lower T-cell dose than planned by the research study, you will no longer be able to participate in this research study. If you 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.

How long will I be in the study?

If you choose to participate in this research study, your participation will take approximately 2 years from screening to the end of the study.

How many other people will be in the study?

It is expected that about 25 people with multiple myeloma will receive CART-19 T-cells as part of this research study, and all will be treated 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 agreeing to participate in this research study, you and your doctor should discuss the current standard treatments for your cancer. The study doctor or a trained member of their staff 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 research study, you will be required to undergo the following tests and evaluations:

Day	Part of Your Standard Medical Care?	Procedures
Screening Enrollment Phase	No	These procedures will check to see if you are eligible to participate in the study and will take approximately 1-2 hours. • Examination of your veins in your arms will be checked by the apheresis unit in order to make sure your veins are adequate to perform the apheresis procedure. • Blood for research analysis- this requires a blood draw of about 1 teaspoon.
	Yes	• Review of your relevant medical history, current medical conditions, and list of medications • Physical examination including an assessment of your vital signs (temperature, blood pressure, heart rate, and blood oxygen levels), height and weight • Routine blood tests- 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), HIV, hepatitis B, and hepatitis C. This requires a blood draw of about 1 tablespoon. • Blood/urine pregnancy test- if you are female and able

Day	Part of Your Standard Medical Care?	Procedures
		to bear children. If a blood test is performed, this requires a blood draw of about 1 teaspoon. • MUGA (Multi Gated Acquisition Scan)/Echocardiogram test- to assess your heart function • Electrocardiogram (EKG) • Pulmonary function test- to measure how well your lungs are working.

Reporting of a positive HIV, hepatitis B and hepatitis C test: As indicated above, 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 infection to the City of Philadelphia Health Department/PA Department of Health. We would report your name, gender, racial/ethnic background, and the month and year you were born.

Once you have completed the screening visit, your study doctor will determine whether it is safe for you to enter 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 and vitamins. This is very important. • Tell your study doctor or study staff if you have any unusual symptoms any time, even outside the visit period.		
Apheresis After enrollment and prior to ASCT	No	Apheresis 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. This apheresis visit will take ~4 hours in total and the apheresis procedure will take ~ 3 hours to complete.

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 will use your T-cells collected from the other study if they are acceptable to make your CART-19 T-cells for this study. If the veins in your arms are not adequate for the procedure, a special apheresis catheter may be inserted into the large vein in your neck for the collection. At this visit, the following procedures will be performed: • Review of current medical conditions and list of medications • Routine blood tests- requires a blood draw of about 1 teaspoon. • Blood for research analysis- requires a blood draw of about 2 tablespoons. • Vital signs (temperature, blood pressure, heart rate, and blood oxygen levels)
Pre-ASCT Within 4 weeks prior to your ASCT	No	At this visit, the following procedures will be performed: • Blood for research analysis- this requires a blood draw of about 2 tablespoons.
	Yes	• Skeletal survey ○ Additional imaging studies (i.e. CT scan, etc.) to be performed per routine care if felt to be clinically appropriate. • Bone marrow biopsy/aspirate- to assess your disease and measure the myeloma cells in your bone marrow. Part of this bone marrow sample (about 2 teaspoons) will also be used for research purposes. • Blood tests to measure your myeloma protein levels (requires about 2 teaspoons of blood). • 24 hour urine sample to measure myeloma protein levels in the urine. • Routine blood tests- to assess your blood cell counts and blood chemistry levels. This requires a blood draw of about 1 tablespoon.

