H-47757- INTERLEUKIN-15 ARMORED GLYPICAN-3-SPECIFIC CHIMERIC ANTIGEN RECEPTOR EXPRESSING AUTOLOGOUS T CELLS AS IMMUNOTHERAPY FOR CHILDREN WITH SOLID TUMORS (AGAR)

Concise and Focused Presentation

You are being asked to participate in this study because you have a solid tumor which has come back or has not gone away after treatment, including the standard treatment we know for these diseases. We want to see if specially designed immune cells called IL 15 GPC3-CAR cells (AGAR T cells) made from your blood to help treat your cancer.

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 infusion of AGAR T cells. You will have follow up visits 1 week, 2 weeks, 3 weeks, 4 weeks and 8 weeks after the injection, every 3 months for 1 year, every 6 months for 4 years and then every year for the next 10 years. If your cancer responds to therapy and there are no serious side effects, what are called dose limiting toxicities (DLT), we would allow for up to 3 additional treatments at that same dose.

Potential Risks:
- A small percentage of patients that receive this type of therapy develop a life -threatening complication known as a cytokine release syndrome (CRS). This complication causes high body temperature, increased heart rate, and low blood pressure. This complication can be life threatening. There are treatments for this complication that may or may not be effective.
- To get the antibody (GPC3) 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 and acts as a vector (a carrier of the gene). 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.
- There is a slight risk of the loss of confidentiality.
- There may also be other side effects that we cannot predict.

Potential benefits:
- 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..

Participation in this study is voluntary. You may choose to receive other experimental treatments or palliative care.

Background

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.

In this document, the term "you" signifies either you or your child.

H-47757- INTERLEUKIN-15 ARMORED GLYPICAN-3-SPECIFIC CHIMERIC ANTIGEN RECEPTOR EXPRESSING AUTOLOGOUS T CELLS AS IMMUNOTHERAPY FOR CHILDREN WITH SOLID TUMORS (AGAR)

This is a clinical trial, a type of research study. Your doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family . You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to participate in this study because you have a solid tumor which has come back or has not gone away after treatment, including the standard treatment we know for these diseases. We are asking you to volunteer to be in a research study using special immune system cells called AGAR T cells, a new experimental treatment.

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

We have found from previous research that we can put a new gene (a tiny part of what makes-up DNA and carries your traits) into T cells that will make them recognize cancer cells and kill them. In the lab, we made several genes called a chimeric antigen receptor (CAR), from an antibody called GC33. The antibody GC33 recognizes a protein found on the solid tumor you have. This CAR is called GPC3-CAR. To make this CAR more effective, we also added a gene that includes IL15. IL15 is a protein that helps CAR T cells grow better and stay in the blood longer so that they may kill tumors better. The mixture of GPC3-CAR and IL15 killed tumor cells better in the laboratory when compared with CAR T cells that did not have IL15 .This study will test T cells that we have made (called genetic engineering) with GPC3-CAR and the IL15 (AGAR T cells) in patients with GPC3-positive solid tumors such as yours.

T cells made to carry a gene called iCasp9 can be killed when they encounter a specific drug called Rimiducid. We will insert the iCasp9 and IL15 together into the T cells using a virus that has been made for this study. The drug (Rimiducid) is an experimental drug that has been tested in humans with no bad side-effects. We will use this drug to kill the T cells if necessary due to side effects.

This study will test T cells genetically engineered with a GPC3-CAR and IL15 (AGAR T cells) in patients with GPC3-positive solid tumors.

The AGAR T cells are an investigational product not approved by the Food and Drug Administration.

This research study is sponsored by Baylor College of MedicineThis research study is funded by Cancer Prevention & Research Institute Of Texas

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 AGAR T cells that is safe, to see how long they last in the body, to learn what the side effects are and to see if the AGAR T cells will help people with GPC3-positive solid tumors.

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

Approximately 15-24 subjects will participate in the treatment part of this study.

We have previously collected up to 180 mL (approximately 12 tablespoons) of your blood. We used this blood to grow T cells. We grew the T cells and used a retrovirus (a special virus that can insert the GPC3 CAR and IL15 genes into the T cells) to genetically engineer them. After the CAR and IL15 genes were put into the T cells, we made sure that they could kill GPC3 positive solid tumor cells in the laboratory.

