H-44526- ANCHOR: ALLOGENEIC NATURAL KILLER T-CELLS EXPRESSING CD19 SPECIFIC CHIMERIC ANTIGEN RECEPTOR AND INTERLEUKIN-15 IN RELAPSED OR REFRACTORY B-CELL MALIGNANCIES

Concise and Focused Presentation

- We are asking you to take part in a research study to treat blood or lymph gland cancers (leukemias or lymphomas) that have a protein called CD19.
- We want to see if specially designed immune cells called CD19-CAR NKT cells made from healthy individuals can help treat those cancers.
- If you take part in the study, you will visit the clinic several times for treatment and to have blood drawn to find out how you respond to the treatment. The study will last 15 years after your last infusion of NKT cells. You will visit the clinic initially approximately every week or every other week for six weeks. Later blood draws and tests can be done where you live.
- Your doctors will follow you after your infusions.
- This study has possible risks:
  - -- These NKT cells might attack other parts of your body and cause graft versus host disease.
  - -- The NKT cells might not last long because they do not grow well in your body or because your immune system might attack them. This means the cells might not treat your cancer.
  - -- You could develop potentially fatal problems, including one or both of two conditions: cytokine release syndrome (CRS) and neurotoxicity. CRS is a group of symptoms associated with the release of substances that cause inflammation called cytokines into the blood circulation.
  - -- A loss of confidentiality.

We may not know all the risks.

- Potential benefits:
  - -- The cells may attack your cancer and get rid of it, at least temporarily.

You may choose not to take part in this study.

Background

In this document, the term "you" signifies either 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 blood cancer called acute lymphoblastic leukemia (throughout the rest of this consent form this disease will be referred to as "Leukemia"). Your leukemia has come back or has not gone away after treatment. Because there is no standard treatment for your cancer at this time, you are being asked to volunteer to be in a gene transfer research study using special immune cells. A gene transfer study places a new set of instructions (a new gene) in cells so that they start making a new component. You may have already thought a lot about being in this study. You may even have already made a decision about whether to be in the study. Even 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 disease, antibodies and immune cells, hoping that they will work together. Antibodies are types of proteins that protect the body from bacterial and other diseases. Immune cells, also called lymphocytes, are special infection-fighting blood cells that can kill other cells including tumor cells. Both antibodies and lymphocytes have been used to treat patients with cancer. They have shown promise, but have not been strong enough to cure most patients.

The antibody used in this study is called anti-CD19. It first came from mice that have developed immunity to human leukemia. This antibody sticks to leukemia cells because of a substance on the outside of these cells called CD19. CD19 antibodies have been used to treat people with lymphoma and leukemia. For this study, the anti-CD19 antibody has been changed so that instead of floating free in the blood it is now joined to the NKT cells, a special type of lymphocytes that can kill tumor cells but not very effectively on their own. When an antibody is joined to a T cell in this way it is called a chimeric receptor. In the laboratory, we have also found that NKT cells work better if we also add proteins that stimulate lymphocytes, such as one called CD28. Adding the CD28 makes the cells last for a longer time in the body but maybe not long enough for them to be able to kill the leukemia cells. We believe that if we add an extra stimulating protein, called IL-15, the cells will have an even better chance of killing the leukemia cells.

In this study we are going to see if this is true by putting the anti-CD19 chimeric receptor with CD28 and the IL-15 into NKT cells grown from a healthy individual. We call these cells ANCHOR cells. We will infuse these cells into patients that have lymphomas or leukemias that have CD19 on their surface. The ANCHOR cells are investigational products not approved by the Food and Drug Administration.

Baylor College of Medicine has a financial interest with Kuur Therapeutics, LLC, a licensee of Baylor College Medicine patented technologies. The study staff (Dr. Heslop and Dr. Brenner) also have a financial interest in the development of the study drug. They may benefit financially if this research leads to future treatment options. Please feel free to ask the study team if you have any questions about this relationship.

This research study is sponsored by Baylor College of MedicineThis research study is funded by National Cancer Institute

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 biggest dose of ANCHOR cells that is safe, to see how long the ANCHOR cells last, to learn what their side effects are and to see whether this therapy might help people with lymphoma or leukemia.

Procedures

The research will be conducted at the following location(s):

Baylor College of Medicine, TCH: Texas Children's Hospital, and TMH: The Methodist Hospital.

Approximately 48 subjects may be treated on this study.

Earlier, a healthy donor gave us blood to make ANCHOR cells in the laboratory. These cells were grown and frozen for later use. To make the ANCHOR cells, we took the donor blood and stimulated it with growth factors to make the NKT cells grow. To get the CD19 antibody, CD28 and IL-15 into the NKT cells, we infected them with a virus, called a retrovirus. This virus cannot grow and infect other cells, but delivered a new genetic message into the ANCHOR cells that provides the instructions for the cells to make the CD19 antibody, CD28 and IL-15. This new genetic message will also help us find the ANCHOR 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. If you cannot visit the clinic, you may be contacted by the research coordinator or physician.

When you enroll on this study, you will be assigned a dose of ANCHOR cells. This is a dose escalation study. This means that at the beginning, patients will be started on the lowest dose (1 of 4 different levels) of ANCHOR cells. Once that dose schedule proves safe, the next group of patients will be started at a higher dose. This process will continue until all 4 dose levels are studied. If the side effects are too severe, the dose will be lowered or the infusions will be stopped.