Day	Part of Your Standard Medical Care?	Procedures
		• Autologous stem cell collection- your bone marrow stem cells will be collected. This process entails administration of medications to move the stem cells from your bone marrow to your bloodstream, and additional apheresis procedures to remove the stem cells from your body. Your doctor will choose the combination of medications you will receive and the number of apheresis procedures you will undergo. This procedure is required prior to ASCT and would be performed even if you were not participating in this study.
Autologous Stem Cell Transplant (ASCT) Day -2 to 0	Yes	You will be admitted to the Hospital of the University of Pennsylvania for your autologous stem cell transplant. Routine hospital admission procedures will be performed. Melphalan chemotherapy will be administered 1-2 days prior to your stem cell transplant per routine care. The purpose of the melphalan chemotherapy is to kill the multiple myeloma plasma cells prior to your transplant. One to two days after you receive melphalan chemotherapy, your autologous stem cells that were previously collected will be given back to you by intravenous infusion.
Pre-Infusion Approximately 1 week prior to your CART-19 T-cell infusion	No	These procedures will take approximately 2 hours. • Bone marrow biopsy/aspirate- to assess your disease and measure the myeloma cells in your bone marrow. Part of this bone marrow sample (about 2 teaspoons) will also be used for research purposes. • Blood will be collected for clinical lab tests (to evaluate how fast your blood clots and to assess whether you have any active infections) and for research analysis. This requires a blood draw of about 2 ½ tablespoons. • Pregnancy test- if you are female and able to bear children. If required, this requires a blood draw of about 1 teaspoon. • A Respiratory Virus Panel (RVP) to test for the flu will be performed ~ 10 days prior to infusion of your T cells –

Day	Part of Your Standard Medical Care?	Procedures
		this test involves swabbing of your throat and nostrils using a cotton swab. ○ 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 a course of this medication. ○ If your RVP test is positive and you have flu symptoms you will need to complete a course of Tamiflu and all clinical symptoms must be resolved before you can receive your T cells.
	Yes	• Review of current medical conditions and list of medications • Physical examination including an assessment of your vital signs • Skeletal survey ○ Additional imaging studies (i.e. CT scan, MRI, etc.) to be performed per routine care if felt to be clinically appropriate. • Blood tests to measure your myeloma protein levels (requires about 2 teaspoons of blood). • 24 hour urine sample to measure myeloma protein levels in the urine. • Routine blood tests- to assess your blood cell counts and blood chemistry levels. This requires a blood draw of about 1 tablespoon.
Chemotherapy Visit Approximately 3 days before your CART-19 T-cell Infusion	No	You will receive a dose of chemotherapy called cyclophosphamide prior to your CART-19 T-cell infusion. The purpose of the chemotherapy is to "make room" to help the CART-19 T-cells expand and grow in your body. Cyclophosphamide is given intravenously (through a vein in your arm), and you will also receive nausea medications and intravenous fluids before and after the cyclophosphamide infusion. At this visit, the following procedures will also be performed. The entire visit will last about 4 hours. • Blood tests- to assess your blood cell counts and blood

Day	Part of Your Standard Medical Care?	Procedures
		chemistry levels. This requires a blood draw of about 1 tablespoon.
	Yes	• Review of current medical conditions and list of medications • Physical examination including an assessment of your vital signs
CART-19 T-cell Infusion Approximately 60 days after your stem cell transplant.	No	1-4 days after you completed chemotherapy your modified CART-19 T-cells will be given back to you in your vein. Some people can get sick from the chemotherapy side effects so your doctor will need to examine you and may choose to delay your CART-19 T-cell infusion until you feel better. Your CART-19 T cell infusion will be given as one infusion. In order to reduce potential side effects of the CART-19 treatment, you may also receive acetaminophen (e.g., Tylenol) and/or diphenhydramine (e.g., Benadryl), prior to this infusion. The CART-19 T-cells will take 20 minutes or less to go into your vein. You will also undergo the following assessments: • Review of current medical conditions and list of medications • Physical examination and vital signs (temperature, blood pressure, heart rate, and blood oxygen levels) will be taken before, during, and after each infusion, and then about every 15 minutes for 1 hour, and then at 2 hours and 3 hours or until satisfactory and stable after the infusion. • Blood tests- to assess your blood cell counts and blood chemistry levels. This requires a blood draw of about 1 tablespoon. • CART-19 T-Cell infusion • Blood for research analysis- collected before and approximately 1-2 hours after the CART-19 T- cell infusion (~ 4 tablespoons) You will be allowed to go home if, 3 hours after your

