PRINCIPAL INVESTIGATOR: James N. Kochenderfer, M.D.

STUDY TITLE: A Phase I Clinical Trial of T Cells Expressing a Novel Fully-Human Anti-BCMA CAR for Treating Multiple Myeloma

STUDY SITE: NIH Clinical Center

Cohort: Affected Patients

Consent Version: 04/26/2021

WHO DO YOU CONTACT ABOUT THIS STUDY?

James Kochenderfer, MD. by phone at 240-760-6062 or Email: kochendj@mail.nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

The immune system plays many important roles in the body such as helping the body fight infections. The immune system is also known to affect cancer cells. "T" lymphocytes, or T cells, are a type of white blood cell and a major component of the immune system. T cells have been shown to be capable of recognizing and destroying a number of different cancers. Unfortunately, most cancers have developed ways of escaping the monitoring by the immune system for foreign or abnormal cells and continue to grow in an uncontrolled manner. Thus, we are looking at ways to manipulate the immune system, in particular the T cell component, so that it will more efficiently

recognize and kill tumor cells. We have developed an experimental procedure for patients with multiple myeloma that has progressed despite standard therapies. This procedure uses your own blood cells. Specifically, it uses your own T cells which are manipulated in a research lab and then given back to you. The purpose of this study is to see if it is safe to administer these T cells to people with multiple myeloma. This T cell therapy is a type of "gene therapy" and is very closely monitored by the Food and Drug Administration (FDA) and other regulatory agencies. The risks of gene therapy will be described later in this document.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You have been diagnosed with multiple myeloma that has not been controlled with standard therapies, meaning that the cancer cells are growing despite your prior treatments or, if you did achieve a remission, the cancer has come back after your most recent treatment. Treatment for multiple myeloma that persists after standard therapies is primarily aimed at improving quality and perhaps length of life because multiple myeloma is almost never curable. Unfortunately, multiple myeloma usually develops resistance to standard treatment options and ultimately becomes completely resistant to conventional therapies. Thus, there is a need to find new approaches for the treatment of multiple myeloma.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 42 patients will take part in this research study.

DESCRIPTION OF RESEARCH STUDY

What will happen if you take part in this research study?

Before you begin the study

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. However, there are some extra exams, tests and procedures that you will need to have if you take part in this study. If you have had some of them recently, they may not need to be repeated.

These tests include:

- Medical history
- Physical examination
- Routine blood tests
- Pregnancy test if you are woman who can have children
- Blood tests for viruses and other disease-causing organisms
- Echocardiogram and EKG of your heart
- Bone marrow biopsy
- CT scan (at locations of your disease) or PET scan, MRI of your brain

During the study

Once it is determined that you are eligible and you agree to participate by signing the study consent, you will undergo an apheresis procedure that will remove cells from your blood. Apheresis is a procedure for obtaining certain blood cells, such as white blood cells, without removing most blood cells. It is a process people undergo when giving routine platelet donations. Some people need an IV (intravenous catheter, a small plastic tube that is put into a vein) inserted into each arm for this collection and some people need a temporary special apheresis "central line" just for the one-day collection.

Next, we will manipulate your cells in a laboratory so that they are capable of recognizing your multiple myeloma. Specifically, we will genetically modify your T cells and grow them in the laboratory. We will be using a type of virus (retrovirus) that encodes a gene for an anti-B-cell maturation antigen (BCMA) receptor in making these anti-BCMA T cells. Your multiple myeloma cells express the BCMA protein on their surface. Multiple myeloma is a cancer of plasma cells. Normal plasma cells make antibodies, which play a role in fighting infections. Normal plasma cells also express the BCMA protein. This BCMA protein will serve as a target for the anti-BCMA T cells.

This study will be conducted as a "dose escalation". The purpose of dose escalation is to determine the safe dose of anti-BCMA T cells. There are five dose levels of anti-BCMA T cells. The first patients enrolled get the smallest dose and the dose is increased when a level has been determined to be safe. You can discuss this with the study doctors to find out which dose of anti-BCMA T cells you will be receiving.