Several studies suggest that any infused immune cells need room to be able to proliferate and accomplish their functions and that this may not happen if there are too many other cells in circulation. Because of that, you will receive treatment with cyclophosphamide and fludarabine. These drugs will decrease the numbers of your own immune cells before we infuse the ANCHOR cells. Although we do not expect any effect on your tumor with the dose that you will receive, these drugs are part of many regimens that are used to treat lymphoma or leukemia. We would prefer that you not receive other chemotherapy or treatment with steroids until 6 weeks after your cell infusion but you can do so if your doctor thinks it is medically necessary.

You will be given an injection of ANCHOR cells into the vein through an IV at the assigned dose. Before you receive the injection, you may be given a dose of Benadryl and Tylenol. The injection will take about 1-10 minutes. We will follow you in the clinic after the injection for up to 2 hours. You will need to stay in Houston for 4 weeks after the ANCHOR cell infusion so we can monitor you for side effects. You will have follow-up visits (3 times per week at weeks 1, 2, 3, 4, and once during week 6; months 3, 6, 9, and 12; twice a year for 4 years and then once a year for the next 10 years - for a total of 15 years) and scheduled disease evaluations after the ANCHOR cell infusion (at week 4 and then as clinically needed).

The treatment will be given by the Center for Cell and Gene Therapy at Houston Methodist Hospital or Texas Children's Hospital.

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

- Physical exam and History
- Blood tests to measure blood cells, kidney and liver function
- Measurements of your tumor by scans and/or bone marrow studies
- A urine or serum pregnancy test, when applicable

Medical tests during and after treatment--
You will receive standard medical tests when you are getting the infusions and afterwards. These visits are required as normal follow up for your disease and treatment. The length of the visits will vary and depend on the amount of time necessary to properly evaluate and treat you for your condition and your related symptoms. The evaluations that will be done at these visits include:

- Physical exams and History
- Blood tests to measure blood cells, kidney and liver function
- Measurements of your tumor by scans at 4-6 weeks, 3 months , 6 months, 9 months and 12 months
- If you have disease in the bone marrow, measurements of your tumor by bone marrow studies at 8-12 weeks, 6 months, 9 months and 12 months after the infusion
- To learn more about the way the ANCHOR cells are working and how long they last in the body, extra blood will be drawn. The total amount on any day is about 12 teaspoons (60 ml). This volume is considered safe but may be decreased if you are anemic (have a low red blood cell count). This blood may be drawn from a central line if you have one. On the day you receive the cells, blood will be taken before the cells are given and a few hours afterwards. Other blood will be drawn one week after the infusion, 2 weeks, 3 weeks (optional), 4 weeks, and 6 weeks after the infusion, at 3 months, at 6 months, at 9 months, at 1 year, twice a year for 4 years, then yearly for the next 10 years - for a total of 15 years. The total blood drawn during your participation in this study will not exceed 340 teaspoons.
- During the time points listed above, if the ANCHOR cells are found in your blood above a certain amount, an extra 5 ml of blood may need to be collected for additional testing.
- If you have a biopsy of your tumor or bone marrow studies while you are on this study, we may ask to have a piece for research purposes.

If you develop a second cancer, a biopsy sample of the cancer tissue will be tested (if a sample can be obtained).

You will receive supportive care for any acute or chronic toxicities, 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.

The remaining blood and/or tissue samples that are not needed directly for you could be used to help researchers learn about this disease. The specimens will be kept until the samples are exhausted. These specimens and information about your circumstances may be shared with other cancer

researchers or third party laboratories.

Samples will be kept at Baylor College of Medicine indefinitely. 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. This consent form is not legally binding and proper consent for an autopsy will be obtained from your next of kin in the event of your death.

Baylor College of Medicine has a licensing agreement with a third party for the commercialization of NKT cells for cancer immunotherapy. Baylor College of Medicine has an interest in the outcome of the study and positive outcomes can financially benefit the institution, but the institution has taken steps to not let this interfere with the way the study is conducted or your safety.

Clinically Relevant Research Results

The results generated from this research study are not expected to have any clinical relevance to you.

Sharing and Future Research Studies with Identifiable Private Information

Information that identifies you may be removed from your identifiable private information collected as part of this research, and after such removal, your information may be used for future research studies or distributed to another investigator for future research studies without additional consent/authorization from you.

Sharing and Future Research Studies with Identifiable Biospecimens

Information that identifies you may be removed from your identifiable biospecimens collected as part of this research, and after such removal, your biospecimens may be used for future research studies or distributed to another investigator for future research studies without additional consent/authorization from you.

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, 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.)
- Full Social Security #
- Billing or financial records
- Identifiable biospecimens

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, TMH: The Methodist Hospital, and NATIONAL CANCER INSTITUTE (NCI) 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

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. 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.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

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 may not use the Certificate to withhold that information.

Information regarding study participation will be included in your medical records.

The Certificate of Confidentiality will not be used to prevent disclosure of child abuse, neglect, or harm to self or others to state or local authorities.

Baylor College of Medicine, TCH: Texas Children's Hospital, 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, 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, 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, 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, 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, NATIONAL CANCER INSTITUTE (NCI) 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, 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: Dr. Carlos A. Ramos, Feigin Tower, 1102 Bates Street, Suite 1760, 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

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.