Day	Part of Your Standard Medical Care?	Procedures
		infusion, you feel well and have not experienced unexpected reactions to the infusion.
Post CART-19 Infusion Follow-up Days 64, 67, 70, 74, and 81	No	• Blood for research analysis including tests for detection of CART-19 T-cells (requires a blood draw of about 2 tablespoons) • <u>Day 64, Day 67 and Day 70 visits only</u>: ○ Routine blood tests- blood cell counts and blood chemistry levels. This requires a blood draw of about 1 tablespoon.

	Yes	• Review of your current medical conditions and list of medications
		• Physical examination including an assessment of your vital signs
		• <u>Day 74 and Day 81 visits only</u>:
		  ○ Routine blood tests- blood cell counts and blood chemistry levels. This requires a blood draw of about 1 tablespoon.
		• <u>Day 74 only</u>:
		  • Blood tests to measure your myeloma protein levels (requires about 2 teaspoons of blood).
		  • 24 hour urine sample to measure myeloma protein levels in the urine.

Post Infusion Day 88 (approximately 1 month after your CART-19 infusion)	No	The following procedures will be done: • Blood for research analysis including tests for detection of CART-19 T-cells (requires a blood draw of about 4 tablespoons).
	Yes	• Review of your current medical conditions and list of medications • Physical examination including an assessment of your vital signs • Routine blood tests- blood cell counts and blood chemistry levels. This requires a blood draw of about 1 tablespoon. • Blood tests to measure your myeloma protein levels (requires about 2 teaspoons of blood). • 24 hour urine sample to measure myeloma protein levels in the urine.

Day	Part of Your Standard Medical Care?	Procedures
		• Approximately 90 days after your stem cell transplant (about 1 month after your CART-19 infusion), your study doctor will discuss starting oral lenalidomide (a pill) as a maintenance treatment. This is done because studies have shown that uses of medicines like lenalidomide may help to keep the myeloma under control longer after transplant. Lenalidomide is approved for use in your disease after stem cell transplant and will be administered per routine care.
Post Infusion Month 4	No	• Blood for research analysis including tests for detection of CART-19 T-cells (requires a blood draw of about 2 tablespoons)
	Yes	• Review of current medical conditions and list of medications • Physical examination including an assessment of your vital signs • Routine blood tests- blood cell counts and blood chemistry levels. This requires a blood draw of about 1 tablespoon. • Bone marrow biopsy/aspirate- to assess your disease and measure the myeloma cells in your bone marrow. Part of this bone marrow sample (about 2 teaspoons) will also be used for research purposes. • Skeletal survey ○ Additional imaging studies (i.e. CT scan, MRI, etc.) to be performed per routine care if felt to be clinically appropriate. • Blood tests to measure your myeloma protein levels (requires about 2 teaspoons of blood). • 24 hour urine sample to measure myeloma protein levels in the urine.
Post Infusion Months 5, 6, 8, 11, 14 + 17	No	• Blood for research analysis including tests for detection of CART-19 T-cells (requires a blood draw of about 2 tablespoons)
	Yes	• Review of current medical conditions and list of medications • Physical examination including an assessment of your

