## Informed Consent Coversheet

| | |
|---|---|
| **Official Study Title:** | CELL THERAPY FOR HIGH RISK T-CELL MALIGNANCIES USING CD7-SPECIFIC CAR EXPRESSED ON NON-EDITED T CELLS (CRIMSON-NE) |
| **NCT Number:** | NCT03690011 |
| **Document Date:** | 12/03/2025 |

H-43761- CELL THERAPY FOR HIGH RISK T-CELL MALIGNANCIES USING CD7-SPECIFIC CAR EXPRESSED ON NON-EDITED T CELLS (CRIMSON-NE)

**Concise and Focused Presentation**

* We ask you to take part in a gene transfer research study to treat a type of blood cancer called T-cell leukemia or lymphoma (lymph gland cancer).

* You are eligible to take part in this research study because your cancer has come back or has not gone away after treatment and there is no standard treatment for your cancer at this time.

* This research study combines two different ways of fighting disease, antibodies and T cells, hoping that they will work together. Antibodies are types of proteins that protect the body from bacterial and other diseases. T cells, also called T lymphocytes, are special infection-fighting blood cells that can kill other cells including tumor cells. We want to see if these cells will kill the tumor cells. When an antibody is joined to a T cell in this way, it is called a chimeric receptor, or "CAR T-Cell."

* If you take part in the study you will receive chemotherapy drugs for 3 days to prepare your body for the T cells. We will then give you an intravenous infusion of the T cell product and monitor you. You will have blood drawn to find out how you respond to the treatment.

* Your participation in this study will last for 15 years since it uses a T cell product that contains a new gene.

* This study has possible risks
- The chemotherapy drugs given may cause side effects.
- The T cells might not last long because your immune system might attack them. This means the cells might not treat your cancer.
- You may experience a treatable side effect called cytokine release syndrome that can lead to fever, difficulty breathing, low blood pressure requiring medication, and treatment in the intensive care unit.
- You may experience symptoms such as confusion, difficulty speaking or other serious neurological side effects.

- Gene transfer is experimental and we may not know all the risks. Please read the consent form for more details on the risks and let your doctor know if you have any questions.

* Potential benefits:
- The cells may kill the tumor cells.

You may choose not to take part in this study.

**Background**

In this document "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 T-cell leukemia or lymphoma (lymph gland cancer). Throughout

the rest of this consent these 2 diseases will be referred to as "T-cell Leukemia or Lymphoma." Your T-cell leukemia or lymphoma has come back or has not gone away after standard of care treatment.

As there are limited or no remaining standard treatments available to treat your cancer, you are being asked to volunteer to be in a gene transfer research study using special immune cells to create a specialized immune cell that will recognize a protein called CD7 that is expressed on the outside surface of the leukemia or lymphoma cells in your body.

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 you make your final decision.

The body has different ways of fighting infection and disease. No one way seems perfect for fighting cancers. This research study combines two different ways of fighting disease, antibodies and T cells, hoping that they will work together. Antibodies are types of proteins that protect the body from bacteria and other diseases. T cells, also called T lymphocytes, are special infection-fighting blood cells that can kill other cells including 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.

T lymphocytes can kill tumor cells but there normally are not enough of them to kill all the tumor cells. Some researchers have taken T cells from a person's blood, grown more of them in the laboratory and then given them back to the person.

The antibody used in this study is called anti-CD7. It first came from mice that have developed immunity to human leukemia. This antibody sticks to T-cell leukemia or lymphoma cells because of a substance on the outside of these cells called CD7. CD7 antibodies have been used to treat people with T-cell leukemia and lymphoma. For this study, anti-CD7 has been changed so that instead of floating free in the blood it is now joined to the T cells. When an antibody is joined to a T cell in this way it is called a chimeric receptor or "CAR T cell".

In the laboratory, we have found that T cells work better if we also add proteins that stimulate T cells, such as one called CD28. Adding the CD28 makes the cells grow better and last longer in the body, thus giving the cells a better chance of killing the leukemia or lymphoma cells.

In this study we are going to attach the CD7 chimeric receptor with CD28 added to it to your T cells. We will then test how long the cells last. These CD7 chimeric receptor T cells with CD28 are investigational products not approved by the Food and Drug Administration.

There are conflicts of interest which pertain to this study. More information is in the Subject's Right's section below.

This research study is sponsored by Baylor College of Medicine. This research study is funded by Cancer Prevention & Research Institute of Texas (CPRIT) and the Leukemia & Lymphoma Society.