Potential Side Effects of the CD19 Antibody
There are several antibodies that are similar to CD19 and 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 NKT cells. One other side effect is that the antibody may react with normal cells such as normal immune system cells called B cells that have CD19 on their surface as well as the cancer cells. If the ANCHOR cells worked very well they could kill your normal B cells as well as the lymphoma and leukemia cells. In that case you would not have B cells to make antibodies that help you fight infection and may have a higher risk of some types of infection. We will check your antibody levels and if these are low we will replace with a product called IVIg that contains antibodies. You would need to get IVIg every 6-8 weeks.

Potential Side Effects of CD28:
There are no known side effects of CD28.

Potential Side Effects of the NKT cells
Similar types of immune cells have been given to patients with cancers and infections. Usually the patients have no problems with the infusions. With the increased doses of 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.

Anti-CD19 CAR T cells when used in patients with lymphoma and chronic leukemia are known to cause side effects. Common side effects include Cytokine-release syndrome (CRS) and Neurotoxicity. We do not know if NKT cells will be associated with these symptoms but this is a likely possibility.

CRS is a group of symptoms associated with the release of substances that cause inflammation called cytokines into the blood circulation. CRS can affect many different parts of the body, and most patients will have at least some of the symptoms listed below. Severe or life-threatening cases requiring life support (intensive care), blood pressure medications, dialysis, or ventilators (breathing machines) have occurred in approximately 25% of subjects. Specific symptoms have included:
- General: fever and tiredness
- Heart: rapid or irregular heart rate, decreased heart function, cardiac arrest, heart muscle injury, or very low blood pressure. These events may be life threatening and require special medications or procedures to restore blood circulation including CPR.
- Lungs: shortness of breath and low oxygen supply sometimes requiring supplemental oxygen and/or insertion of a breathing tube and placement on a ventilator (breathing machine) to help with breathing
- Blood vessels: vascular leak syndrome (in which the fluid in your bloodstream leaks out of circulation

into other areas of your body)
- Kidneys: low urine output and kidney failure, sometimes requiring dialysis
- Stomach/liver/intestines: liver dysfunction (e.g., changes in AST/ALT), nausea, vomiting, diarrhea

Neurotoxicity is a group of symptoms involving the brain and spinal cord. Most patients will have at least some of the symptoms listed below. Severe or life-threatening cases have occurred in approximately 25% of subjects. Specific symptoms have included confusion, difficulty speaking or understanding speech, prolonged or pronounced sleepiness, tremors (shaky hand or other body part), facial droop, seizures which may be prolonged, inability to control bladder or bowel, weakness in arms and/or legs, difficulty or inability to walk, anxiety and dizziness. Neurotoxicity can also lead to difficulty breathing and low oxygen levels, requiring insertion of a breathing tube and placement on a ventilator (breathing machine) to assist with breathing and may be potentially life-threatening.

In addition to the above-mentioned supportive medical care for patients who develop CRS and/or Neurotoxicity, medications will be used that specifically treat both conditions.

As you are receiving NKT cells from an unrelated donor, there is the possibility that these donor NKT cells or residual T cells in the cellular product might try to attack other parts of your body and cause graft versus host disease (GVHD). GVHD occurs when cells from the immune cell donor (graft) recognize that your body's tissues (host) are different from those of the donor. When this happens, cells from the donor may attack your skin, liver and/or intestines. If you have GVHD after the ANCHOR cells have been given, we will treat you appropriately.

Conversely, because the ANCHOR cells could be recognized as being foreign by your body and destroyed by the immune system, we modified them so that they do not express proteins that are usually involved in immune rejection. While we hope this will improve ANCHOR cell function, this could also increase the likelihood for side effects. However, we do not know if this will be the case or not.

Potential Side Effects from the IL-15:
NKT cells genetically engineered to produce IL-15 have not been tested in humans. Other cell types, for example T cells, which were genetically engineered to produce IL-15 have not been tested in humans. Infusing IL-15 to humans has been studied in humans and was associated with low blood pressure, changes in liver enzyme levels and decrease in platelet count at higher doses. In some animal studies, when IL-15 was produced in immature T cells, the T cells divided rapidly and, in some experiments, these immature T cells became leukemia cancer cells. In the laboratory, NKT cells carrying the anti-CD19 receptor and IL-15 were safe and did not grow and divide in the absence of tumors.

Side Effects of the Gene Transfer:
To get the antibody to attach to the surface of the NKT cell, we must deliver the gene for the antibody into the NKT 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 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. 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 havebeen 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.

Potential Side Effects of Dimethyl sulfoxide (DMSO):
The preservative called DMSO that we may use to freeze the cells in is breathed out through the lungs. You will have a funny taste in your mouth for a few minutes after getting the cells. Some people say this tastes like garlic. It may also make your breath smell like garlic.

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.

Risk of tumor biopsy:
Risks vary based on the site of the tumor. The specific risks of your tumor biopsy will be discussed with you. In general the risks of a tumor biopsy include bleeding, bruising, and infection.

Risk of bone marrow aspirate:
The risks include pain, bleeding and infection.

