Informed Consent Coversheet

Official Study Title:	ADMINISTRATION OF HER2 CHIMERIC ANTIGEN RECEPTOR EXPRESSING T CELLS FOR SUBJECTS WITH ADVANCED SARCOMA (HEROS)
NCT number:	00902044
Date of Consent:	03/30/2020

H-24489- ADMINISTRATION OF HER2 CHIMERIC ANTIGEN RECEPTOR EXPRESSING T CELLS FOR SUBJECTS WITH ADVANCED SARCOMA (HEROS)

Background

In this consent form, "you" signifies you or your child.

You are invited to take part in a research study. Please read this information and feel free to ask any questions before you agree to take part in the study.

You have a type of cancer called sarcoma. Your sarcoma has not responded or has come back after treatment. Because there is no standard treatment for your cancer at this time or because the currently used treatments do not work fully in all cases, you are being asked to volunteer to take part in a gene transfer research study using special immune cells. You may have already thought about being in this study when we collected blood to make the cells used in this study. You may even have made a decision about whether to be in the study. If this is true for you, it is important that we give you this information and talk about it before we start you in the study.

The body has different ways of fighting infection and disease. No single way seems perfect for fighting cancers. This research study combines two different ways of fighting cancer: antibodies and T cells. Antibodies are types of proteins that protect the body from infectious diseases and possibly cancer. T cells, also called T lymphocytes, are special infection-fighting blood cells that can kill other cells, including cells infected with viruses and tumor cells. Both antibodies and T cells have been used to treat patients with cancers. They have shown promise, but have not been strong enough to cure most patients.

We have found from previous research that we can put a new gene into T cells that will make them recognize cancer cells and kill them. We now want to see if we can put a new gene in these cells that will let the T cells recognize and kill sarcoma cells. The new gene that we will put in makes an antibody specific for HER2 (Human Epidermal Growth Factor Receptor 2) that binds to sarcoma cells. In addition it contains CD28, which stimulated T cells and make them last longer.

In other clinical studies using T cells, some investigators found that giving chemotherapy before the T cell infusion can improve the amount of time the T cells stay in the body and therefore the effect the T cells can have. Giving chemotherapy before a T cell infusion is called lymphodepletion since the chemotherapy is specifically chosen to decrease the number of lymphocytes in the body. Decreasing the number of your lymphocytes first should allow the T cells we infuse to expand and stay longer in your body, and potentially kill cancer cells more effectively.

The chemotherapy we will use for lymphodepletion is a combination of cyclophosphamide and fludarabine. Cyclophosphamide and fludarabine are the chemotherapy agents most commonly used for lymphodepletion in immunotherapy clinical trials.

In the past you have signed a consent form that allowed us to put on your T cells the HER2 chimeric receptor with CD28 (HER2-CD28 T cells). We now want to see if these cells can survive in your blood and affect the tumor. These HER2-CD28 T cells are an investigational product not approved by the Food and Drug Administration.

H-24489- ADMINISTRATION OF HER2 CHIMERIC ANTIGEN RECEPTOR EXPRESSING T CELLS FOR SUBJECTS WITH ADVANCED SARCOMA (HEROS)

This research study is sponsored by Baylor College of Medicine. This research study is funded by Alex's Lemonade Stand, Stand Up 2 Cancer/ St. Baldrick's Foundation, Cookies for Kids' Cancer and Triumph Over Kid Cancer Foundation

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.

Purpose

The purpose of this study is to find the largest safe dose of HER2-CD28 T cells, to learn what the side effects are, and to see whether this therapy might help patients with sarcoma. Another purpose is to see if it is safe to give HER2-CD28 T cells after lymphodepleting chemotherapy. We will also study how the rest of your immune system responds following treatment with CAR T cells and what the effects are on the tumor when tumor tissue is available for testing following treatment.

Procedures

The research will be conducted at the following location(s):
Baylor College of Medicine, TCH: Texas Children's Hospital, TCH: Texas Children's Hospital General Clinical Research Center, and TMH: The Methodist Hospital.

Approximately 44 people may be treated on this study.

Earlier, you gave us blood to make HER2-CD28 T cells. These cells were grown and frozen for you. To get the HER2 antibody (and the CD28) to attach to the surface of the T-cell, we inserted the antibody gene into the T-cell. This is done with a virus called a retrovirus that has been made for this study and will carry the antibody gene into the T cell. This virus also helps us find the T cells in your blood after we inject them. Because you have received cells with a new gene in them you will be followed for a total of 15 years to see if there are any long term side effects of gene transfer.

