INSTITUTE: National Cancer Institute

STUDY NUMBER: 14-C-0022 PRINCIPAL INVESTIGATOR: Stephanie L. Goff, MD

STUDY TITLE: A Phase II Study for Metastatic Melanoma Using High Dose Chemotherapy Preparative Regimen followed by Cell Transfer Therapy Using Tumor Infiltrating Lymphocytes Plus IL-2 with the Administration of Pembrolizumab in the Retreatment Arm

Continuing Review Approved by the IRB on 10/16/19
Amendment Approved by the IRB on 03/11/19 (K) Date posted to web: 10/19/19

Standard

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary**.**

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, 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). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

Why is this study being done?

Your doctor has told you that you have been diagnosed with metastatic melanoma. We have developed an experimental therapy that involves taking cells called lymphocytes from patients' tumors, growing them in the laboratory in large numbers, and then giving the cells back to the patient. These cells are called Young Tumor Infiltrating Lymphocytes, or Young TIL and the therapy is called cell therapy. Before receiving the cells, the patients receive 2 chemotherapy drugs to temporarily suppress the immune system to improve the chances that the tumor fighting cells

will be able to survive in the body. After the cells are given, the patients receive aldesleukin (IL-2) to help the tumor fighting cells stay alive longer. The purpose of this study is to see if these tumor fighting cells (young TIL) with the administration of aldesleukin can cause metastatic melanoma tumors to shrink and to evaluate the toxicity of this treatment.

Why are you being asked to take part in this study?

You are being asked to participate in this study because you have been diagnosed with metastatic melanoma.

How many people will take part in this study?

Up to 64 patients will be enrolled in this study.

Description of Research Study

Stages 1 is performed under the companion protocol, 99-C-0128 (Evaluation for NCI Surgery Branch Clinical Research Protocols), to which you have already enrolled.

Stages 2-5 are performed under this protocol.

The Cell protocol has several stages:

Stage	Timeframe	Location	Comments & Instructions
1. Work up	1-2 weeks	Inpatient and out patient	Scans, x-rays, labs and other tests as needed
2. Chemotherapy (day -7 to -3)	1 week	Inpatient	Receive IV chemotherapy to prepare your immune system for the cells
3. Cells and aldesleukin (Day 0-4)	1-4 days	Inpatient and possibly ICU	Receive the TIL cells IV and then high dose aldesleukin about every 8 hours for up to 12 doses
4. Recovery	1-3 weeks	Inpatient unit	Recover from the effects of treatment
5. Follow -up	Ongoing until disease progression	Outpatient	Return to clinic for physical exam, review of side effects, labs, scans every 1-3 months for the first year and then every 6 months.

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

Before you begin the study:

The following procedures are conducted under 99-C-0128 or 03-C-0277.

Cell Harvest and Growth

You underwent a procedure to take a piece of your tumor either from a biopsy or during surgery, so we can grow TIL from your tumor cells in the laboratory while enrolled on our companion protocol 03-C-0277 (Cell Harvest and Preparation for Surgery Branch Adoptive Cell Therapy Protocols). Sometimes we are unable to successfully grow the cells needed for this procedure. If your cells do not grow, you will not be able to receive the cell infusion. We usually know after about 4 weeks whether the cells will grow well enough to be used as an experimental treatment on this protocol. At the time we determine that your cells are not growing, we will inform you and discuss your options with you. Several medications are used during the preparation of your cell product, be sure to tell your doctor if you are allergic to any antibiotics.

Work-up

Prior to receiving the experimental treatment, you will undergo many tests. We will evaluate you for eligibility for participation on this trial with a physical examination, CT and/or MRI scans, x-rays, EKG, heart and lung function tests, and blood tests. Patients who have a positive HIV blood test will not be eligible for this protocol because it may put them at higher risk of developing infections. If you are a woman, you will undergo a pregnancy test. You may be admitted to the hospital for these tests. However, you will be allowed to leave on pass on the days that you are not having tests performed.