Potential Side Effects of Lymphodepleting Chemotherapy with cyclophosphamide and fludarabine

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 (IV) include:

Likely:
Loss of appetite; Nausea or the urge to vomit; Decreased number of red blood cells, white blood cells, and/or platelets (a blood cell that helps clot blood); Muscle weakness of the whole body; Cough; Shortness of breath; Fatigue or tiredness; Fever; Infection; Pain; Increased risk of unusual infections lasting more than 6 months.

Less likely:
Skin rash with the presence of macules (flat discolored area) and papules (raised bumps); Diarrhea; Irritation or sores in the lining of the mouth, voice box, throat, and windpipe; Vomiting; Peripheral Neuropathy - commonly known as "pins and needles," where part of the body (typically a foot or hand) begins to tingle and becomes numb, or "falls asleep"; Blurred vision, double vision and/or loss of vision (blindness); Fear of light; Inflammation of the lungs that may cause difficulty breathing and can be life-threatening; Chills; An increase in the number of a type of white blood cell (called eosinophils) in the blood; Agitation or restlessness; Confusion; Weakness or paralysis (loss of muscle function) caused by damage to peripheral nerves (those nerves outside of brain and spinal cord); Inflammation (swelling and redness) or degeneration of the peripheral nerves (those nerves outside of brain and spinal cord) causing numbness, tingling, burning; Pain of the urinary tract; Inflammation (swelling and redness) of the paranasal sinuses which may or may not be a result of infection.

Rare but serious:
Severe rash with redness, pain and/or blisters. When pressure is applied to an area, the skin will detach from the lower layers; A rare autoimmune disorder called Evan's syndrome in which the body makes antibodies that destroy the red blood cells, platelets and white blood cells; Sudden damage to the red blood cells (hemolytic anemia) which could cause a rapid decrease in the number of red blood cells such that you may be tired, weak, feel short of breath, and may require a blood transfusion; Coma

and/or abnormal brain function; Convulsion or seizure; Blindness; A rare disorder that damages the material that covers and protects nerves in the white matter of the brain. The disorder may cause headaches, loss of coordination, clumsiness, loss of language ability, memory loss, vision problems, and weakness of the legs and arms that gets worse; Inflammation (swelling and redness) of the bladder not due to urinary tract infection; Severe potentially life-threatening damage to the lungs which can lead to fluid in the lungs; Bleeding from the lungs. Kidney damage which may require dialysis.

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 urine or serum pregnancy test prior to entry into this study.

You have been informed that either you or your partner(s) must utilize one of the more effective birth control methods during the study and for six months after the study is concluded. These consist of total abstinence, oral contraceptives "the pill", intrauterine devices (IUDs), contraceptive implants under the skin, or contraceptive injections. If one of these methods cannot be used, contraceptive foam with a condom is allowed. In addition, the male partner should use a condom.

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.

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

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 the ANCHOR cells may begin to kill the cancer cells. This could make the cancer grow more slowly, or get smaller, or go away (at least 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 leukemias or lymphomas. 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 preparation or manufacture of the ANCHOR cells, nor will you be charged for the laboratory studies done to monitor the how well these cells are working and to measure how long they stay in your body. You and/or your insurance company may be charged for some research related costs including the chemotherapy and infusion of the cells. You and/or your insurance company will be responsible for medical services provided that are part of the standard of care for your cancer (including some supportive care treatments, laboratory, and disease evaluations). Financial counseling is available if needed.

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

Research Related Injury

If you are injured as part of your participation in this study, there are no plans to pay you.

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, CARLOS RAMOS, 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: CARLOS ALMEIDA RAMOS at (713) 441-1450 during the day and 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.

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.

In addition, study data is sent to the company, March Biosciences, Inc. They will not have access to any information that could identify you.

Financial Conflict of Interests: The following investigators were determined to have financial conflicts based on their relationship with immuno-oncology companies that make cell-based immunotherapy products, which is the focus of this research:

-Dr. Helen Heslop has relationships with these entities: Marker Therapeutics, LLC (Scientific Advisor/ Scientific Advisory Board, Business Ownership/ Equity Interest) and March Biosciences, Inc. (Consulting, Equity).

-Dr. Cliona Rooney has relationships with these entities: Marker Therapeutics, LLC (Scientific Advisor/ Scientific Advisory Board, Business Ownership/ Equity Interest) and March Biosciences, Inc.

Dr. Malcolm Brenner, Dr. Rooneys spouse, has relationships with these entities Marker Therapeutics, LLC (Business Ownership/Equity Interest) and March Biosciences (Leadership, Income).

-Dr. LaQuisa Hill has a speaker agreement with Kite Pharma, Inc.

-Dr. Maksim Mamonkin has relationships with these entities: Amgen, Inc. (Industry speaking Events),

Galapagos NV (Industry Speaking Events), March Biosciences, Inc. (Income, Leadership, and Consulting), and NKILT Therapeutics (Income and Consulting).

Neither Marker Therapeutics nor Kite Pharma are involved with this protocol.