You will receive fludarabine and cyclophosphamide for 2 days, fludarabine alone for an additional 3 days, and 2 days of rest before receiving the HER2-CD28 T cells.

The fludarabine and cyclophosphamide will be given intravenously (through a needle inserted into a vein or your port-a-cath).

The HER2-CD28 T cells will be given into the vein through an IV line. Before you receive the injection, you may be given a dose of Benadryl (Diphenhydramine) and Tylenol (Acetaminophen). The injection will take between 1 and 10 minutes. We will follow you in the clinic after the injection for 1 to 4 hours. The treatment will be given by the Center for Cell and Gene Therapy at Texas Children's Hospital or Houston Methodist Hospital. We will follow you in the clinic after the T-cell injection and also follow results of your disease evaluations with your primary doctor.

Medical tests before treatment--
Before being treated, you will receive a series of standard medical tests:

Physical exam
Blood tests to measure blood cells, inflammation, kidney and liver function
Routine heart function test (Echocardiogram)
Measurements of your tumor by routine imaging studies. We will use the imaging study that was used before to follow your tumor (Computer Tomogram (CT), Magnetic Resonance Imaging (MRI), or Positron Emission Tomograhy(PET/CT))
Chest X-Ray

Medical tests during and after treatment--
You will receive standard medical tests when you are getting the infusions and after:
Physical exams
Blood tests to measure blood cells, kidney and liver function
Routine heart function test (Echocardiogram) at 6 weeks after the infusion
Measurements of your tumor by routine imaging studies 6 weeks after the infusion

To learn more about the way the HER2-CD28 T cells are working and how long they last in the body, an extra amount of blood, based on your weight, up to a maximum of 60 ml (12 teaspoons) of blood will be taken on the day of the T-cell infusion, before and at the end of the T-cell infusion, 1, 2, 4 and 6 weeks after the T-cell infusion and every 3 months for 1 year, every 6 months for 4 years, then yearly for a total of 15 years. One additional blood sample might be drawn 3 to 4 days post the T-cell infusion; this is optional. For children, the total amount of blood drawn will not be more than 3ml (less than 1 teaspoon) per 1 kg of body weight on any one day. This volume is considered safe, but may be decreased if you are anemic.

During the time points listed above, if the T cells are found in your blood at a certain amount an extra 5ml of blood may need to be collected for additional testing.

If you tolerate the treatment well and have no significant decline in your health, you may receive additional doses of the T cells at 6 to 12 week intervals if you wish. Before the second and third T-cell infusion, you are eligible to receive the same lymphodepleting chemotherapy as before your initial T-cell infusion. After each T-cell infusion, you will be monitored as described above.

After treatment if you have stable disease (the tumor did not grow) or there is a reduction in the size of your tumor on imaging studies, this may indicate that the treatment is helping to control your tumor. If your tumor is bigger after treatment, this may be due to progression of your tumor (the treatment is not effective) or may be due to inflammation around the tumor causing it to look bigger (called pseudo-progression) before it gets smaller. After the first infusion, we will discuss your tumor imaging results with you to help you make the best decision about whether it may be beneficial to receive additional T cell treatments.

If you have a tumor biopsy or resection performed any time while you are on study, a sample of this will be used for research purposes (if a sample can be obtained). If there is a medical reason for you to undergo tumor resection, this may be done as early as 4 weeks after T cell treatment.

If you develop a second abnormal growth, significant blood or nervous system disorder during the trial, a biopsy sample of the tissue will be tested (if a sample can be obtained).

You will receive supportive care for acute or chronic toxicity, including blood components or antibiotics, and other intervention as appropriate.

If you decide to withdraw at any time during the study both samples and data collected during your participation will be maintained.

These specimens and information about your circumstances may be used in other research being conducted in immune therapy. Although there will be a record identifying under what circumstances these specimens were obtained, under all circumstances your identity will be kept confidential. There is a small risk for the loss of confidentiality. However, study personnel will make every effort to minimize this risk.

In the event of your death, we will request permission to perform an autopsy to learn more about the effect of this experimental treatment on your tumor. Proper consent for an autopsy will be obtained from your next of kin in the event of your death.