Day	Part of Your Standard Medical Care?	Procedures
		vital signs • Routine blood tests- blood cell counts and blood chemistry levels. This requires a blood draw of about 1 tablespoon. • Blood tests to measure your myeloma protein levels (requires about 2 teaspoons of blood). • 24 hour urine sample to measure myeloma protein levels in the urine.
Post Infusion Month 20	No	• Blood for research analysis including tests for detection of CART-19 T-cells (requires a blood draw of about 2 tablespoons)
Post Infusion Month 24	No	• Blood for research analysis including tests for detection of CART-19 T-cells (requires a blood draw of about 2 tablespoons)
	Yes	• Review of current medical conditions and list of medications • Physical examination including an assessment of your vital signs • Routine blood tests- blood cell counts and blood chemistry levels. This requires a blood draw of about 1 tablespoon. • Bone marrow biopsy/aspirate- performed if determined to be clinically appropriate by your study doctor. Part of this bone marrow sample (about 2 teaspoons) will also be used for research purposes. • Skeletal survey ○ Additional imaging studies (i.e. CT scan, MRI, etc.) to be performed per routine care if felt to be clinically appropriate. • Blood tests to measure your myeloma protein levels (requires about 2 teaspoons of blood). • 24 hour urine sample to measure myeloma protein levels in the urine.

You will be required to travel to the Hospital of the University of Pennsylvania for each of the study visits. Once you have had your CART-19 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 telephone by a member of the study team to assess any potential toxicity.

Additional Research Samples: 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 likely effects from the CART-19 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-specified time points.

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.

Long-Term Follow-Up Study: After you complete this research study, you will be asked to enroll in a separate long-term follow-up research study that will look for possible side effects of the gene modified CART-19 T-cells. If you choose to participate in the long-term follow-up research study, you will sign a new separate consent form. The long-term follow-up research study will consist of semi-annual evaluations (every six months) for up to five years followed by annual evaluations thereafter for up to 10 more years.

The purpose of this long-term follow-up study is to monitor the health status of individuals, such as you, who received their own cells that had been changed using a lentiviral vector (also known as gene-modified cells). The Food and Drug Administration (FDA) has issued guidelines requiring long-term follow-up for up to 15 years of all subjects who received gene therapy. The long-term follow-up study is an important in monitoring you for development of a new cancer and Replication Competent Lentivirus (RCL). Both are very rare, unexpected events and are described in more detail in the "What are the possible risks or discomforts?" section that follows.

Request for Autopsy:
In order for the study doctors to learn more about your disease and the safety and function of the CART-19 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?

The list of side effects below contains the most common side effects seen in people that have received CART-19 T-cells (over 200 adults and children as of August 2016). This research may involve risks that are currently unforeseeable, so 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 at any signs of fever or other new abnormal symptoms. Treatment on this research study may have risks we don't know about and may require you to go into the hospital so the study team can monitor these side effects.

The following side effects may be observed with CART-19 T-cells. 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.

More Common:

Significant Decrease in B-Cell Counts:
CART-19 kills cancerous B-cells but can also kill normal B-cells. This happens because CART-19 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.

Infusion Reactions:
Like other types of transfusions, the infusion of T cells can cause a reaction. This can include:

- Fever
- Chills
- Nausea
- Hives or other rashes
- Changes in blood pressure
- Altered taste: one of the ingredients in the product may lead to an unusual taste in your mouth and odor to your breath; this is temporary and may last 1-2 days post infusion.

Cytokine Release Syndrome (CRS)/Macrophage Activation Syndrome (MAS):
Rapidly growing activated CART-19 T-cells release proteins and chemicals called cytokines. Release of large amounts of certain cytokines can cause a “cytokine release syndrome”.

Macrophage activation syndrome is an activation of your immune system associated with the cytokine release syndrome. Cytokine release syndrome can cause a severe flu-like syndrome. Symptoms of this severe flu-like syndrome 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 requiring dialysis. People can also have trouble breathing and dangerously low blood pressure. Some people need to be treated with a ventilator (a breathing machine). Many people with severe flu-like syndromes have had to be cared for in an intensive care unit at the hospital. This reaction 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 the cytokine release syndrome and macrophage activation syndrome (steroid treatment or other medicines). Unfortunately, these medicines could get rid of the CART-19 T-cells and prevent them from working. The best time to administer medications to treat the cytokine release syndrome and macrophage activation syndrome is not currently known. In addition, these medications may weaken the immune system increasing the chance for potential serious infections (including but not limited to pneumonia).