After you have had cells removed from your blood, you will receive 2 FDA approved drugs (chemotherapy) named cyclophosphamide and fludarabine. These drugs will be administered to you through a "central line" (or tube) placed in a large vein in your arm or chest once a day for 3 days. The two drugs are given one after the other with each infusion lasting about 30 minutes. The purpose of the chemotherapy is to enhance the activity of the anti-BCMA T cells. This is a standard chemotherapy regimen that is often used to treat certain types of leukemia. The chemotherapy can be administered on an outpatient basis, which means hospital admission is not necessary to receive this chemotherapy. If you are removed from the protocol before receiving the CAR T cells, you may be eligible for re-enrollment in the study.

Two days after the chemotherapy ends, you will be admitted to the hospital as an inpatient and receive the anti-BCMA T cells. The anti-BCMA T cells will be given to you as a single intravenous (IV) infusion. You will need to have a "central line", and IV catheter (or tube) placed in a large vein in your arm or chest for this infusion. This may be the same "central line" that was used for the chemotherapy. All patients that participate in this study will be required to stay in the hospital for close observation and testing for at least 9 days after the cell infusion, and patients must stay within 60 minutes driving distance for 2 weeks after the cell infusion. This is because in our experience with similar treatments we have noticed side-effects including fevers, fatigue, low blood pressure, and others that have been most severe between 6 and 9 days after cell infusion. You may have to stay in the hospital longer to manage these side effects if they occur. During this time-period, you must be willing to agree to intensive care treatment that can include drugs that support your blood pressure, chest compressions, a machine to assist your kidneys, and being attached to a breathing machine.

You will be closely watched during the anti-BCMA cell infusion for signs of a reaction. While other types of genetically-modified T cells have been administered to many patients, infusion of anti-BCMA T cells is a new approach that is being evaluated in this protocol. There is always a chance that we will not be able to genetically-modify your cells or be able to grow the cells in the laboratory. If we are not able to successfully prepare the minimum number of cells that we believe are needed to help control the tumor in our first attempt to produce the cells, we will make a second attempt to produce the cells if you give us permission to do so even if you have already received the chemotherapy part of the protocol at the time. This second attempt to produce cells will probably not be necessary.

For patients who still have disease after receiving anti-BCMA T cells the first time, repeated infusions might be possible. In order for a repeat infusion to be possible, you must not have experienced severe toxicities with their first infusion, and you must meet the original eligibility requirements for enrollment on the trial. Repeat treatments will also include the same chemotherapy as the first treatment. A maximum of 2 total treatments can be administered to any one patient.

When you are finished taking the drugs (treatment)

You will need to come for a clinic visit two weeks after your cell infusion, for blood work, urine tests, and a brief visit with one of our doctors. You will also need to return to clinic for evaluation of your overall health and your multiple myeloma 1, 2, 3, 4, 6, 9 and 12 months after the cell infusion. These visits will also include a health and multiple myeloma assessment including blood test, urine tests, and possible disease imaging.

After 12 months, follow up for patients with ongoing responses, which means the multiple myeloma has not progressed, will continue every 6 months for up to 5 years after your T-cell infusion. At the follow-up visits we will evaluate your general health, and we will assess your multiple myeloma. Blood will be drawn at all follow-up visits (~4 tablespoons). Note that all of these follow-up visits are only required for patients with ongoing responses.

If your multiple myeloma progresses, you will be removed from the study to pursue other options. As long as your multiple myeloma does not progress, we ask that you do not take any other treatments. We also ask that you do not take any corticosteroid medications such as prednisone or dexamethasone. If you do take other treatments or if you take corticosteroids, we will not be able to interpret the results of the anti-BCMA T cells, and you will be removed from the study. You will also be followed by your home oncologist who will receive a detailed summary of your case and blood tests and other investigations that need to be performed and potential problems that may arise. We encourage early communication of any problems with us so that we can assist in deciding the best treatment approach.