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 a dose of chimeric T cells that is safe, to learn what the side effects are and to see whether this therapy might help people with T-cell leukemia or lymphoma.

**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 3-27 subjects may be treated on this study.

Earlier, you gave us blood to make CD7 CD28 chimeric receptor-T cells in the laboratory. These cells were grown and frozen for you. To make the T cells we took your blood and stimulated it with growth factors to make the T cells grow. To get the CD7 antibody and 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. To ensure the T cells grow well in the lab, we add small amounts of medications that are often used to treat patients with cancer or other illnesses. These medications are washed off of the cells prior to injecting them into your body. Because you will 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 CD7 chimeric receptor-T cells. Several studies suggest that the infused T cells need room to be able to proliferate (grow) and accomplish their functions and that this may not happen if there are too many other T cells in your blood. Because of that, you will receive two chemotherapy medications prior to receiving the CD7 chimeric receptor-T cells. One medication is called cyclophosphamide and the other fludarabine. You will receive 3 daily doses of each drug, ending at least one day before you receive the chimeric receptor-T cells. These drugs will decrease the numbers of your own T cells before we infuse the CD7 chimeric receptor T cells and also will help decrease the number of other cells that may interfere with the chimeric receptor-T cells working well. Although we do not expect any effect on your tumor with the doses that you will receive, these drugs are part of many regimens that are used to treat leukemia or lymphoma. We would prefer that you not receive other chemotherapy or treatments for your cancer until 4 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 cells into the vein through an IV at the assigned dose. Before you receive the injection, you will be given a dose of Benadryl and Tylenol. The injection will take about 1-10 minutes. You will
be monitored for at least 3 hours post infusion, and you will have to remain locally for at least 3 weeks after the infusion. If you experience any side effects (see section on risks below), you may have to be

hospitalized for evaluation and management. If restaging studies show you have achieved a complete response (measured by bone marrow or radiology scans 4-6 weeks after the infusion), your primary oncology doctors may decide you should proceed to bone marrow transplant, at which time you will be removed from the treatment portion of the study.

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

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
- Testing of your blood for certain viral infections
- An ultrasound of your heart to make sure your heart function is appropriate for the study if you have not had one recently

YOU WILL RECEIVE STANDARD MEDICAL TESTS DURING TREATMENT AND AFTER:

- Physical exams and History
- Blood tests to measure blood cells, kidney and liver function
- Measurements of your tumor by scans and/or bone marrow studies 4 weeks after the infusion

To learn more about the way the CD7 chimeric receptor-T cells are working and how long they last in the body, extra blood will be drawn. The total amount on any day is about 10 teaspoons (50 mL) or no more than 3 mL per 2.2 pounds body weight in children. This volume is considered safe but may be decreased if you are anemic (decreased number of red blood cells). This blood may be drawn from a central line if you have one. Blood will be taken before you start the chemotherapy a few days prior to the cell infusion. On the day you receive the cells, blood will be taken before the cells are given and several hours afterwards. Other blood will be drawn one week after the infusion, 2 weeks, 3 weeks, 4 weeks 6 and 8 weeks after the infusion, at 3 months, at 6 months, at 9 months, at 1 year, every 6 months for 4 years, then yearly for a total of 15 years. The total blood drawn during your participation in this study will not exceed 280 teaspoons.

If you have a biopsy of your tumor or bone marrow studies in the future after completing this study, we may ask to have a piece of tumor or bone marrow to look for CD7 chimeric receptor-T cells.

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.

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

**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.)
- 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, BAYLOR COLLEGE OF MEDICINE (BCM) and their representatives, CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS (CPRIT) and their representatives, and LEUKEMIA & LYMPHOMA SOCIETY 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, 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, BAYLOR COLLEGE OF MEDICINE (BCM) and their representatives, CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS (CPRIT) and their representatives, LEUKEMIA & LYMPHOMA SOCIETY 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: LaQuisa Hill, MD
Center for Cell and Gene Therapy
Houston Methodist Hospital
6565 Fannin Street, Suite A6-080
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.