Research related health information

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you sign this document, you give permission to people who give medical care and ensure quality from Baylor College of Medicine, TCH: Texas Children's Hospital, TCH: Texas Children's Hospital General Clinical Research Center, and TMH: The Methodist Hospital to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Specific information concerning HIV
- Demographic information (name, D.O.B., age, gender, race, etc.)
- Billing or financial records

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, TCH: Texas Children's Hospital, TCH: Texas Children's Hospital General Clinical Research Center, TMH: The Methodist Hospital, ALEX'S LEMONADE STAND and their representatives, COOKIES FOR KIDS' CANCER and their representatives, ST. BALDRICK'S FOUNDATION and their representatives, STAND UP TO CANCER (SU2C) and their representatives, and TRIUMPH OVER KID CANCER FOUNDATION and their representatives.

Agents of the U.S. Food and Drug Administration may inspect the research records including your health information. Agents of regulatory agencies such as the U.S. Department of Health and Human Services will be permitted to inspect the research records including your health information.

A Data and Safety Monitoring Board will have access to the research records including your health information.

Use or Disclosure Required by Law

Your health information will be used or disclosed when required by law.

Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability and conducting public health surveillance, investigations or interventions.

Baylor College of Medicine, TCH: Texas Children's Hospital, TCH: Texas Children's Hospital General Clinical Research Center, and TMH: The Methodist Hospital are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine, TCH: Texas Children's Hospital, TCH: Texas Children's Hospital General Clinical Research Center, and TMH: The Methodist Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

Please note that the research involves treatment. You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment. To maintain the integrity of this research study, you generally will not have access to your personal health information related to this research until the study is complete. However, your health information that is necessary to your care will be provided to you or your physician. At the conclusion of the research and at your request, you generally will have access to your health information that Baylor College of Medicine, TCH: Texas Children's Hospital, TCH: Texas Children's Hospital General Clinical Research Center, and TMH: The Methodist Hospital maintain in a designated record set, which means a set of data that includes medical information or billing records used in whole or in part by your doctors or other health care providers at Baylor College of Medicine, TCH: Texas Children's Hospital, TCH: Texas Children's Hospital General Clinical Research Center, and TMH: The Methodist Hospital to make decisions about individuals. Access to your health information in a designated record set is described in the Notice of Privacy Practices provided to you by representatives of the specific institution where you are being enrolled into this research study which are: Baylor College of Medicine, TCH: Texas Children's Hospital, TCH: Texas Children's Hospital General Clinical Research Center, and TMH: The Methodist Hospital.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, ALEX'S LEMONADE STAND and their representatives, COOKIES FOR

KIDS' CANCER and their representatives, ST. BALDRICK'S FOUNDATION and their representatives, STAND UP TO CANCER (SU2C) and their representatives, TRIUMPH OVER KID CANCER FOUNDATION and their representatives, regulatory agencies such as the U.S. Department of Health and Human Services, FDA, Baylor College of Medicine, Data and Safety Monitoring Board, TCH: Texas Children's Hospital, TCH: Texas Children's Hospital General Clinical Research Center, and TMH: The Methodist Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: Nabil Ahmed, MD
1102 Bates Street Feigin Center,
Suite 1770, Houston, TX 77030

This authorization does not have an expiration date. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

Potential Risks and Discomforts
Risk of Blood draws: Pain/discomfort at the site of the needle stick. Bruising and/or bleeding at the site of the needle stick. There is also a very small risk of infection at the site of the needle stick.

While on this research study you are at risk for side effects from the treatments. There may also be other side effects that we cannot predict. Other drugs will be given to make side effects less serious and less uncomfortable. Many side effects will go away shortly after treatment is stopped, but in some cases, side effects may be long lasting or permanent. Some side effects may be life threatening.

Patients are watched carefully and treatment is stopped if serious side effects develop.

Side Effects of HER2-specific Therapies:
There are several antibodies that are similar our HER2-CD28 T cells that have been given to patients with cancer. Some people who have received these antibodies have had temporary muscle and back pain, fever and chills, shaking, chest pain and labored breathing, wheezing, and nausea or vomiting. These side effects are unlikely in this study where the antibody is stuck to the T cells.