Gene-therapy-specific follow-up

Because we do not know the long-term side effects of gene therapy, we will collect your blood over the next several years, frequently at first and then less frequently. We can obtain the blood needed for these studies at your regular follow-up visits as long as you are on the study. If you are removed from the study, we still need to conduct these gene-therapy follow-up visits according to FDA regulations and will request your permission to enroll you in a protocol that would allow us to follow you for this reason only. If you return to your referring physician after receiving therapy

here, we will ask you to have your physician send your blood specimens here for this testing, which will decrease the inconvenience to you. This testing will determine if the cells have grown or changed in your body. We will test your blood immediately before you receive the cells, and then at 3, 6, and 12 months (2 teaspoons each time). We may also collect your blood (2 teaspoons each time) over the next several years after 12 months if you have had any previous tests that show a retrovirus in your blood. According to FDA requirements, we need you to return annually to the NIH for a physical examination for five years after you receive the cells. After that time, we will be sending you a questionnaire to get information regarding your health for the next ten years, for a total follow-up time period of 15 years. For this reason, we ask that you continue to provide us with a current address and telephone number, even after you complete this research study. At the time of your death, no matter the cause, we may request permission for an autopsy in order to obtain vital information concerning the safety of this experimental therapy approach. Please discuss this request with your family to inform them of your wishes.

BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this therapy would affect your baby or your unborn child. If you are a woman who can become pregnant or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for at least 4 months after your last research treatment. If the anti-BCMA T cells are still detected in your blood longer than 4 months after your treatment, your doctors will recommend that you not become pregnant until the anti-BCMA T cells are not detectable in your blood. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once. If you are a man, you should not donate sperm during the study treatment and for 4 months after you finish your last research treatment.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

TESTS FOR RESEARCH

An important part of this study is testing the effects of this treatment on your tumor and immune system. The following blood samples and tests will be done while you participate in this study:

HOW WILL MY SAMPLES AND DATA BE USED?

This study aims to perform laboratory studies (research) to better understand how the immune system fights cancer cells and to make more effective cell treatments. We plan to keep some of your specimens and data that we collect while you are participating on this study to use in our research labs.

We will use some of the samples we collect (blood, tissue) to perform a number of genetic tests. This includes RNA sequencing on your samples. The human genome is the material in our cells that includes thousands of genes. Genes are the building blocks of our cells that make and maintain our body. A gene provides instructions to individual cells to make proteins through a middle step of making RNA. Proteins are the substances that are involved in all of our body's chemical processes.

The purpose of RNA sequencing is to learn about the expression of different genes in your cancer cells and in your CAR T cells. Our goal is not to look into genetic abnormalities that could be inherited by you or passed along to your children, but in the course of studying gene expression, there is a slight chance that we could find evidence of an inherited disorder or a genetic disorder that could be passed along to your children. The slight possibility of this happening is covered below under "Incidental and Secondary Findings".

Incidental and Secondary Findings

Because we might accidentally collect a small amount of normal tissue when we sample your tumor, it is possible, but unlikely, that we could identify possible changes in your RNA that are not related to this research. These are known as "incidental medical findings".

- Genetic changes that are related to diseases
- Genetic changes that are not known to cause any disease
- Genetic changes that are new and of uncertain clinical importance. This means that we do not know if they could cause or contribute to a disease or if they are normal variations.

The analyses that we perform in our laboratory are for research purposes only; they are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing. Changes that we observe unrelated to our research may or may not be valid. Therefore, we do not plan to inform you of the results of testing on your samples that is performed in our research lab. However, in the unlikely event that we discover a finding that is believed to be clinically important based on medical standards at the time we first analyze your results, we will contact you. This could be many years in the future. We will ask if you would like to meet with a credentialed genetic healthcare provider for genetics education and counseling (either in clinic or via phone conference). The NIH will offer to pay for confirmation of the incidental genetic finding. You will have an additional tube of blood drawn to verify the findings we have seen in our lab. If the results are verified, you will be re-contacted and offered a referral to a genetic healthcare provider to discuss the results.

It is possible that none of the studies described above in this section will be performed.

Storage and release of samples, genomic data, and health information

Portions of your samples, genomic data, and health information will be stored for an unlimited period of time to be used in future research.