Side Effects of CD7 Antibody:

CD7 and several other antibodies that are similar to CD7 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. One other side effect is that the antibody may react with normal cells such as normal immune system cells, mainly T cells, which have CD7 on their surface as well as the cancer cells. If the CD7 chimeric receptor-T cells worked very well, they could kill your normal T cells as well as the leukemia or lymphoma cells. In that case you would not have T cells to help you fight infection and may have a higher risk of some types of infection. We will check your T cell numbers and how well they respond to common viruses in the laboratory. If you develop a serious infection due to low numbers of normal T cells that have been killed by the CD7 chimeric-receptor T cells, we will administer appropriate treatment for the infection, but may also give steroids or other anti-T cell medications to kill the CD7-chimeric T cells. There is a much smaller chance that the CD7 chimeric receptor-T cells may reduce the number of normal natural killer (NK) cells (another type of immune cell) that express CD7 on their surface, which could affect your body's ability to fight infection. If you have persistently low numbers of T cells and you are in complete remission from your leukemia or lymphoma, your primary oncologist may decide to proceed with bone marrow transplant. The chemotherapy required immediately prior to bone marrow transplant (conditioning chemotherapy) would eliminate the chimeric-receptor T cells, thus eliminating any risks associated with them.

Side Effects of T cells attached to CD28:

There are no known side effects of CD28. CD28 has been attached to chimeric T cells targeting CD19 (on the surface of B-cell leukemia and lymphoma) and given to over 400 patients. CD19 chimeric receptor-T cells when used in patients with leukemia and lymphoma are known to cause side effects. Common side effects include Cytokine Release Syndrome (CRS) and neurotoxicity. CRS typically occurs when the chimeric-receptor T cells come into contact with tumor and are expanding in the body, and is more likely to occur in patients with large amounts of leukemia or lymphoma. Details of these side effects follow:

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 (due to kidney failure), 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 cardiopulmonary resuscitation (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 some patients with large tumors or large amounts of tumor cells, the T cells have caused inflammation leading to CRS-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.

Most patients who experience CRS have gone on to have tumor shrinkage. There have been some cases of death due to CRS. With increased doses of T cells, there is a possibility that the harmful effects could increase, though in previous studies it appears the risk of CRS is more related to the

amount of tumor in the body. We have seen very minimal problems related to increasing the dose of T cells.

We did have one patient who experienced significant neurotoxicity following treatment on this study. This patient developed symptoms of confusion and agitation. Imaging of the patient brain and spinal cord showed changes that have been seen in the past with neurotoxicity related to CAR T cells, but also in patients with cancer progression in the brain. We were unable to determine whether the neurotoxicity was related to treatment or disease progression.

You will be monitored closely for any early signs of CRS, neurotoxicity, or other potential side effects (and must remain locally for at least 3 weeks after receiving the chimeric-receptor T cells, as this is the most likely time period for it to occur). 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. These include a medication that blocks the cytokine most commonly elevated in CRS (IL-6), steroids, and other anti-inflammatory medications.

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 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 haveshown this risk to be very low with the type of retrovirus we are using.

More recently in experimental studies, 12 cases of cancer and two cases of a pre-leukemia syndrome (myelodysplastic syndrome) have been reported in children who received a retroviral vector and gene to treat X-linked Severe Combined Immunodeficiency (SCID) (like the "boy in the bubble"), the Wiskott-Aldrich Syndrome (WAS) or Chronic Granulomatous Disease (CGD), all diseases that affect the immune defenses of patients affected by them. While most of the children who participated in the SCID study appear to have been cured of their disease, one child developed leukemia (a form of cancer of the blood) approximately 30 months after receiving the gene therapy treatment; this child appeared to be responding to treatment for leukemia, but the child later died. A second child developed leukemia 34 months after receiving the gene therapy treatment. There are now a total of five children that are known to have developed leukemia in these SCID trials. A group of experts in the field of gene therapy looked at the test results and concluded that gene therapy caused the leukemia in the children. Seven of 10 children treated for WAS also developed leukemia, which was also likely caused by the gene therapy. Finally, 2 CGD patients treated in a gene therapy trial developed pre-leukemia, also

possibly caused by the gene therapy. One patient died from severe infection 27 months after gene therapy and the second one underwent successful allogeneic bone marrow transplantation.

This risk of this problem occurring in this study should be very low because many genes need to be changed for a cell to turn cancerous. The gene we plan to use is different from the genes used in the studies described above. Importantly, the cases of leukemia described above occurred after gene transfer to stem cells. In this study, we are transferring genes to T cells, which has not been associated with development of cancer thus far. Furthermore, over the past 15 years we have and others have treated over 1000 patients with genes to mark cells (the integrated gene marks the cells and allow the cells to be identified from unmarked cells). None have developed any signs of cancer related to the treatment. But even though gene marking has not caused any patients any problems to date, we do not know for certain what the risk is that this treatment will contribute to getting another cancer. For this reason we will need to follow you for 15 years.