LYMPHODEPLETION CHEMOTHERAPY:

Several studies suggest that the infused T cells need room to be able to increase in numbers/multiply and accomplish their functions and that this may not happen if there are too many other T cells in circulation . Because of that, you will receive treatment with lymphodepletion chemotherapy. This chemotherapy means you will receive both cyclophosphamide (Cytoxan) and fludarabine. You will receive these drugs for 3 days before receiving the T-cell infusion. These drugs will decrease the numbers of your own T cells before we infuse the AGAR T cells.

WHAT THE INFUSION WILL BE LIKE:

After making these cells, they were frozen. If you agree to participate in this study, at the time you are scheduled to be treated, the cells will then be thawed and injected into you over 5 to 10 minutes. You will receive the AGAR T cells 48 to 72 hours after completing the chemotherapy. You will only get one dose of AGAR T cells. You may be pretreated with Tylenol (acetaminophen) and Benadryl (diphenhydramine). Tylenol and Benadryl are given to prevent a possible allergic reaction to the T cell administration.

If we need to stop the AGAR T cells due to bad side effects, we have inserted a gene called iCasp9 into the AGAR T cells. This allows us to eliminate the AGAR T cells in the blood when the gene comes into contact with a medication called Rimiducid. The drug Rimiducid is not yet FDA approved, and is an experimental drug, but it has been tested in humans with no bad side-effects. We will only use this drug to kill the T cells if necessary due to side effects. Since we do not know exactly what dose will effectively

stop AGAR T cells in individual patients, we will start at a low dose with the ability to increase the dose three times based on how the patient is doing.

This is a dose escalation study, which means that we do not know the highest dose of AGAR T cells that is safe. To find out, we will give the cells to at least 3 participants at one dose level. If that is safe, we will raise the dose given to the next group of participants. The dose you will get will depend on how many participants get the agent before you and how they react. The investigator will tell you this information. If your cancer responds to therapy and there are no DLTs, we would allow for up to 3 additional treatments at that same dose. This will help you think about possible harms and benefits. Since the treatment is experimental, what is likely to happen at any dose is not fully known.

All the treatments will be given by the Center for Cell and Gene Therapy at 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.
- Pregnancy test (if you are a female who can get pregnant)
- If you are infected with the hepatitis B virus (HBV) we will do a test to measure the levels of the virus
- Measurements of your tumor by scans and the tumor marker alfa-fetoprotein (AFP), if your tumor produces this protein. Tumor markers are molecules in the blood that are higher when a person has certain cancers

Medical tests during and after treatment:
You will receive standard medical tests when you are getting the infusions and after :
- Physical exams and History
- Blood tests to measure blood cells, kidney and liver function
- If you are infected with thehepatitis B virus (HBV) we will repeat the test and monitor the levels of the virus
- Measurements of your tumor by scans (4 - 6 weeks after the infusion) and AFP (if applicable at 1, 2, 3 and 4 weeks after the infusion).
- Tumor biopsy between 2-4 weeks after the infusion and as clinically indicated thereafter. For additional clinically indicated tumor biopsies we will ask for a portion of the sample for research.

FOLLOW-UP STUDIES:

We will follow you during and after each injection. To learn more about the way the T cells are working in your body, up to 60 mL (up to 12 teaspoons, no more than 3mL/kg/day) of blood will be taken from you before the chemotherapy, before the T-cell infusion, 1 to 4 hours after the infusion, 3 to 4 days after the infusion (this time point is optional) at 1 week, 2 weeks, 3 weeks, 4 weeks and 8 weeks after the injection, every 3 months for 1 year, every 6 months for 4 years and then every year for the next 10 years. Total participation time for this study will be 15 years.

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

We will use this blood to look for the frequency and activity of the cells that we have given ; that is, to learn more about the way the T cells are working and how long they last in the body . We will also use this blood to see if there are any long-term side effects of putting the new gene (chimeric antigen receptor, CAR) into the cells. In addition to the blood draws, because you have received cells that have had a new gene put in them, you will need to have long term follow up for 15 years so we can see if there are any long-term side effects of the gene transfer.

Once a year, you will be asked to have your blood drawn and answer questions about your general health and medical condition. The investigators may ask you to report any recent hospitalizations, new medications, or the development of conditions or illness that were not present when you enrolled in the study and may request that physical exams and/or laboratory tests be performed if necessary.

When tumor biopsy is performed for clinical reasons we will request permission to obtain excess sample to learn more about the effects of the treatment on your disease .

In the event of death, we will request permission to perform an autopsy to learn more about the effects of the treatment on your disease and if there were any side effects from the cells with the new gene.