Leukapheresis

Leukapheresis is a procedure that allows us to remove certain types of blood cells from you and return the rest of your blood. It is a very common procedure that is done routinely here with very few risks. During leukapheresis, blood is removed from you through a needle in your arm, circulated through a machine that divides whole blood into red cells, plasma (the serum part), and lymphocytes (or white cells), and then the plasma and red cells are returned to you through a second needle in your other arm. The procedure takes between 4-5 hours to complete. Rarely, people may experience lightheadedness or dizziness. We ask that you eat prior to the procedure to prevent this. The white blood cells collected before treatment may be used to help grow the cells and after the treatment, can be tested to see how the therapy has affected your immune system.

Catheter insertion

Prior to beginning the experimental cell treatment, you will have an intravenous (IV) catheter placed in your upper chest. The area will be numbed with an anesthetic before the catheter is put in.

During the Study

The following procedures will be performed under this protocol.

Chemotherapy Regimen (Day -7 through Day -3):

After we have grown the cells to large numbers in the laboratory, you will be admitted to the hospital to begin your experimental treatment. You will be given two chemotherapy medicines, cyclophosphamide and fludarabine, to make space in your immune system so the cells can work without any interference from the cells in your immune system. (These medicines will not treat your cancer.) These medicines may cause your tumor to shrink some, but this shrinkage is anticipated to be only partial and only for a short time. The main purpose of the chemotherapy is to see if we can make the cells more effective in fighting cancer tumors. Animal experiments have indicated that this can make the cells more effective in fighting cancer tumors, and we think this is true in humans. In arm 1, you will receive the cyclophosphamide into your catheter over 1 hour for two days (Day -7 and Day -6) and then the fludarabine will be given for 30 minutes every day for five days (Day -7 through Day -3). The side effects of these medicines are described on the following pages.

Cell Infusion and Aldesleukin Regimen (Day 0 through Day 5)

All patients will be given the cells through their IV over 20-30 minutes two to four days after the last dose of chemotherapy. Within 24 hours after your cell infusion you will be given high dose aldesleukin through one of the IVs. It will be given as a 15-minute infusion about every 8 hours for up to four days after the cell infusion. Aldesleukin is a cell growth factor and it is thought that it will help the cells live longer in your body.

The day after your cells are infused, we may give you G-CSF (filgrastim) as a shot or injection under the skin every day to stimulate your blood cells until they increase to a sufficient number. We will watch you closely during this entire time for any side effects of this experimental regimen. We will discuss the side effects below and we will include in your care all the medicines and treatments to prevent as many of these side effects as we can and to make you as comfortable as we can.

When you are finished taking the drugs (treatment)

Recovery

You will recover in the hospital until you are well enough to go home. This usually takes 7-21 days after you have received cells or your last dose of IL-2; however, you may need to stay in the hospital for longer than this before you are well enough to go home. We will continue to give you support medications, do laboratory tests, and watch you closely for any side effects until we feel your condition is stable.

In addition to the laboratory tests to monitor your condition, we will remove between 1 and 9 teaspoons of blood daily to study the effects of this regimen on your immune system. The maximum amount of blood for research is approximately 2.3 cups in 8 weeks.

Follow up and Evaluation of Experimental Regimen

You will need to continue to take Bactrim, an antibiotic, for at least 6 months following your treatment to prevent you from catching a certain type of pneumonia seen in patients who have low white blood cell counts. You will also need to take Valtrex, an anti-viral, for at least 6 months following your treatment to prevent any type of herpes simplex virus, like shingles. We will ask you to return to the NIH Clinical Center frequently after you are discharged approximately 6 and 12 weeks following treatment and then if you are responding to the treatment, every 3 months x3, then every 6 months x5 years and then as determined by your physician. The follow up visits will take up to 2 days. At each visit you will have lab tests, imaging studies and a physical examination. At some of your follow up visits, you may undergo leukapheresis or have about 8 tubes of blood drawn (4 tablespoons) so that we can see the effect this therapy has had on your immune system and if the cells we gave you are still alive. If you are unwilling or unable to travel to the NIH Clinical Center we will contact you by phone or e-mail and we may ask you to send us lab, imaging, and physical exam reports. If your tumor appears to be growing, we will look for other investigational therapies you may be eligible for, or refer you back to the care of your local physician.