RESEARCH BLOOD SAMPLES

Blood will be drawn frequently during your treatment. Most of the blood draws will be to monitor your health during and after the cell infusion. In addition, some blood samples will be drawn for

research purposes. Additional blood draws might be necessary to investigate T cell responses and serum cytokine levels in cases of clinical events such as rapid regressions of malignancy or toxicity. These samples will be used to study how your immune system is affected by the cell therapy. Some of the samples may be sent to investigators outside of the NIH for future research. In general, 4 tablespoons will be drawn at each clinic visit or every Monday, Wednesday, and Friday during the inpatient stay. There will also be about a 1 tablespoon draw the day you receive the cells and the first Sunday afterwards. On one occasion before the treatment a larger amount of blood (8 tablespoons) will be drawn. The NIH has set a limit on the maximum amount of blood that can be taken for research. This limit is based on your age. For adults, no more than 37 tablespoons can be taken over an 8-week period.

Bone Marrow Biopsies

Before you begin treatment on this protocol and at the time of the 14-day, 2-month, and 6-month, 18-month, 30-month, and 42-month follow up appointments, bone marrow biopsies will be scheduled. These biopsies are required for participation on the study to evaluate your tumor and clinical status, but also for research tests.

Possible Additional Biopsies

In very rare instances, we may also ask your permission to perform an additional biopsy for research or clinical purposes. These additional biopsies could be bone marrow biopsies or biopsies of tumors that could be multiple myeloma. The tissue from this biopsy will be used for research purposes, to determine whether there is evidence of an immune response to the tumor or to determine if a newly discovered tumor is actually multiple myeloma. Any biopsies would only be performed with your permission, and if the biopsy is determined to be safe by the Principle Investigator of this trial and the additional physician or physicians that would actually perform the biopsy. Some of the samples may be used for other or future research conducted by the investigational team or other researchers. This future research might directly study malignancy of the same type that you have, or it could focus on other areas of research. Your permission for this will be obtained at the time of the biopsy.

CT SCAN

You may have a CT (Computed Tomography) scan of areas with lesions/plasmacytomas at 1-month, 2-month, 3-month, 4-month, 6-month, 9-month and 12 months after T cell infusion. This may include areas such as the head, neck, chest, abdomen and pelvis. (only if a plasmacytoma/lesion was detected before treatment). If it is necessary, we may use contrast agent enhanced CT scans. The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures showing the inside of your body. During the procedure, you will need to lie still on a table inside the CT machine. The table will move you in and out of the machine during the scan and you will be instructed to hold your breath. The scan itself will only take a few minutes to complete, the entire visit will take about 30 minutes.

PET SCAN

You may have a PET (Positron Emission Tomography) scan at 2-month, 6-month, 9-month and 12-months after T cell infusion if needed to stage disease. The PET scanner is a doughnut-shaped

machine that uses x-rays combined with a dose of a radioactive substance (tracer) to create computer pictures showing the inside of your body.

Before the scan, you will have a radioactive substance injected into your arm after which, you will need to wait for approximately 30 minutes for the substance to be absorbed. After 30 minutes, you'll lie on a narrow, padded table and be positioned for the scan. The scan itself is painless and won't make much noise. During this time, you will need to lie very still. It will take about another 30 minutes to complete.

ROUTINE SPINE MRI

Routine Spine MRI (Magnetic Resonance Imaging) will be done at of areas with lesions/plasmacytomas at 1-month, 2-month, 3-month, 4-month, 6-month, 9-month and 12 months after T cell infusion. You will have an MRI done at NIH clinical center. During part of the MRI you will receive gadolinium, a contrast agent, through an intravenous (IV) catheter (small tube). An MRI creates pictures of the inside of your body using strong magnets instead of x-ray energy. At the time of each scan you will be asked to fill out a screening form to verify that it is safe for you to have the scan. You will also be asked to remove any metallic objects you may be wearing (for example, watches, earrings or piercings) and possibly to change into a hospital gown. Then you'll be asked to lie on a narrow bed that will move into the MRI scanner. Once you are comfortable, the table will be moved into the scanner (the scanner is a long, narrow tube that is open at each end). You will need to lie still on the table during the scan which will take about 30 minutes to complete. You will hear normal "hammering" or clicking and squealing noises during the scan. While in the scanner you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the technician running the scan the entire time and will be provided an emergency button to squeeze at any time if you decide you want the scan to stop.