These relationships mean that these individuals may stand to profit financially from the results of this study. These relationships have been independently reviewed, and to minimize any potential influence on the conduct of this study, these individuals' activities on this study have been restricted. There is oversight on this study from individuals who are not invested and are not expected to benefit financially. You can ask any questions you would like to decide whether you wish to continue participating in this study.
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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

TREATMENT CONSENT FORM (Arm A: NON-ALL)

H-44526- ANCHOR: ALLOGENEIC NATURAL KILLER T-CELLS EXPRESSING CD19 SPECIFIC CHIMERIC ANTIGEN RECEPTOR AND INTERLEUKIN-15 IN RELAPSED OR REFRACTORY B-CELL MALIGNANCIES

Concise and Focused Presentation

- We are asking you to take part in a research study to treat blood or lymph gland cancers (leukemias or lymphomas) that have a protein called CD19.
- We want to see if specially designed immune cells called CD 19-CAR NKT cells made from healthy individuals can help treat those cancers.
- If you take part in the study, you will visit the clinic several times for treatment and to have blood drawn to find out how you respond to the treatment. The study will last 15 years after your last infusion of NKT cells. You will visit the clinic initially approximately every week or every other week for six weeks . Later blood draws and tests can be done where you live.
- Your doctors will follow you after your infusions.
- This study has possible risks:
-- These NKT cells might attack other parts of your body and cause graft versus host disease .
-- The NKT cells might not last long because they do not grow well in your body or because your immune system might attack them. This means the cells might not treat your cancer.
-- You could develop potentially fatal problems, including one or both of two conditions: cytokine release syndrome (CRS) and neurotoxicity. CRS is a group of symptoms associated with the release of substances that cause inflammation called cytokines into the blood circulation.
-- A loss of confidentiality.

We may not know all the risks.

- Potential benefits:
-- The cells may attack your cancer and get rid of it, at least temporarily.

You may choose not to take part in this study.

Background

In this document, the term "you" signifies either 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 lymph gland cancer called non-Hodgkin lymphoma or you have a blood cancer called chronic lymphocytic leukemia (throughout the rest of this consent form these diseases will be referred to as "Lymphoma"). Your lymphoma has come back or has not gone away after treatment. Because there is no standard treatment for your cancer at this time, you are being asked to volunteer to be in a gene transfer research study using special immune cells. A gene transfer study places a new set of instructions (a new gene) in cells so that they start making a new component. You may have already thought a lot about being in this study. You may even have already made a decision about whether to be in the study. Even 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 disease , antibodies and immune cells, hoping that they will work together. Antibodies are types of proteins that protect the body from bacterial and other diseases. Immune cells, also called lymphocytes, are special infection-fighting blood cells that can kill other cells including tumor cells. Both antibodies and lymphocytes have been used to treat patients with cancer. They have shown promise, but have not been strong enough to cure most patients.

The antibody used in this study is called anti-CD19. It first came from mice that have developed immunity to human lymphoma. This antibody sticks to lymphoma cells because of a substance on the outside of these cells called CD19. CD19 antibodies have been used to treat people with lymphoma and leukemia. For this study, the anti-CD19 antibody has been changed so that instead of floating free in the blood it is now joined to the NKT cells, a special type of lymphocytes that can kill tumor cells but not very effectively on their own. When an antibody is joined to a T cell in this way it is called a chimeric receptor. In the laboratory, we have also found that NKT cells work better if we also add proteins that stimulate lymphocytes, such as one called CD28. Adding the CD28 makes the cells last for a longer time in the body but maybe not long enough for them to be able to kill the lymphoma cells. We believe that if we add an extra stimulating protein, called IL-15, the cells will have an even better chance of killing the lymphoma cells.

In this study we are going to see if this is true by putting the anti-CD19 chimeric receptor with CD28 and the IL-15 into NKT cells grown from a healthy individual. We call these cells ANCHOR cells. We will infuse these cells into patients that have lymphomas or leukemias that have CD19 on their surface. The ANCHOR cells are investigational products not approved by the Food and Drug Administration.

Baylor College of Medicine has a financial interest with Kuur Therapeutics, LLC, a licensee of Baylor College Medicine patented technologies. The study staff (Dr. Heslop and Dr. Brenner) also have a financial interest in the development of the study drug. They may benefit financially if this research leads to future treatment options. Please feel free to ask the study team if you have any questions about this relationship.

This research study is sponsored by Baylor College of MedicineThis research study is funded by National Cancer Institute

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 biggest dose of ANCHOR cells that is safe , to see how long the ANCHOR cells last, to learn what their side effects are and to see whether this therapy might help people with lymphoma or leukemia.

Procedures

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

Approximately 48 subjects may be treated on this study.

Earlier, a healthy donor gave us blood to make ANCHOR cells in the laboratory . These cells were grown and frozen for later use. To make the ANCHOR cells, we took the donor blood and stimulated it with growth factors to make the NKT cells grow. To get the CD19 antibody, CD28 and IL-15 into the NKT cells, we infected them with a virus, called a retrovirus. This virus cannot grow and infect other cells, but delivered a new genetic message into the ANCHOR cells that provides the instructions for the cells to make the CD19 antibody, CD28 and IL-15. This new genetic message will also help us find the ANCHOR 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. If you cannot visit the clinic, you may be contacted by the research coordinator or physician.

When you enroll on this study, you will be assigned a dose of ANCHOR cells. This is a dose escalation study. This means that at the beginning, patients will be started on the lowest dose (1 of 4 different levels) of ANCHOR cells. Once that dose schedule proves safe, the next group of patients will be started at a higher dose. This process will continue until all 4 dose levels are studied. If the side effects are too severe, the dose will be lowered or the infusions will be stopped.