Side Effects of Cyclophosphamide (Cytoxan):

Lowered white blood cell count (cells that fight infection) that may lead to fever and infection needing hospitalization and/or treatment with IV antibiotics, lowered platelet count (cells that help the blood to clot) which may lead to bruising or bleeding, lowered red blood cell count (cells that carry oxygen) (anemia) which could cause tiredness or shortness of breath. You may need a red blood cell and/or platelet transfusion if your blood counts are too low.

You could also experience one or more of the following:

Likely:
- Loss of appetite
- Nausea
- Vomiting
- Fewer white blood cells in the blood.
- A low number of white blood cells, which may make it easier to get infections.
- Hair loss
- Decreased ability of the body to fight infections
- 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 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 to Unborn Children from Cyclophosphamide:
Toxicities or defects in a developing fetus have been noted in humans receiving cyclophosphamide (alone or in combination with other anticancer agents). These toxicities may include chromosome abnormalities, multiple anomalies, and low birth weight. Cyclophosphamide is also excreted into breast milk and may cause potential adverse effects, to infants who breast-feed, related to immune suppression, growth problems, and carcinogenesis.

Side Effects of Fludarabine
Risks and side effects related to fludarabine include:

Likely:
- Loss of appetite
- Nausea or the urge to vomit
- Decreased number of red blood cells, white blood cells (neutrophil/granulocyte), 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

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
- 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

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.

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.

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 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. 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 injection of the CD7 CD28 chimeric receptor-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 and/or your insurance company will be responsible for medical services provided that are not part of the research study, but are part of the standard of care for your cancer.

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

This institution may use your biospecimens (even if identifiers are removed) for commercial profit, however, the institution does not plan to pay royalties (share with you in the commercial profit) to you if a

commercial product is developed from any biospecimens (blood or tissue) obtained from you during 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, LAQUISA HILL, 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: RAYNE HELEN ROUCE at 832-822-4716 or LaQuisa Hill at 832-824-4670 during the day and 832-822-4242 (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.

Financial Conflict of Interests:
Baylor College of Medicine and Stand Up to Cancer is providing funding for this research study. The following investigators were determined to have financial conflict based on their relationships with immune-oncology companies that make cell-based immunotherapy products, which is the focus of this funded research:
- Dr. Brenner has relationships with these entities: Allogene (Income, Stock Options), Allovir (Equity), Bellicum Pharmaceuticals (Intellectual Property Ownership), Bluebird BIO. Inc. (Scientific advisory board), Marker Therapeutics, LLC. (Equity), Memgen, LLC (Income), Tessa Therapeutics (Income, Equity), Turnstone Biologics (Income), Walking Fish (Income, Stock Options).
- Dr. Heslop has relationships with these entities: Allovir (Business Ownership/Equity Interest), Gilead Sciences, Inc. (Scientific Advisor/Scientific Advisory Board), Kiadis Pharma (Scientific Advisor/Scientific Advisory Board, Stock Options), Marker Therapeutics, Llc (Equity), Novartis (Consulting, Advising), Tessa Therapeutics Pte. Ltd. (Consulting, Advising)
- Dr. Rooney has relationships with these entities: Allogene (Income), Allovir (Equity), Bellicum Pharmaceuticals (Intellectual Property Ownership), Bluebird BIO. INC. (Scientific advisory board), Marker Therapeutics, LLC. (Equity), Memgen, LLC. (Income), Tessa Therapeutics (Income), Tumstone Biologics (Income), Walking Fish (Income)
-Bambi Grilley, BS, RPh, RAC, CIP, CCRC, CCRP owns a consulting company, QB Regulatory Consulting, LLC that develops, implements and conducts protocols for external sponsors.
-Dr. Lapteva is a Scientific advisor for Tessa Therapeutics Pte. Ltd.
-Dr. LaQuisa Hill has a relationship with March Biosciences, Inc. (Income).

Some of the companies listed may no longer be in existence.

Confidentiality:

It is possible that in the future a commercial or not-for-profit enterprise will help us further develop this product and may end up sponsoring the product with the FDA. If that happens, we will share your data in a manner that will not be identifiable to them.

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.

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-43761- CELL THERAPY FOR HIGH RISK T-CELL MALIGNANCIES USING CD7-SPECIFIC CAR EXPRESSED ON NON-EDITED T CELLS (CRIMSON-NE)

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<br>Parent or Guardian | Date |
| Investigator or Designee Obtaining Consent | Date |
| Witness (if applicable) | Date |
| Translator (if applicable) | Date |