RISKS OR DISCOMFORTS OF PARTICIPATION

What side effects or risks can I expect from being in this study?

Because the BCMA protein is found on normal plasma cells as well as on your cancer, the anti-BCMA T cells might cause a fleeting or prolonged decrease in the number of normal plasma cells. A small number of B cells also express BCMA, so a slight decrease in B-cell counts might occur. Because plasma cells make antibodies that are involved in protection against infections, this decrease in plasma cell number might lead to a greater risk of infections because of low blood antibody levels. We do not know if a decrease in normal plasma cells will cause problems with infections and several steps can be taken to deal with an increased risk of infection or actual infections, such as giving antibodies intravenously, which is a standard treatment given to many patients with immune deficits.

The anti-BCMA T cells we will be giving you are exposed to a type of virus (retrovirus) in order to insert the anti-BCMA gene that gives the T cells the ability to recognize multiple myeloma. Although this retrovirus is not active, there is the rare possibility that it may cause infection. This has never happened to any of the hundreds of patients who received T cells that were modified with similar viruses. The anti-BCMA T cells could also cause you to develop another type of cancer in your blood cells, although we think this is very unlikely because it has never happened in the hundreds of patients who have received genetically-modified T cells.

Patients who received cell infusions aimed at BCMA and targets other than BCMA have experienced a variety of side-effects. Most of these patients have developed fever and fatigue that can last for up to 2 weeks after cell infusion. Some patients that have received similar treatments have developed low blood pressure. In a minority of patients developing low blood pressure, a temporary decrease in kidney function also occurred. Several patients developed temporary confusion, headaches, or weakness. One patient developed severe, but temporary, muscle twitching. Three patients developed a temporary inability to speak, which resolved completely after a few days. One patient developed a temporary decrease in heart function. His heart function subsequently returned to normal levels. One patient developed tumor lysis syndrome, which is a release of toxic substances from tumor cells that are being destroyed. This tumor lysis syndrome was successfully treated and caused no long-term problems for the patient. Patients at risk of tumor lysis syndrome on the anti-BCMA T-cell study will receive medication to prevent this complication. Chemotherapy is part of this protocol. The chemotherapy part of this study can cause decreased blood count, nausea, and hair loss. The decreased blood counts due to chemotherapy can lead to infections and bleeding.

Potential risks of anti-BCMA T cells infusion include:

Likely:	**Less Likely:**	**Rare:**
• Fever • Chills • Fatigue • Low immunoglobulin levels	• Headache • General feeling of being unwell (malaise) • Temporary decreased kidney function • Temporary weakness or difficulty speaking • Low blood pressure • Fainting • Tumor lysis syndrome (rapid breakdown of tumor that can cause side-effects) • Possible intensive care unit admission • Fast heart rate • Possible kidney damage that will most likely be temporary • Possible breathing problems that might in rare cases require mechanical ventilation (breathing machine) • Cytokine release syndrome (release of substances from T cells that can cause many side-effects) including • Fever • Fast heart rate • Low Blood Pressure • Possible intensive care unit admission • Rare cases, death.	• Muscle pain, twitching • Death • Permanent kidney damage • Coma • Temporary liver damage • Extreme weakness of the arms and legs • Muscle damage • Long-term debilitation • Difficulty breathing • Diarrhea • Breakdown in red blood cells

Likely:	Less Likely:	Rare:
	• Temporary decreased cardiac function, or abnormal heart rhythms • Prolonged (a month or more) low blood counts including low white blood cells and platelets • Temporary changes in bleeding tests • Temporary changes in liver function tests • Temporary low calcium, phosphorous, albumin in the blood • Increased risk of infection • Other neurologic problems	

There are no data available at this time to guide us in how humans might respond to this type of cell infusion. As this is a new experimental therapy, side effects that we do not anticipate that may cause your condition to worsen may be encountered.

