Official Study Title: A Phase I/II Study Evaluating SJCAR19 (CD19-Specific CAR Engineered Autologous T-Cells) in Pediatric and Young Adult Patients ≤ 21 Years of Age With Relapsed or Refractory CD19+ Acute Lymphoblastic Leukemia

CTG Number: NCT03573700

Document Date: 10/25/2022

Informed Consent for Research

SJCAR19: A PHASE I/II STUDY EVALUATING SJCAR19 (CD19-SPECIFIC CAR ENGINEERED AUTOLOGOUS T-CELLS) IN PEDIATRIC AND YOUNG ADULT PATIENTS ≤ 21 YEARS OF AGE WITH RELAPSED OR REFRACTORY CD19$^+$ ACUTE LYMPHOBLASTIC LEUKEMIA

NOTE: *When we say "you" in this document, we mean "you or your child."*

1. Why am I being asked to take part in this research study?

You are being asked to volunteer for this research study because you have a type of cancer, acute lymphoblastic leukemia (ALL), which has been difficult to treat (refractory) or has returned (relapsed) even after very intensive therapy with chemotherapy and/or stem cell transplant. This consent form gives you information about the study, which will be discussed with you in detail. Please take your time making a decision and feel free to discuss it with your friends and family. Before agreeing to take part in this research study, it is important that you read this consent form that describes the study. After you understand the study, and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep.

2. Why is this study being done?

SJCAR19 is a research study evaluating the use of chimeric antigen receptor (CAR) T cell therapy, a type of cellular therapy, for the treatment of your type of cancer. The body has different ways of fighting infection and disease. CAR therapy combines two of the body's basic disease fighters: antibodies and T Cells. For this type of therapy, peripheral (circulating) immune cells are collected and then undergo a manufacturing process to engineer them to more effectively kill cancer cells. SJCAR19 is a CAR therapy cellular product which is created in the lab by genetically modifying your T cells in such a way that allows the T cells to recognize cancer cells and attack them like an antibody would. The SJCAR19 product will be manufactured at the St. Jude Children's Research Hospital's Good Manufacturing Practice (GMP) facility, using a viral vector (derived from a modified human immunodeficiency virus (HIV)) to deliver the antibody-gene (derived using a modified mouse protein) to the immune cells.

The main purpose of this study is to determine:

1. The largest dose of SJCAR19 that is safe to give,
2. How long SJCAR19 cells last in the body,
3. The side effects of SJCAR19, and
4. Whether or not treatment with SJCAR19 is effective in treating people with refractory or relapsed ALL.

3. What are my rights in this study?

Before you learn about this study, it is important that you know the following:

- Whether or not you take part in this study is entirely up to you.
- You may leave the study at any time.
- You may take time to consider whether or not you would like to take part in this study and any options that are available to you.
- The persons in charge of this study (called the principal investigators and researchers) are Dr. Aimee Talleur and Dr. Stephen Gottschalk. They can be reached by phone at 901-595-3300. Please feel free to call them if you have questions at any time.
- If you choose not to be in the study, or to leave the study at any time, you may still be able to get routine medical care at St Jude.
- This study is sponsored by and done at St. Jude Children's Research Hospital.

4. What will be done in this study?

This study contains 3 phases. The first part is called the "Collection Phase," the second the "Manufacturing Phase" and the third the "Treatment Phase." Each phase of the study will be explained to you in detail, and will each have a separate consent.

Each phase is briefly outlined below:

- The **Collection Phase** refers to your blood cells being collected, and possibly frozen, via a process called apheresis. The cells are for use in the Manufacturing and Treatment phases of the study at a later time.
- The Manufacturing Phase refers to your blood cells being engineered to improve their ability to recognize and kill cancer cells. This process occurs in the GMP using the cells that were previously collected. The final cell product is referred to as SJCAR19.
- The Treatment Phase refers to the portion of the study in which you receive an infusion of the SJCAR19 cells that were made in the Manufacturing Phase; chemotherapy is often given for several days prior to the cellular infusion. You are then monitored for any possible side effects, as well as effectiveness, of the treatment. SJCAR19 is not yet been approved by the FDA, similar cell products have been tested by other institutions.

This consent form gives you information about the first part of the study, the "Collection Phase." Before you can receive these cells back in the treatment phase, you will need to sign a "Manufacturing Phase" consent form giving permission to manufacture the SJCAR19 product, and a "Treatment Phase" consent form prior to receiving the SJCAR19 product. You will be given copies of these consent forms to review, and your doctor will discuss it with you once it has been determined that enough cells have been collected to manufacture the SJCAR19 product and it has been determined that you are eligible to continue further in this research study. Some patients may not meet criteria for all 3 phases of the study.