In addition, we would like to ask for your permission to use tumor biopsy for research purposes only. Associated risk with the biopsy will be discussed with you in detail in a procedure specific consent form. We will test the sample to see if the AGAR T cells can be found in the tumor and what effect they had on the tumor cells.

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

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

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

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 and TCH: Texas Children's 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, CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS (CPRIT) and their representatives, and NATIONAL INSTITUTES OF HEALTH (NIH) 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 and TCH: Texas Children's Hospital are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine and TCH: Texas Children's 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 and TCH: Texas Children's 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 and TCH: Texas Children's 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 and TCH: Texas Children's 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, CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS (CPRIT) and their representatives, NATIONAL INSTITUTES OF HEALTH (NIH) 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, and TCH: Texas Children's 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: DAVID STEFFIN at the Feigin Tower, 1102 Bates Street, Suite 1760 Houston, TX 77030 or at dhsteffi@texaschildrens.org.

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 the T cells:

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

It is possible that the T cells will cause an allergic reaction , which could include itching, rash and shortness of breath (potentially life-threatening).

A small percentage of patients that receive this type of therapy develop a life -threatening complication known as a cytokine release syndrome (CRS). This complication causes high body temperature,

increased heart rate, and low blood pressure. This complication can be life threatening. There are treatments for this complication that may or may not be effective.

In addition, a small percentage of patients, who have received a particular type of T cell that attacks leukemia, a type of blood cancer, have developed drowsiness, sleepiness, or have become unresponsive. This complication can also be life threatening.

Potential side effects from IL15:
T cells that have been had a gene added to make extra IL 15 have not been tested in humans. Other cell types, for example Natural Killer cells which were genetically engineered to produce IL -15, have been tested in humans and were safe in patients with cancer. Infusing IL15 has been studied in humans and was associated with low blood pressure, changes in liver enzyme levels and decrease in platelet (tiny blood cell fragments that help your body form clots to stop bleeding) count at higher doses. In some animal studies, when IL15 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, T cells carrying the GPC3-CAR and IL15 were safe and did not grow and survive long time in the absence of GPC3-positive tumor cells and did not themselves become cancerous.

Potential side effects of Rimiducid infusion:
Rimiducid can be used to kill the T cells if necessary due to side effects. This drug has been tested in humans and has not caused any bad effects, but we do not know if there may be side-effects in patients treated with GPC3-CAR T cells. The drug is experimental and has not been licensed by the FDA.

Potential 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 and acts as a vector (a carrier of the gene). 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 (conditions when a patient's immune system is not working properly). 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.

Risks to Unborn Children
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.

Side Effects of Cyclophosphamide (Cytoxan) 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:
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.

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; 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.

As mentioned above, cyclophosphamide and fludarabine cause low blood count. If you have chronic Hepatitis B, there is a risk that your Hepatitis B virus infection flares up. To prevent this from occurring you will receive an FDA-approved medication, called anti-viral, to prevent this (if you are not already receiving it) for 2 weeks prior to the T-cell infusion until 6 weeks after the infusion. Side effects (less than 1 in 10) of anti-virals in general include indigestion, diarrhea, feeling dizzy, tired, or week, headache, problems sleeping, and changes in blood tests.

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.

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

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: you may choose not to participate in the study, receive other experimental treatments or choose to receive palliative care..

Subject Costs and Payments

You will not be charged for the preparation or manufacture of the AGAR T CELLS , nor will you be charged for the laboratory studies done to monitor the how well these T cells are working and to measure how long they stay in your body or the pregnancy test (if applicable). You/your insurance company will not be charged for the cost of the rimiducid. You or your insurance company may be charged for some research related costs including the infusion of the product and the chemotherapy (fludarabine and cyclophosphamide). 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. 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 (3) 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, DAVID STEFFIN, 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: DAVID STEFFIN at 832-824-4233 during the day and at 832-826-0860 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.

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

The National Institutes of Health (NIH) and the National Cancer Institute (NCI) may have access to your records for research purposes. Coded information may be provided to the NIH/NCI such as your Patient ID, your Zip code, your country and your birth date (month and year). However, in the event of an audit, the 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-47757- INTERLEUKIN-15 ARMORED GLYPICAN-3-SPECIFIC CHIMERIC ANTIGEN RECEPTOR EXPRESSING AUTOLOGOUS T CELLS AS IMMUNOTHERAPY FOR CHILDREN WITH SOLID TUMORS (AGAR)

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