Retreatment

If your tumor does not shrink or shrinks and then recurs following the initial treatment and you have previously received pembrolizumab or nivolumab, you may receive one additional treatment. The second treatment may start at least 6- 8 weeks after your last dose of IL-2. In the retreatment arm we want to see if patients whose tumor has not responded to either pembrolizumab or TIL therapy might respond to the combination of these 2 therapies. We think that the pembrolizumab may help the cells that we give you last longer. You will receive the high dose chemotherapy regimen described above and you will receive pembrolizumab the prior to receiving your cells and then every three weeks for a total of 4 doses. The side effects of pembrolizumab are listed below and the research nurse will give you a hand out describing the side effects as well. We do not anticipate that the pembrolizumab will increase the side effects from the TIL or the aldesleukin but as we have not given these agents together before, we do not know if this will be true. We will monitor you very carefully for any increase in side effects and provide treatment as needed.

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 medicine 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 four months after your blood tests show no evidence of the cells. Male participants should also refrain from sperm donation during this period. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

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

Risks or Discomforts of Participation

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

The risks and discomforts of this research study can be significant. This experimental treatment can lead to long-term decrease in your immune function. It is also possible that you may lose your fertility following this experimental treatment. It is possible, although unlikely, that this experimental treatment may cause your death.

We will discuss the side effects of this experimental treatment with you. You will be given medicines, transfusions, and treatments to prevent or treat the side effects including drugs to prevent and/or treat different types of infections. We will try to make you as comfortable as possible. You should talk to your study doctor about any symptoms that you experience while taking part in the study.

Cell Infusion

Based on our experience giving similar types of TIL cells grown in the laboratory, you may experience the following side effects:

- Fever, chills and shortness of breath, which may last for a few hours (common)
- Autoimmune reaction such as loss of skin pigment (known as vitiligo) or inflammation of the eye (uveitis) which may require the use of steroid eye drops. You may also experience other side effects that we don't yet know about

Aldesleukin (IL-2)

When IL-2 is given through an intravenous catheter, it can make you feel like you have the flu. It can also cause confusion and mental status changes making you unable to make sound decisions. Prior to beginning treatment, we will ask you to complete a Durable Power of Attorney so that a person of your choosing can make health care decisions for you in case you develop these side

effects. In our experience giving IL-2 to over 2,000 patients we have found that these side effects go away within a few days of stopping the IL-2.

Medications

The side effects of cyclophosphamide, fludarabine, high dose IL-2 and some of the other medications you will receive are listed below:

Cyclophosphamide and Fludarabine side effects:

Common	Less Common	Rare
▪ Changes in blood counts including: low red cell count (causing fatigue and shortness of breath), low platelet count (increasing the risk of bleeding and bruising), decrease in white blood cells (increasing the risk of infection and the need for treatment with antibiotics or other treatment) ▪ Loss of appetite, nausea, vomiting, ▪ Diarrhea, stomach pain ▪ Mouth sores ▪ Hair loss ▪ Fatigue ▪ Muscle or joint aches	▪ Bleeding ▪ Infection ▪ Bladder irritation with bloody urine ▪ Severe allergic reaction (difficulty breathing/swelling) ▪ Headache or dizziness ▪ Sweating ▪ Swelling of arms or legs ▪ Skin changes, rash, blisters ▪ Weakness ▪ Hearing loss	▪ Heart damage ▪ Lung damage ▪ Kidney damage ▪ Inflammation of the eye resulting in blindness ▪ Inflammation of nervous system resulting in death ▪ Epstein Barr Virus Lymphoma. This can be fatal (Two patients on other studies in the Surgery Branch developed EBV lymphoma, and one died as a result of this disease.) ▪ Loss of fertility ▪ Two out of the first 81 patients enrolled on the initial young TIL study died from complications resulting from suppression of the immune function which resulted in a severe infection (one of these patients also received radiation as part of their treatment regimen).