In addition, some participants 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 some instances, these problems resolved when we treated the participants with medications that reverse the cytokine release syndrome.

Significant decreases in blood counts, including neutropenia (low white blood cell count), anemia (low red blood cell count), and thrombocytopenia (low platelet counts) are routinely seen. This will be related to the chemotherapy you receive prior to the CART-19 infusion, and may be related to the CART-19 infusion as well. 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.

<u>Possible risk of neurological side effects</u>:
The use of CART-19 T-cells may cause side effects that affect your nervous system including:

- Headache
- Difficulty speaking (aphasia)
- Delirium, confusion, decreased alertness- which may be mild to severe
- Hallucinations
- Seizures (uncontrollable shaking/convulsions)
- 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 and bleeding in the brain

Typically these events have been associated with cytokine release syndrome/macrophage activation syndrome (CRS/MAS) as described above, however patients have also experienced neurological side effects that are not associated with CRS/MAS which may be related to CART-19 T-cells or other factors related to their disease or care. While most neurological side effects have improved, there is a possibility that you will experience side effects that will not improve and may result in death.

Additional Risks (Less Common):
If your T-cells grow rapidly it is possible that the CART-19 T-cells will multiply in your body. This can be a good thing. However, it is possible that the growth of the CART-19 T-cells will be excessive, in which case your doctor may wish to kill the CART-19 T-cells. This can be done by giving drugs called corticosteroids. If the CART-19 T-cell growth is not controlled by the corticosteroid treatment, your doctor will recommend chemotherapy, similar to what is usually administered for your tumor.

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 cells.

Tumor Lysis Syndrome:
Tumor lysis syndrome 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.

Additional risks:

Autologous Graft-vs-Host Disease (GVHD): In prior studies in which activated T cells were given after ASCT for multiple myeloma, some patients (approximately 15%) developed a syndrome of fever, rash, and/or diarrhea called autologous GVHD. Autologous means that the cells collected are collected from the same person who receives the cells. This syndrome is due to T cells causing inflammation in the skin or gastrointestinal tract. Autologous GVHD can occur after ASCT even without additional infusion of activated T cells, but activated T cells seem to increase the risk of autologous GVHD. Treatment of autologous GVHD may require the use of medications called steroids. Steroids may kill CART-19 cells or prevent them from working as intended.

Potential risk of autoimmune disease:
The use of CART-19 T-cells could potentially result in an illness which doctors call "autoimmune disease". Our bodies have an immune system that protects us from disease and infection. When you have an autoimmune disease, your immune system attacks your body by mistake and you can get sick. 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.

Potential risk of other cancers:
There is a chance that the insertion of the CAR gene into some regions of your DNA may activate a neighboring gene or genes. Depending on the type(s) of neighboring gene(s) activated, there may be a risk of uncontrolled cell growth that could result in cancer. We do not know if and what specific genes may be activated by integration of the lentivirus vector used in this protocol and if these would cause a new cancer.

Cancers due to a type of viral vector different than that used in this protocol has occurred in a gene transfer research study conducted in France. Several children with a disease called X-linked Severe Combined Immunodeficiency (SCID) that received gene modified cells developed a leukemia-like malignant disease (cancer) due to the vector DNA. Some that developed the leukemia were successfully treated while others were not. However, most of the children with X-linked SCID who received gene modified cells have not developed a leukemia-like disease.

While this risk is rare, 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.

Other cancers have been observed in patients who have received CAR Therapy. The relationship to the CAR therapy is not known at this time.

Potential risks associated with a Replication Competent Lentivirus or "RCL":
The lentiviral vector that is used to transfer the CART-19 gene 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 with the CART-19 or another gene modified T cells using lentiviral vector has developed an RCL.