At this time you are only agreeing to have your blood cells collected, and possibly frozen, for potential future use on this research study. Your doctors have already reviewed your medical history, clinical status and determined you are eligible and prepared to have your blood cells collected during a procedure called apheresis. This review has included but was not limited to confirming your age, diagnosis type, blood tests, and a physical examination.

This collection phase has the following parts, which are explained below this list:

- Blood cell collection
- Blood cell processing

a) Blood cell collection. As stated before, your blood cells will need to be collected during a process called apheresis. This process uses a machine to take blood from a vein, usually in one of the arms. The machine divides the blood into parts, such as plasma, platelets, white blood cells, and red blood cells. For this procedure, we will take some of your white blood cells. The rest will then be mixed together and given back to you through a different vein. The white blood cells will then be sent to a lab at St. Jude to be processed.

Each session of apheresis takes between 3 to 8 hours each day until enough cells are collected. It is often done in 1 day; however, more days or donations may be needed to collect enough cells. During apheresis, the staff will give you drugs to keep your blood from clotting in the machine. These drugs, citrate or heparin, might be given either alone or together. The staff will also give you calcium to prevent the side effects of low calcium related to the citrate. During the donation, you will need to lie fairly still in a recliner chair or in a bed located in the St. Jude Blood Donor Center. You will be able to sleep, or watch TV or a movie. One (1) or two (2) family members or friends may visit with you during the donation. You may have drinks or snacks brought to you, but someone will have to help you eat or drink because you will not be able to move your arms.

The apheresis procedure will not use up your body's supply of white blood cells. Most people have enough white blood cells to stay healthy. About one (1) week after donation, their bodies will have made enough new white blood cells to replace what they gave.

Sometimes the veins in the arms are not large enough for the apheresis needles. You may temporarily need a special catheter (a small, flexible tube) called a central venous line. This catheter may be placed in one of the veins in or near your neck or groin, and it will be removed when enough cells have been collected. If you need a central venous line, you will be asked to sign a separate consent form for that procedure.

Because we are growing your cells in the laboratory, we will also need to take blood to test for infectious viruses such as hepatitis and HIV (the virus that causes AIDS), and we will also ask you to fill in a questionnaire that is given to blood donors. Consenting to this study means that you are also giving us permission to test for HIV, West Nile Virus and other infectious agents. Health authorities (for example, CDC, public health department) will need to be informed if test results indicate you have HIV and/or hepatitis or other certain infectious diseases. If any of these tests are positive, your doctor will tell you. If you have HIV, you will not be eligible to be on this study. If more than the required number of cells are collected for SJCAR19 production, studies looking at the immunologic content of the apheresis product will also be performed, for both quality and research purposes. These research tests will not require additional blood samples to be collected from you.

b) Blood cell processing. Your collected blood cells may be frozen or they could be used fresh to manufacture the SJCAR19 product. Manufacturing of the product will be described in another consent form. For the purposes of this collection phase, processing would include standard counting of cells and checking for germs. If there are enough cells after collection and processing, your cells will be frozen and stored in the laboratory here at St. Jude Children's Research Hospital until you are ready for the SJCAR19 product to be manufactured and infused. If after all apheresis collections are completed and processed, there are *not* enough cells remaining to use, or if you do not meet the criteria to continue with the study, your product will be frozen and placed in storage for potential future use on this research study.

5. What are my other choices if I do not take part in this study?

Potential alternatives to taking part in this research study are:

- Treatment with an FDA approved CAR therapy (manufactured by Novartis).
- Continue to receive standard chemotherapy with or without hematopoietic cell transplant.
- Other experimental treatments using new drugs or methods, if available.
- Supportive care (such as transfusions for low blood counts, medications for pain, antibiotics for infections or hospice care).
- No further treatment.

The researcher in charge of the study can tell you about the disease and the benefits of other treatment options. Please feel free to ask the researcher about the disease and its outcomes. If you decide not to get more treatment, the disease will likely get worse.

6. How many people will take part in this study?

We expect that 30 patients will take part in this study over the next few years.

7. How long will I be in this study?

The collection phase of this study will be complete once your blood cells have been collected, processed and stored. If enough cells are collected, you may be allowed to continue to the next phase of manufacturing the SJCAR19 product and will need to provide additional consent in order to continue. If not enough cells are collected or you do not meet criteria to proceed to the Manufacturing Phase of the study, your cell product will be frozen and placed in storage here at St. Jude Children's Research Hospital.