Pembrolizumab – side effects (retreatment only)

COMMON, SOME MAY BE SERIOUS
In 100 people receiving MK-3475 (pembrolizumab), more than 20 and up to 100 may have:
• Tiredness

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving MK-3475 (pembrolizumab), from 4 to 20 may have:

- Nausea
- Infection
- Loss of appetite
- Pain in back
- Joint stiffness
- Cough
- Swelling and redness of the skin

MK-3475 (pembrolizumab) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Anemia which may require blood transfusion
- Pain in lymph nodes
- Blood clot which may cause bleeding, confusion, paralysis, seizures and blindness
- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness
- Diarrhea
- Sores in the mouth which may cause difficulty swallowing
- Pain in belly
- Sores in the bowels
- Chills, fever
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving MK-3475 (pembrolizumab), from 4 to 20 may have:

nausea or vomiting; drowsiness; pain in the right upper belly

- Pain or swelling of the joints
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Fluid in the joints
- Pain in chest
- Lung problems (pneumonitis and other conditions). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Skin: itching; acne; rash (can be severe); blisters and peeling on the skin, mouth; skin changes; hives

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RARE, AND SERIOUS

In 100 people receiving MK-3475 (pembrolizumab), 3 or fewer may have:

- Feeling of "pins and needles" in arms and legs
- Redness, pain or peeling of palms and soles

MK-3475 (pembrolizumab) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Heart problems including swelling and heart failure. Symptoms and signs of heart problems may include: Shortness of breath, swelling of the ankles and body.
- Swelling and redness of the eye
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Reaction during or following a drug infusion which may cause fever, chills, rash
- Damage to organs in the body when donor cells attack host organs which may cause yellowing of eyes and skin, itchy dry skin
- Damage to organs in the body when the body produces too many white

cells

- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in a coma
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs.
- Swelling of the brain (encephalitis/meningitis) which may cause headache, confusion, sleepiness, seizures, and stiff neck
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
- Swelling or tenderness of blood vessels

Additionally, since pembrolizumab was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab.

These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of this side effect:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling

If you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GvHD), which may include diarrhea, skin rashes, and liver damage, after receiving pembrolizumab. Sometimes this condition can lead to death.

If you have had a solid organ transplant (for example, if you have received a kidney or heart transplant), you may experience rejection of the transplanted organ. Your doctor will monitor you and should tell you what signs and symptoms you should report depending on the type of organ transplant that you have had.

IL-2 (aldesleukin) side effects

Common	Less common	Rare
▪ Fever, chills, and fatigue ▪ Lowered platelet and red blood cell levels that may require transfusions ▪ Significant fluid retention causing weight gain (as much as 20 pounds). ▪ Low blood pressure ▪ Increased heart rate ▪ Low urine output ▪ Swelling in your extremities, ▪ Fluid in your lungs that can require oxygen ▪ Dry mouth, nausea, vomiting and diarrhea; ▪ Rash, itching; and changes in skin or hair pigmentation, called vitiligo; ▪ Changes in mental status, including confusion, difficulty sleeping or vivid dreams; this can be severe and require sedation and monitoring in the ICU	▪ Decrease in thyroid function that may require daily thyroid hormone replacement; ▪ Abnormal kidney and liver function that can be severe; ▪ Abnormal heartbeats or low blood pressure that may require treatment in the ICU. ▪ Breathing problems which may need monitoring in ICU and insertion of a breathing tube.	▪ Bowel perforation (a hole) requiring longer hospitalization or surgery. This is more common in patients who have previously received anti-CTLA-4 antibody. You will have a colonoscopy and biopsy before treatment if you have previously received anti-CTLA-4 antibody. ▪ Autoimmune disease, where your immune system attacks cells in organs of your body. Should this occur, you will be treated with steroids to stop the immune response. ▪ Damage to the heart muscle or heart attack ▪ Loss of blood flow to the extremities due to medicines used to treat very low blood pressure and shock. In one instance a patient had to have her lower arm amputated after treatment with these medicines. ▪ IL-2 is mixed with human albumin which could cause an allergic reaction or potentially transmit viral infections, although we have not had this occur.