To minimize the possibility of you developing an RCL, the lentiviral vector and the CART-19 T-cells will both be tested for RCL. You will also be monitored throughout the study for RCL. If the test used to detect components of a RCL is positive during any of these visits, you will be notified and requested to return for additional blood tests for your safety. A single positive

blood test does not mean that you have an active RCL. However, if your blood tests for RCL continue to remain positive, you will undergo additional testing to determine whether or not you have developed an active RCL. During this time, you will be closely monitored in the clinic. Should the additional testing show that you have an active RCL, medical and research experts will work with you to design the best care available based upon your health.

Potential risks associated with HIV:
The lentiviral vector that is used to transfer the CART-19 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 HIV positive.

Risks associated with 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 CART-19 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 CART-19 T-cells, and that this may result in the loss of CART-19 T-cells from your body.

Development of anti-mouse antibodies may prevent you from getting other therapies that use mouse derived antibodies in the future.

Reproductive risks:
The effects of CART-19 on pregnancy and child development are unknown. Therefore, there could be serious harm to unborn children (or children who are breast-feeding) and it could also jeopardize the health of the mother.

If you are capable of becoming pregnant, you will undergo a pregnancy test prior to entry into the research study and again prior to your CART-19 T-cell infusion. If you are found to be pregnant or breast-feeding at that time you will not be allowed to participate in the research study.

If you are a female participant in the study and are capable of becoming pregnant, you MUST use at least one method of birth control during the entire time you participate in the study, including long-term follow-up. If you are male, you MUST use at least one method of birth control during the entire time you participate in order to avoid impregnating a female.

Examples of highly effective birth control methods include any of the following:

- Total abstinence (no sexual relations)
- Female sterilization- surgical removal of both ovaries (woman's 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 (i.e. vasectomy)
- Condoms (male or female) with or without a spermicidal agent
- Diaphragm or cervical cap with spermicide
- An 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 be taken off the research study. Your study doctor will follow your pregnancy until outcome to monitor your safety.

If you are a male participant and your partner becomes pregnant, you must tell the study doctor as soon as possible.

The following side effects may be observed following cyclophosphamide administration:

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 (in ability to have children)
- Acute hemorrhagic cystitis (inflammation of the bladder causing blood in the urine)

Less common (1-10%):

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

Risks associated with apheresis (uncommon):
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, you will be given a drug called ACD (acid-citrate-dextrose). 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: nausea, vomiting, fainting, seizures, blood loss, infection, skin rash, flushing, hives, numbness and tingling, or swelling of your feet and ankles.

Risk of bone marrow biopsy/aspirate:
This procedure is commonly done to diagnose or monitor subjects with blood and bone marrow diseases. It is important for you to be aware of the following risks:

- Discomfort or bruising at the biopsy site, which often lasts for 1-4 days after the procedure.
- Bleeding from the biopsy site, which is usually only a small amount that has stopped by the end of the procedure. More serious bleeding is possible but happens rarely.
- Pain, redness or swelling at the biopsy site. Some pain may be long-lasting.
- Infection at the biopsy site, which is very rare.
- Rarely, the biopsy needle damages other nearby structures
- The aspiration needle may break within the bone and cause infection or bleeding, or enter (penetrate) the breastbone (sternum) during sternal aspirations and cause heart or lung problems.

Risks associated with blood draws (uncommon):
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 54 ½ tablespoons (about 3 ½ cups) of blood will be drawn for research purposes during your participation in this study.

Risks associated with 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).

Risks of autologous stem cell transplantation:
ASCT is a standard therapy for multiple myeloma that your doctor has recommended that you receive, whether or not you decide to participate in this study. Therefore, the risks of ASCT are not particular to this study. Nonetheless, it is important that you understand the risks and potential toxicities of ASCT. Your study doctor will review these with you, and you will be asked to sign a separate informed consent document that outlines the risks and potential toxicities of autologous stem cell transplant. Some of these risks are potentially fatal, but the overall risk of dying due to complications of ASCT is low, <3%. CART-19 T cells are not expected to increase or decrease the risks associated with ASCT.