Potential risks of cyclophosphamide:

Likely:	Less Likely:	Rare:
• Low blood counts	• Nausea and vomiting • Painful and bloody urination • Sterility • Water retention • Hair Loss	• Heart damage • Secondary leukemia (a different type of cancer) • Skin rash • Bleeding

Potential risks fludarabine:

Likely:	Less Likely:	Rare:
• Low blood counts	• Long-term reduction of lymphocyte counts which could increase the risk of infection. • Infection	• Damage to the nervous system • Causing seizures, coma and even death • Inflammation in the lungs • Kidney damage

Gene Therapy Risk of Cancer and Other Diseases:

The risks of gene therapy causing new disease are unknown. It is possible that the gene therapy may cause an immune system, blood, or neurological disorder, or cause a new cancer in your blood

cells to develop. It is unknown if you will develop any of these disorders, but you need to be aware of this possible risk. Children in France and England received gene therapy for a particular disease of the immune system. In these children, stem cells were genetically modified (in contrast to the research offered in this trial where T cells are genetically modified). Most of the children were cured, but 5 out of 22 children developed leukemia and one died. Experts who examined this case thought that the gene therapy caused the leukemia in these children. To monitor you for this risk we will be testing your blood as previously described.

Procedure Risks

Blood draws: Side effects of drawing blood include pain and bruising in the area where the blood was drawn, lightheadedness, or rarely fainting due to transient lowering of blood pressure. If you feel dizzy, you should lie down for a few minutes to avoid hurting yourself if you fall. Infection at the blood-drawing site could also occur.

Intravenous Catheter: In order to receive this treatment, you will need to have a central venous catheter. This catheter is placed under the skin of the chest wall and enters a major vein in the chest. There are several types of catheters including those which must be removed after each cycle of chemotherapy (temporary type) and those which may be kept for the duration of therapy (permanent type). These options will be discussed with you. The risks associated with placing some catheters include pain, bleeding, infection and collapsed lung. The long- term risks of the catheter include infection and clotting of your veins. If these occur, it may be necessary to remove the catheter. These risks will be explained to you in more detail at the time of insertion.

Bone marrow aspiration and biopsy: A bone marrow biopsy is performed by inserting a needle into a bone of the hip. In the aspiration part of the procedure, a small amount of liquid bone marrow is removed, and in the biopsy part, a tiny solid piece of bone marrow is removed. You may feel a pressure sensation when the needle is being inserted and a pulling sensation and brief pain as the marrow is withdrawn. The amount of marrow taken is very small and will not change your body's ability to form blood cells. Potential complications of this procedure are local bleeding, pain at the site, and infection. Both of these are very rare. Bleeding can be stopped by applying local pressure and an infection can be treated with antibiotics.

Apheresis:

The risks of apheresis are similar to whole blood donation and include pain and bruising at the needle insertion site in the arms, lightheadedness, dizziness, nausea, and rarely fainting due to a rare reflex reaction to needle placement and to the temporary decrease in blood volume during apheresis. You may also feel tingling around your mouth or in your fingers caused by a blood thinner given during the procedure. The nurses will give you a calcium containing antacid to chew to reduce the tingling. All the symptoms usually go away within a few minutes of stopping the procedure. We ask that you eat a meal before coming to donate, and avoid caffeine, to prevent lightheadedness or dizziness that might occur. You will be asked to remain in the chair/bed for a few minutes after the donation is completed, and to sit down and relax for about 15 minutes after the donation. This is done so that staff can observe you to make sure that you feel entirely well before you leave our department.

What are the risks of radiation from being in the study?

During your participation in this research study, you may be exposed to radiation from CT scans of your head, neck, chest, abdomen and pelvis, and 18FDG-PET/CT scans each year. The amount of radiation exposure you will receive from these procedures is equal to approximately 16.9 rem. A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans and 18FDG-PET/CT scans that you get in this study will expose you to the roughly the same amount of radiation as 56 years' worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 1.7 out of 100 (1.7%) and of getting a fatal cancer is 0.8 out of 100 (0.8%).

You may not participate in this study if you are pregnant. If you can become pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time

Contrast Agent enhanced CT scans risks:

If contrast dye is used, there is a chance of developing an allergic reaction from the contrast material, which may cause symptoms ranging from mild itching or a rash to severe difficulty breathing, shock or rarely, death. The contrast material may also cause kidney problems. The study doctors will do a blood test prior to the test to confirm that it is safe you to receive the contrast.