Support Medications – side effects		
Common	Less common	Rare
Filgrastim (To increase production of white blood cells)		
▪ Bone Pain	▪ Severe headache	▪ Severe breathing problems ▪ Rupture of your spleen
Bactrim (To prevent a specific type of pneumonia)		
	▪ Fever ▪ Nausea, vomiting, ▪ Skin rash with itching ▪ reduced number of white blood cells ▪ Allergic reaction	
Fluconazole: (To prevent fungal infections)		
▪ Headache ▪ Nausea, vomiting, diarrhea, abdominal pain ▪ Itching		▪ A skin disorder called Stevens Johnson Syndrome, which can be fatal ▪ Liver damage which may be permanent

Acyclovir and Valacyclovir		
	▪ Temporary decrease in kidney function which may not cause any symptoms ▪ Nausea, vomiting, diarrhea, constipation ▪ Pain and irritation at place of injection	▪ Skin rash, hives, itching ▪ Tremors, dizziness, confusion, seizures ▪ Fatigue ▪ Blood in the urine

Potential Benefits of Participation

Are there benefits to taking part in this study?

The aim of this study is to see if this new experimental treatment will cause your tumors to shrink. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the effect of this

treatment on your type of cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may benefit others in the future who have cancer.

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 for treatment:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment; or getting comfort care which is also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by 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.

Please talk to your doctor about these and other options.

Stopping Therapy

Your doctor may decide to take you off this study under the following circumstances:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you become pregnant
- if you experience side effects from the treatment that are considered too severe
- if new information becomes available that shows that another treatment would be better for you

In this case, you will be informed of the reason for that decision.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular doctor first. If you refuse to participate or withdraw from the protocol or at the completion of the protocol, we will attempt to offer you participation in other NIH protocols if these are available, or will refer you to your home physician for further management.

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. However, according to FDA guidelines, information collected on you up to that point may still be provided to the Sponsor. 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 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 cannot be recalled and destroyed.

Research Subject's Rights

What are the costs of taking part in this study?

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. 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 Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

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 National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- NIH Intramural Institutional Review Board
- The study Sponsor, Center for Cancer Research or their agents
- Iovance Biotherapeutics, Inc.

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.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or
- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

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 additional information 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.

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.

The National Institutes of Health and the research team for this study are using the cell product developed by the NCI Surgery Branch through collaboration with Iovance Biotherapeutics, Inc. The company also provides financial support for this study.

Use of Specimens and Data for Future Research

Blood and tissue collected during the course of this study will be used for future research and will be stored, tracked and disposed of under our companion protocol 03-C-0277, (Cell Harvest and Preparation for Surgery Branch Adoptive Cell Therapy Protocols) on which you have already been enrolled.

In addition, 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 they 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.

OTHER PERTINENT INFORMATION

1. Confidentiality. 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.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The 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 National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. 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, Stephanie L. Goff, M.D., Building 10 CRC, Room 3-5840, Telephone: 240-760-6214. If you have any questions about the use of your specimens or data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

You may also call the Clinical Center Patient Representative at 301-496-2626.

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

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/ Legal Representative — Date

Print Name

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/Guardian — Date

Print Name

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian — Date

Print Name

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM OCTOBER 16, 2019 THROUGH OCTOBER 8, 2020.

Signature of Investigator — Date

Print Name

Signature of Witness — Date

Print Name