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.

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

Your other choices may include:

- Getting treatment or care for your leukemia 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. This includes the cost of your CART-19 infusion and the pre-infusion cyclophosphamide.

This research study also requires that you receive certain standard medical tests/procedures 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. This includes all costs related to your stem cell transplant including the pre-transplant melphalan chemotherapy, your hospital stay, and any associated tests/procedures. 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 study?

All side effects, injuries or illnesses that occur while you are taking part in this 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 his/her 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.

The University of Pennsylvania will offer you the care needed to treat side effects and/or injuries that occur while you are 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.

Research-related injuries or illnesses that occur while you are taking part in this research study: In the event of a bodily injury or illness directly resulting from the CART-19 T-cells or a medical procedure required for this study, Novartis, will cover the cost of all reasonable, unreimbursed, and necessary medical expenses to treat this injury or illness. Novartis will not provide payment for injuries unrelated to the research study, or which are a result of your underlying disease or any pre-existing medical conditions. If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.
You may receive bills for the care of injuries/illnesses that occur during your participation in this study. If you have questions about these bills, contact the study team. Provide them with copies of these bills so they can inquire if these costs are covered by the research study.

Financial compensation for such things as traveling, parking, lost wages, disability or discomfort due to injury will not be provided.

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. This research study may also be stopped at any time by your physician, the study Sponsor, study Funder or the Food and Drug Administration (FDA) without your consent because:

- The Primary 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, Study Funder, 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. Withdrawal will not interfere with your future care.

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

The investigator and staff involved with the study will keep your personal health information collected for the study strictly confidential. 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.

Electronic Medical Records and Research Results

What is an Electronic Medical Record and/or a Clinical Trial Management System?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.
A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research

study. The creation of this EMR is required for your participation in this research study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Information related to your participation in the research study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

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

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*. 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.

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
- Information from a physical examination that generally also includes blood pressure reading, heart rate, breathing 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.

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 Investigator's study team

- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.).
- Authorized members at the University of Pennsylvania, School of Medicine who coordinate this study and support research operations.

Who, outside of the School of Medicine, might receive my information?

- The funding sponsor (Novartis Pharmaceuticals) and its 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 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 the School of 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 University of Pennsylvania procedures developed to protect your privacy.

How long may the School of 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, the School of 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.

How will my research samples be used and stored for the purposes of this study?

As outlined above, you will have blood and tissue samples collected as part of your participation in this research study. These samples will be stored at the University of Pennsylvania for research purposes. Your authorization for the use and storage of your research samples does not expire. However, you may withdraw or take away your permission to use and store these samples at any time. After your participation in this study has ended and all research analysis on these samples is complete, these samples may be destroyed at any time without notice.

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

[redacted]

Informed Consent Form and HIPAA Authorization

Phase 2 Study of Autologous T Cells Engineered to Express an Anti-CD19 Chimeric Antigen Receptor (CART-19) Following First-line Autologous Stem Cell Transplantation for High-risk Multiple Myeloma

[redacted]

[redacted]

[redacted]

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

A copy of this Informed Consent Form and HIPAA Authorization will be given to you. By signing this document you are permitting the School of Medicine 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

About Using Blood and Tissue for Research

In addition to the research study and the analysis of blood and tissue outlined above, researchers are also interested in using blood, tissue, fluid, remaining unmanufactured T-cells (from your apheresis collection), unused manufactured CART-19 T-cells or other specimens that may be obtained from you while you are participating on this research study. Research tests may be developed during the time you are on the research study or, in some cases, years later. We ask that you give approval for these tests to be performed using these specimens. Because it is not possible for you or the researchers conducting this research study to know what will be discovered in the future and what additional tests may be appropriate at that time, we ask that you give your permission to 1) use these additional samples for future research; and 2) conduct studies on them in the future without your being contacted for permission for each test. These tests may provide additional information that will be helpful in understanding your disease or response to treatment and/or cancer, but it is unlikely that what we learn from these studies will have a direct benefit for you. These studies may benefit patients in the future. You will not receive the results of any testing performed on your samples.