There is one report of a patient who received a dose of HER2-specific T cells that is 100 X-fold greater than the highest dose on this study and died. If low doses of HER2-CD28 T cells worked very well they could attack tissue that expresses low amounts of HER2 such as the heart. Observed side effects of HER2-specific therapies on the heart in patients with other cancers included decreased heart function. This mainly occurred in patients who had pre-existing heart disease. To treat the side effects of infused T cells we would give you doses of steroids which we hope would kill the T cells but they may still be

able to cause serious damage.

There are no known risks of CD28 as part of the chimeric receptor.

Side Effects of the T cells:
Similar types of T cells have been given to patients with cancers and infections. Usually the patients have no problems with the infusions. With the increased doses of T cells, there is a possibility that the harmful effects could increase, though in previous studies we have seen very minimal problems. In some patients with large tumors, the cells have caused inflammation leading to fever and flu-like symptoms, as well as swelling within the tumor. This swelling could be potentially dangerous and even life threatening depending on the site of the tumor.

A small percentage of patients that receive this type of therapy develop a life threatening complication known as a cytokine release syndrome (CRS). This complication causes high body temperature, increased heart rate, and low blood pressure. This complication can be life threatening. There are treatments for this complication.

In addition, a small percentage of patients, who have received a particular type of T cell that attacks leukemia, a type of blood cancer, have developed drowsiness, sleepiness, or have become unresponsiveness. This complication can also be life threatening. As for CRS, there are treatments available for this complication.

Side Effects of the Gene Transfer:
To get the antibody to attach to the surface of the T cell, we must deliver the gene for the antibody into the T cells. This is done with a virus called a retrovirus that has been made for this study. The retrovirus has been altered so it should not be able to come out of the T cells and infect other cells. When retroviral vectors enter a normal cell in the body, the gene it carries goes into the DNA (genetic material) of the cell. Human DNA contains thousands of genes. When the retrovirus adds the gene it carries into the human DNA this is called integration. Integration can occur anywhere in DNA and most integration does not harm the cell or the study subjects. However, there is a chance that there may be some parts of human DNA where integration may turn on or off other genes. For example, if it turned on a gene that made a substance that caused the cell to grow it might cause uncontrolled increase in the numbers of cells, which could result in cancer. Conversely, if it turned off a gene that made a substance that limits cell growth, it might have the same effect. There was one study in mice where cancer occurred, but most other animal studies have shown this risk to be very low with the type of retrovirus we are using.

Some patients who have received marrow stem cells modified with retroviral vectors to correct immunodeficiency disorders have developed leukemias that are due to the vectors. To date this has only been seen in patients being treated who have received stem cells treated with retroviral vectors for immunodeficiency conditions. No leukemias or other cancers have been seen in hundreds of patients who have received T cells modified with retroviral vectors. However, the risk of developing cancer is a risk of receiving products that contain a retroviral vector.

Side effects of lymphodepletion chemotherapy with cyclophosphamide and fludarabine:

Potential side effects are listed below:
Risks and side effects related to cyclophosphamide include:

Likely:
Loss of appetite, Nausea; Vomiting; Fewer white blood cells in the blood (A low number of white blood cells may make it easier to get infections); Hair loss; Decreased ability of the body to fight infection; Absence or decrease in the number of sperm which may be temporary or permanent which may decrease the ability to have children

Less likely:
Abnormal hormone function which may lower the level of salt in the blood; Abdominal pain; Diarrhea; Fewer red blood cells and platelets in the blood; A low number of red blood cells may make you feel tired and weak; A low number of platelets may cause you to bruise and bleed more easily; Bleeding and inflammation of the urinary bladder; Absence or decrease of monthly periods which may be temporary or permanent and which may decrease the ability to have children; Temporary blurred vision; Nasal stuffiness with IV infusions; Skin rash; Darkening of areas of the skin and finger nails; Slow healing of wounds; Infections.

Rare but serious:
Heart muscle damage which may occur with very high doses and which may be fatal; Abnormal heart rhythms; Damage and scarring of lung tissue which may make you short of breath; A new cancer or leukemia resulting from this treatment; Damage or scarring of urinary bladder tissue; Severe allergic reaction which can be life threatening with shortness of breath, low blood pressure, rapid heart rate, chills and fever ; Infertility which is the inability to have children.

Risks and side effects related to fludarabine include:

Likely (may happen in more than 20% of patients):
Low number of red blood cells (anemia); Low number of white blood cells; Low number of blood platelets; Feeling tired; Nausea (feeling sick to your stomach); Throwing up (vomiting); Weak immune system; Pneumonia; Infection; Bleeding; Pain; Electrolyte imbalance.