For IV contrast if used: You may feel discomfort when the contrast material is injected. You may feel warm, flushed, get a metallic taste in your mouth or, rarely, may make you vomit or feel sick to your stomach.

For oral contrast if used: You may experience vomiting, nausea, cramping, bloating, constipation or diarrhea after drinking the contrast.

Gadolinium enhanced MRI risks:

The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein with pain and swelling.

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives,

and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called "nephrogenic systemic fibrosis (NSF)". This condition always involves the skin and can also involve the muscles, joints and internal organs. NSF has resulted in a very small number of deaths. A blood test of your kidney function may be done within the month before an MRI scan with gadolinium contrast. You will not receive gadolinium for a research MRI scan if your kidney function is below the safe level.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA has issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to years. The effects of the retained gadolinium are not clear. At this time, retained gadolinium has not been linked to health risks in people whose kidneys work well. Some types of gadolinium contrast drugs are less likely to remain in the body than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body, whenever possible. We will also give you additional information called a "Medication Guide." Upon request, we will give you individual information about retained gadolinium we see on your studies.

Non-physical risks of genetic research

Psychological or Social Risks Associated with Return of Incidental or Secondary Findings

As part of the research study, it is possible that you could learn that you have genetic risks for another disease or disability. This may be upsetting and, depending on what you learn, might create a need to make challenging decisions about how to respond.

Although your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, learning your research results could mean something about your family members and might cause you or your family distress. Before joining the study, it may be beneficial to talk with your family members about whether and how they want you to share your results with them.

Privacy Risks Associated with Return of Incidental or Secondary Findings

Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her blood relatives.

Protections against misuse of genetic information

This study involves genetic testing on samples. Some genetic information can help predict future health problems of you and your family and this information might be of interest to your employers or insurers. The Genetic Information Nondiscrimination Act (GINA) is a federal law that prohibits plans and health insurers from requesting genetic information or using genetic information. It also prohibits employment discrimination based on your health information. However, GINA does not address discrimination by companies that sell life insurance, disability insurance, or long-term care

insurance. GINA also does not protect you against discrimination based on an already-diagnosed condition or disease that has a genetic component.

POTENTIAL BENEFITS OF PARTICIPATION

It is unknown at this time whether anti-BCMA T cell infusions will improve survival or have any benefit for patients with multiple myeloma. If accepted by your body, the cell infusion may decrease the amount of your cancer. Your participation in this experimental treatment may also help us advance the understanding and treatment of multiple myeloma.

Alternative Approaches or Treatments

What other choices do I have if I do not take part in this study?

Instead of being in this study, you have these options:

- Getting care for your cancer without being in a study such as other forms of chemotherapy, radiation, stem cell or bone marrow transplantation, or immune therapies.
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

You should discuss with your referring doctor and the NIH doctors whether any of these treatments might represent a reasonable treatment option for your disease.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment (you may also be eligible for a second infusion of the anti-BCMA T cells if this happens)
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- if you become pregnant
- if the study doctor decides to end the study

In this case, you will be informed of the reason therapy is being stopped.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed or returned upon request. However, any samples and data generated from the samples that have

already been distributed to other researchers or placed in the research databases can**not** be recalled and destroyed.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines, but they do not need to report their personal finances to the NIH.

The NIH and the research team for this study have developed anti-BCMA CAR being used in this study. This means it is possible that the results of this study could lead to payments to NIH. By law, the government is required to share such payments with the employee inventors. You will not receive any money from the development of anti-BCMA CAR.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that it may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

Genomic Data Sharing

As part of this research study, we will put your genomic data in a large database for broad sharing with the research community. These databases are commonly called data repositories. The information in this database will include but is not limited to genetic information, race and ethnicity, and sex. If your individual data are placed in one of these repositories, they will be

labeled with a code and not with your name or other information that could be used to easily identify you, and only qualified researchers will be able to access them. These researchers must receive prior approval from individuals or committees with authority to determine whether these researchers can access the data.

Summary information about all of the participants included in this study (including you*)* is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.

NIH policies require that genomic data be placed in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor , NCI Center for Cancer Research, or their agent(s)

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Jim Kochenderfer, M.D., Building 10, Room 12C121, Telephone: 240-760-6062. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.