Additional research on your samples in the future will also 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.

In addition, blood, tissue, fluid, unmanufactured or manufactured CART-19 T-cells or other specimens obtained from you may be used to establish products that could be patented or licensed. There are no plans to provide financial compensation to you should this occur.

Samples will be stored indefinitely. Researchers involved in this research study at the Abramson Cancer Center, the University of Pennsylvania and Novartis will have access to the specimens. These specimens may be used to conduct pilot (new) studies regarding your disease or regarding your response to the kind of treatment you received. Samples may also be sent to other researchers for collaborative studies, including researchers at for-profit agencies. However, prior to shipment, patient identifiers (name, initials and medical record numbers) will be removed, but these samples will still include your unique subject identification number. You will not be given results of these pilot studies or of any future testing performed on your samples.

You have the right to withdraw any unused blood, tissue, fluid, unmanufactured or manufactured CART-19 T-cells from further use by contacting [redacted]. Any blood/tissue/fluid that has already been used for research will be retained.

Please initial next to your choice below.

Initials	
	I AGREE to allow my blood/tissue/fluid and any leftover unmanufactured or manufactured T-cells to be kept for use in research to learn about, prevent, or treat cancer or other diseases.
	I DO NOT AGREE to allow my blood /tissue/fluid or unmanufactured/manufactured T-cells to be kept for use in research to learn about, prevent, or treat cancer or other diseases.

Name of Participant	Signature of Participant	Date
Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date

List of Terms Used in the Consent:

Apheresis - Apheresis is the removal of white blood cells from your blood. In order to collect your cells you must have a needle inserted into each arm. Your blood will be drawn through sterile tubing into a sterile bowl inside a machine that separates your white blood cells from the rest of your blood. Your cells will be collected into a sterile collection bag. During the procedure, the machine works in cycles. In one cycle the machine is drawing blood into the sterile bowl to collect your cells. In the second cycle the machine is returning your red blood cells and platelets (cells that help your blood clot) back to you. The procedure ends with the machine in the return cycle. A solution called acid-citrate-dextrose (ACD) and salt solution (saline) is used during the process to prevent your blood from clotting within the tubing of the machine. A small amount of the solution will also be returned to you along with your red blood cell and platelets. The procedure usually takes between 2-3 hours to complete and trained personnel in the apheresis unit supervise the procedure.

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

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

Bone marrow biopsy and aspirate - A bone marrow aspiration is a procedure in which an area of the hipbone is numbed, and a small sample of bone marrow is removed through a needle. A bone marrow biopsy is similar to a bone marrow aspiration, except a sample of bone is removed through the needle.

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 (EKG) - a test to check for problems with the electrical activity of your heart.

Examination of your veins – a nurse or doctor will look at the veins in your arms to make sure you have good enough veins to undergo a procedure (called apheresis) that will be used to collect your T-cells for the study.

Immune System - the body's defense system against infections and diseases like cancer.
Immunity - protection against a foreign invader (like cancer or a germ).

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, respiratory rate, pulse 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. After the virus enters the cell, it uses an enzyme (called reverse transcriptase) which transforms the RNA into DNA, which can then enter the infected cell's DNA. A lentivirus is a type of retrovirus that can insert itself into both dividing and non-dividing cells.

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

TCR-DNA – the genetic material that is transferred by the lentiviral system and which carries the information for the T-cells to make a new T-cell receptor.

T-cell Receptor *(TCR)* – the surface protein or marker which allows the immune T-cell to recognize and attack a cancer cell or a cell carrying foreign germs.

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.