Several studies suggest that any infused immune cells need room to be able to proliferate and accomplish their functions and that this may not happen if there are too many other cells in circulation. Because of that, you will receive treatment with cyclophosphamide and fludarabine. These drugs will decrease the numbers of your own immune cells before we infuse the ANCHOR cells . Although we do not expect any effect on your tumor with the dose that you will receive , these drugs are part of many regimens that are used to treat lymphoma or leukemia. We would prefer that you not receive other chemotherapy or treatment with steroids until 6 weeks after your cell infusion but you can do so if your doctor thinks it is medically necessary.

You will be given an injection of ANCHOR cells into the vein through an IV at the assigned dose . Before you receive the injection, you may be given a dose of Benadryl and Tylenol. The injection will take about 1-10 minutes. We will follow you in the clinic after the injection for up to 2 hours. You will need to stay in Houston for 4 weeks after the ANCHOR cell infusion so we can monitor you for side effects . You will have follow-up visits (3 times per week at weeks 1, 2, 3, 4, and once during week 6; months 3, 6, 9, and 12; twice a year for 4 years and then once a year for the next 10 years - for a total of 15 years) and scheduled disease evaluations after the ANCHOR cell infusion (at week 4 and then as clinically needed).

The treatment will be given by the Center for Cell and Gene Therapy at Houston Methodist Hospital or Texas Children's Hospital.

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

- Physical exam and History
- Blood tests to measure blood cells, kidney and liver function
- Measurements of your tumor by scans and/or bone marrow studies
- A urine or serum pregnancy test, when applicable

Medical tests during and after treatment--
You will receive standard medical tests when you are getting the infusions and afterwards. These visits are required as normal follow up for your disease and treatment. The length of the visits will vary and depend on the amount of time necessary to properly evaluate and treat you for your condition and your related symptoms. The evaluations that will be done at these visits include:

- Physical exams and History
- Blood tests to measure blood cells, kidney and liver function
- Measurements of your tumor by scans at 4-6weeks, 3 months, 6 months, 9 months and 12 months
- If you have disease in the bone marrow, measurements of your tumor by bone marrow studies at 8-12 weeks, 6 months, 9 months and 12 months after the infusion.
- To learn more about the way the ANCHOR cells are working and how long they last in the body, extra blood will be drawn. The total amount on any day is about 12 teaspoons (60 ml). This volume is considered safe but may be decreased if you are anemic (have a low red blood cell count). This blood may be drawn from a central line if you have one. On the day you receive the cells, blood will be taken before the cells are given and a few hours afterwards. Other blood will be drawn one week after the infusion, 2 weeks, 3 weeks (optional), 4 weeks, and 6 weeks after the infusion, at 3 months, at 6 months, at 9 months, at 1 year, twice a year for 4 years, then yearly for the next 10 years - for a total of 15 years. The total blood drawn during your participation in this study will not exceed 340 teaspoons.
- During the time points listed above, if the ANCHOR cells are found in your blood above a certain amount, an extra 5 ml of blood may need to be collected for additional testing.
- If you have a biopsy of your tumor or bone marrow studies while you are on this study, we may ask to have a piece for research purposes.
- A biopsy of a lymph node will be done at 1-6 weeks after the infusion if possible and will be tested for research purposes.

If you develop a second cancer, a biopsy sample of the cancer tissue will be tested (if a sample can be obtained).

You will receive supportive care for any acute or chronic toxicities, 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.

The remaining blood and/or tissue samples that are not needed directly for you could be used to help researchers learn about this disease. The specimens will be kept until the samples are exhausted. These specimens and information about your circumstances may be shared with other cancer researchers or third party laboratories.

Samples will be kept at Baylor College of Medicine indefinitely. 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. This consent form is not legally binding and proper consent for an autopsy will be obtained from your next of kin in the event of your death.

Baylor College of Medicine has a licensing agreement with a third party for the commercialization of NKT cells for cancer immunotherapy. Baylor College of Medicine has an interest in the outcome of the study and positive outcomes can financially benefit the institution, but the institution has taken steps to not let this interfere with the way the study is conducted or your safety.

Clinically Relevant Research Results

The results generated from this research study are not expected to have any clinical relevance to you.

Sharing and Future Research Studies with Identifiable Private Information

Information that identifies you may be removed from your identifiable private information collected as part of this research, and after such removal, your information may be used for future research studies or distributed to another investigator for future research studies without additional consent/authorization from you.

Sharing and Future Research Studies with Identifiable Biospecimens

Information that identifies you may be removed from your identifiable biospecimens collected as part of this research, and after such removal, your biospecimens may be used for future research studies or distributed to another investigator for future research studies without additional consent/authorization from you.

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, 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.)
- Full Social Security #
- Billing or financial records
- Identifiable biospecimens

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, TMH: The Methodist Hospital, and NATIONAL CANCER INSTITUTE (NCI) 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

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. 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.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

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 may not use the Certificate to withhold that information.

Information regarding study participation will be included in your medical records.

The Certificate of Confidentiality will not be used to prevent disclosure of child abuse, neglect, or harm to self or others to state or local authorities.

Baylor College of Medicine, TCH: Texas Children's Hospital, 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, 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, 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, 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, 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, NATIONAL CANCER INSTITUTE (NCI) 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, 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: Dr. Carlos A. Ramos, Feigin Tower, 1102 Bates Street, Suite 1760, 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

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 .