Less likely (may happen in fewer than 20% of patients):
Diarrhea; Mouth sores; Skin rash; Fever; Swelling of hands and feet; Numbness and tingling in hands and/or feet; Loss of appetite.

Rare but serious (may happen in fewer than 2% of patients):
Changes in vision; Feeling nervous or anxious; Confusion; Cough; Difficulty breathing; Feeling weak; Severe brain injury which can lead to death; Kidney damage that could require dialysis; Coma; New (secondary) cancers.

Acetaminophen (Tylenol): Rarely large doses or long term usage can cause liver damage, rash, itching, fever, lowered blood sugar. These side effects are unlikely at the doses being used for this study.

Benadryl: Drowsiness, dizziness, headache, irritability, stomach upset, vision changes (e.g., blurred vision), decreased coordination, or dry mouth/nose/throat may occur.

Because of potential or unknown effects of the study on a fetus, if you are a woman of childbearing potential, you must have a negative serum pregnancy test prior to entry into this study.

Since this is a research study, there may be risks that are currently unknown. We will watch you very carefully for any side effects. If there are bad side effects, we will stop the treatment.

There is a slight risk of loss of privacy. Research staff and agencies will do everything possible to prevent this risk.

There may be unknown risks or discomforts involved. Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

Potential Benefits

The benefits of participating in this study may be: that your immune system may begin to kill the cancer cells. This could make the cancer grow more slowly, or get smaller, or go away for a while. This benefit is at best only possible, and may not happen to you. Your participation may help the investigators better understand how the immune system can fight this disease. However, you may receive no benefit from participating.

Alternatives

The following alternative procedures or treatments are available if you choose not to participate in this study: other treatments with chemotherapy, radiation, or surgery. Your doctor will discuss these other options with you. Additionally, the same alternatives are available if, after participation in this research project, you are not responding to the therapy. You may also choose to receive no further treatment for your tumor. If this is your decision, your doctor will help manage your symptoms and will discuss this with you.

Subject Costs and Payments

You will not be charged for the manufacture or preparation of the HER2-CD28 T cells, nor will you be charged for the laboratory studies done to monitor how well these T cells are working and to measure how long they stay in your body. You or your insurance company may be charged for some research related costs including the chemotherapy (fludarabine and cyclophosphamide) and infusion of the product. You or your insurance company are responsible for medical services that are part of the standard of care for your cancer.

You will not be paid for taking part in this study.

This institution does not plan to pay royalties to you if a commercial product is developed from blood or tissue obtained from you during this study.

Research Related Injury

You will not be reimbursed for expenses or compensated financially for this injury.

Research personnel will try to reduce, control, and treat any complications from this research. If you are injured because of this study, you will receive medical care that you or your insurance will have to pay for just like any other medical care.

Women of Childbearing Potential

It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. Because of the potential risks involved, you or your partner should not become pregnant while you are participating in this study.

If you are sexually active or become sexually active and can get pregnant or can get your partner pregnant, you must agree to use one of the following forms of birth control every time you have sex and for (6) months afterwards:

* oral contraceptives ("the pill"),
* intrauterine devices (IUDs),
* contraceptive implants under the skin, or contraceptive injections,
* condoms with foam.

Should you become pregnant while on this study, you must immediately notify the study personnel.

The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can choose not to provide this information.

Subject's Rights

Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

The investigator, NABIL AHMED, and/or someone he/she appoints in his/her place will try to answer all

of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: NABIL M AHMED at 832-824-4611 during the day and 832-826-0860 (TCH) or 713-441-1450 (TMH) after hours.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

The National Institutes of Health and the National Cancer Institute may have access to your records for research purposes. Coded information may be provided to the NIH/NCI such as Patient ID, Patient Zip code, Patient country code and Patient Birth date (month/year). However, in the event of an audit NIH/NCI might have access to more information that is part of your research record.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

If your child is the one invited to take part in this study you are signing to give your permission. Each child may agree to take part in a study at his or her own level of understanding. When you sign this you also note that your child understands and agrees to take part in this study according to his or her understanding.

Please print your child's name here _____

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject	Date
Legally Authorized Representative Parent or Guardian	Date
Investigator or Designee Obtaining Consent	Date
Witness (if applicable)	Date
Translator (if applicable)	Date