Potential Side Effects of the CD19 Antibody

There are several antibodies that are similar to CD19 and 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 NKT cells . One other side effect is that the antibody may react with normal cells such as normal immune system cells called B cells that have CD19 on their surface as well as the cancer cells. If the ANCHOR cells worked very well they could kill your normal B cells as well as the lymphoma cells. In that case you would not have B cells to make antibodies that help you fight infection and may have a higher risk of some types of infection. We will check your antibody levels and if these are low we will replace with a product called IVIg that contains antibodies. You would need to get IVIg every 6-8 weeks.

Potential Side Effects of CD28:

There are no known side effects of CD28.

Potential Side Effects of the NKT cells

Similar types of immune cells have been given to patients with cancers and infections. Usually the patients have no problems with the infusions. With the increased doses of 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.

Anti-CD19 CAR T cells when used in patients with lymphoma and chronic leukemia are known to cause side effects. Common side effects include Cytokine-release syndrome (CRS) and Neurotoxicity. We do not know if NKT cells will be associated with these symptoms but this is a likely possibility .

CRS is a group of symptoms associated with the release of substances that cause inflammation called cytokines into the blood circulation. CRS can affect many different parts of the body, and most patients will have at least some of the symptoms listed below. Severe or life-threatening cases requiring life support (intensive care), blood pressure medications, dialysis, or ventilators (breathing machines) have occurred in approximately 25% of subjects. Specific symptoms have included:

- General: fever and tiredness
- Heart: rapid or irregular heart rate, decreased heart function, cardiac arrest, heart muscle injury, or very low blood pressure. These events may be life threatening and require special medications or procedures to restore blood circulation including CPR.

- Lungs: shortness of breath and low oxygen supply sometimes requiring supplemental oxygen and/or insertion of a breathing tube and placement on a ventilator (breathing machine) to help with breathing
- Blood vessels: vascular leak syndrome (in which the fluid in your bloodstream leaks out of circulation into other areas of your body)
- Kidneys: low urine output and kidney failure, sometimes requiring dialysis
- Stomach/liver/intestines: liver dysfunction (e.g., changes in AST/ALT), nausea, vomiting, diarrhea

Neurotoxicity is a group of symptoms involving the brain and spinal cord. Most patients will have at least some of the symptoms listed below. Severe or life-threatening cases have occurred in approximately 25% of subjects. Specific symptoms have included confusion, difficulty speaking or understanding speech, prolonged or pronounced sleepiness, tremors (shaky hand or other body part), facial droop, seizures which may be prolonged, inability to control bladder or bowel, weakness in arms and/or legs, difficulty or inability to walk, anxiety and dizziness. Neurotoxicity can also lead to difficulty breathing and low oxygen levels, requiring insertion of a breathing tube and placement on a ventilator (breathing machine) to assist with breathing and may be potentially life-threatening.

In addition to the above-mentioned supportive medical care for patients who develop CRS and/or Neurotoxicity, medications will be used that specifically treat both conditions.

As you are receiving NKT cells from an unrelated donor, there is the possibility that these donor NKT cells or residual T cells in the cellular product might try to attack other parts of your body and cause graft versus host disease (GVHD). GVHD occurs when cells from the immune cell donor (graft) recognize that your body's tissues (host) are different from those of the donor. When this happens, cells from the donor may attack your skin, liver and/or intestines. If you have GVHD after the ANCHOR cells have been given, we will treat you appropriately.

Conversely, because the ANCHOR cells could be recognized as being foreign by your body and destroyed by the immune system, we modified them so that they do not express proteins that are usually involved in immune rejection. While we hope this will improve ANCHOR cell function, this could also increase the likelihood for side effects. However, we do not know if this will be the case or not.

Potential Side Effects from the IL-15:
NKT cells genetically engineered to produce IL-15 have not been tested in humans. Other cell types, for example T cells, which were genetically engineered to produce IL-15 have not been tested in humans. Infusing IL-15 to humans has been studied in humans and was associated with low blood pressure, changes in liver enzyme levels and decrease in platelet count at higher doses. In some animal studies, when IL-15 was produced in immature T cells, the T cells divided rapidly and, in some experiments, these immature T cells became leukemia cancer cells. In the laboratory, NKT cells carrying the anti-CD19 receptor and IL-15 were safe and did not grow and divide in the absence of tumors.

Side Effects of the Gene Transfer:
To get the antibody to attach to the surface of the NKT cell, we must deliver the gene for the antibody

into the NKT 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 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. 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.

Potential Side Effects of Dimethyl sulfoxide (DMSO):
The preservative called DMSO that we may use to freeze the cells in is breathed out through the lungs. You will have a funny taste in your mouth for a few minutes after getting the cells . Some people say this tastes like garlic. It may also make your breath smell like garlic.

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.

Risk of tumor biopsy:
Risks vary based on the site of the tumor. The specific risks of your tumor biopsy will be discussed with you. In general the risks of a tumor biopsy include bleeding, bruising, and infection.

Risk of bone marrow aspirate:
The risks include pain, bleeding and infection.

Potential Side Effects of Lymphodepleting Chemotherapy with cyclophosphamide and fludarabine
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 (IV) include:

Likely:
Loss of appetite; Nausea or the urge to vomit; Decreased number of red blood cells, white blood cells,and/or platelets (a blood cell that helps clot blood); Muscle weakness of the whole body; Cough; Shortness of breath; Fatigue or tiredness; Fever; Infection; Pain; Increased risk of unusual infections lasting more than 6 months.

Less likely:
Skin rash with the presence of macules (flat discolored area) and papules (raised bumps); Diarrhea; Irritation or sores in the lining of the mouth, voice box, throat, and windpipe; Vomiting; Peripheral Neuropathy - commonly known as "pins and needles," where part of the body (typically a foot or hand) begins to tingle and becomes numb, or "falls asleep"; Blurred vision, double vision and/or loss of vision (blindness); Fear of light; Inflammation of the lungs that may cause difficulty breathing and can be life-threatening; Chills; An increase in the number of a type of white blood cell (called eosinophils) in the blood; Agitation or restlessness; Confusion; Weakness or paralysis (loss of muscle function) caused by damage to peripheral nerves (those nerves outside of brain and spinal cord); Inflammation (swelling and redness) or degeneration ofthe peripheral nerves (those nerves outside of brain and spinal cord) causing numbness, tingling, burning; Pain of the urinary tract; Inflammation (swelling and redness) of the paranasal sinuses which may or may not be a result of infection.

Rare but serious:
Severe rash with redness, pain and/or blisters. When pressure is applied to an area, the skin will detach from the lower layers; A rare autoimmune disorder called Evan's syndrome in which the body makes antibodies that destroy the red blood cells, platelets and white blood cells; Sudden damage to the red

blood cells (hemolytic anemia) which could cause a rapid decrease in the number of red blood cells such that you may be tired, weak, feel short of breath, and may require a blood transfusion; Coma and/or abnormal brain function; Convulsion or seizure; Blindness; A rare disorder that damages the material that covers and protects nerves in the white matter of the brain. The disorder may cause headaches, loss of coordination, clumsiness, loss of language ability, memory loss, vision problems, and weakness of the legs and arms that gets worse; Inflammation (swelling and redness) of the bladder not due to urinary tract infection; Severe potentially life-threatening damage to the lungs which can lead to fluid in the lungs; Bleeding from the lungs. Kidney damage which may require dialysis.

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 urine or serum pregnancy test prior to entry into this study.

You have been informed that either you or your partner (s) must utilize one of the more effective birth control methods during the study and for six months after the study is concluded. These consist of total abstinence, oral contraceptives "the pill", intrauterine devices (IUDs), contraceptive implants under the skin, or contraceptive injections. If one of these methods cannot be used, contraceptive foam with a condom is allowed. In addition, the male partner should use a condom.

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 .

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

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 the ANCHOR cells may begin to kill the cancer cells. This could make the cancer grow more slowly, or get smaller, or go away (at least 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 leukemias or lymphomas. However, you may receive no benefit from participating.. 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 preparation or manufacture of the ANCHOR cells , nor will you be charged for the laboratory studies done to monitor the how well these cells are working and to measure how long they stay in your body. You and/or your insurance company may be charged for some research related costs including the chemotherapy and infusion of the cells. You and/or your insurance company will be responsible for medical services provided that are part of the standard of care for your cancer (including some supportive care treatments, laboratory, and disease evaluations). Financial counseling is available if needed.

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

Research Related Injury

If you are injured as part of your participation in this study, there are no plans to pay you.

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.

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, CARLOS RAMOS, 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: CARLOS ALMEIDA RAMOS at (713) 441-1450 during the day and 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.

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.

In addition, study data is sent to the company, March Biosciences, Inc. They will not have access to any information that could identify you.

Financial Conflict of Interests: The following investigators were determined to have financial conflicts based on their relationship with immuno-oncology companies that make cell-based immunotherapy products, which is the focus of this research:

-Dr. Helen Heslop has relationships with these entities: Marker Therapeutics, LLC (Scientific Advisor/ Scientific Advisory Board, Business Ownership/ Equity Interest) and March Biosciences, Inc. (Consulting, Equity).

-Dr. Cliona Rooney has relationships with these entities: Marker Therapeutics, LLC (Scientific Advisor/ Scientific Advisory Board, Business Ownership/ Equity Interest) and March Biosciences, Inc.

Dr. Malcolm Brenner, Dr. Rooneys spouse, has relationships with these entities Marker Therapeutics, LLC (Business Ownership/Equity Interest) and March Biosciences (Leadership, Income).

-Dr. LaQuisa Hill has a speaker agreement with Kite Pharma, Inc.

-Dr. Maksim Mamonkin has relationships with these entities: Amgen, Inc. (Industry speaking Events), Galapagos NV (Industry Speaking Events), March Biosciences, Inc. (Income, Leadership, and Consulting), and NKILT Therapeutics (Income and Consulting).

Neither Marker Therapeutics nor Kite Pharma are involved with this protocol.

These relationships mean that these individuals may stand to profit financially from the results of this study. These relationships have been independently reviewed, and to minimize any potential influence on the conduct of this study, these individuals' activities on this study have been restricted. There is oversight on this study from individuals who are not invested and are not expected to benefit financially. You can ask any questions you would like to decide whether you wish to continue participating in this study.

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 _____

H-44526- ANCHOR: ALLOGENEIC NATURAL KILLER T-CELLS EXPRESSING CD19 SPECIFIC CHIMERIC ANTIGEN RECEPTOR AND INTERLEUKIN-15 IN RELAPSED OR REFRACTORY B-CELL MALIGNANCIES

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