The total length of the treatment and follow-up for the purposes of the entire study is about one year after you have received the SJCAR19 product on this study. Participants who receive the SJCAR19 treatment at St. Jude are asked to return to the Transplant Clinic, or their local physician, for doctor visits and follow-up evaluations at least once a year for at least 15 years. We want to see if any long term effects of this research treatment occur. After one year from your SJCAR19 treatment, you will be asked to enroll in a long-term follow-up study of children and young adults who have received a gene transfer product at St. Jude Children's Research Hospital to complete the 15 year follow-up. If you choose not to enroll on this long-term follow-up study, we will continue to monitor you on-study on SJCAR19, for up to 15 years post-infusion, per FDA guidance.

8. What risks can I expect from taking part in this study?

Both your disease and its prior treatment may be associated with potentially life-threatening complications, side effects, or death. The main risks during this phase of the treatment are the side effects of the blood cell collection procedure (apheresis). The treatment can cause some, or all, of the side effects listed below. There may also be side effects that we cannot predict.

Side Effects of Apheresis. The apheresis procedure has side effects like the side effects that can happen when people donate blood. These side effects include pain, discomfort and/or infection at the sites where the needles are placed. Also, nausea, fainting or dizziness, and/or blood loss may occur. If the procedure is stopped before it has been completed, it is possible that a part of the blood taken out will not be returned to your body.

After apheresis, your platelet count or white blood cell count may be lower than before the procedure. You may need a transfusion of red blood cells, or platelets; however, this rarely happens. Some smaller people may need blood transfusions through the apheresis machine to keep the level of fluid in the blood balanced. Taking aspirin in combination with a lowered platelet count may increase the chance of bleeding. Therefore, aspirin, medications that contain aspirin or medications that contain ibuprofen (i.e. Motrin®) should not be taken without permission from your physician.

Side effects of citrate and heparin**.** If citrate is used during apheresis, you may have muscle cramping, numbness, a cold feeling, tingling sensations, or feel anxious. In rare cases, citrate can cause seizures. If heparin is used, it may take longer than normal for the blood to clot after the apheresis. This longer clotting time may lead to bleeding in very rare cases.

Side effects of the intravenous catheter (IV) used for apheresis procedure. The side effects of the use of the intravenous catheter include fainting, discomfort and bruising at the site where the catheter is placed. Bleeding or infection may occur at the site, however, this is unlikely.

Side effects of obtaining blood for blood tests. The side effects of obtaining these blood samples include fainting, discomfort and bruising at the site where the needle was placed. Bleeding or infection may occur at the site, however, this is rare. In addition to the discomforts associated with the blood draw, there are psychological risks associated with learning that you have an infectious virus. These psychological risks include an increase in anxiety and depression. In addition, if you learn you have an infectious disease (specifically HIV), it could be difficult for you to get insurance coverage or may impact your current insurance coverage.

Loss of confidentiality. Very rarely, personal information from your records could be given out by accident. This might make you upset, embarrass you, or affect your ability to get insurance. To stop this from happening, we:

- Store records apart from names or other personal information
- Only allow members of the study team to see the records
- Store electronic data only on computers protected with a password and encryption software
- Report study results on the whole group and never identify one single person in any reports

If it is decided that you will be eligible to proceed with manufacturing and treatment phases of this study you should also be aware of these additional risks, which will be discussed in detail at the time you consent for those phases of the study.

Pregnancy and reproduction. The risks of the planned study treatment on reproduction (ability to have a baby or father a baby) in the future are unknown. The effects of the treatment on an unborn or nursing child are also unknown. Females must not be pregnant or nursing (breast-feeding a baby) at any point during this study, including the collection phase. Females of childbearing age must have a negative pregnancy test before starting collection. If you think you may have become pregnant at any point, you must notify your doctor immediately. If you become pregnant, you may be taken out of the study.

Likewise, there may be risks associated with male participants fathering a child while receiving this treatment. Some medications cause DNA damage. This may be passed on to children through sperm resulting in possible birth defects or babies with abnormalities.

Participants who are able to have a child or father a child must use an effective form of birth control while receiving this treatment. Effective forms of birth control include oral contraceptive pills, condoms, and abstinence (not having sexual intercourse). The study doctor will discuss effective forms of birth control with you. Birth control methods should be continued for at least 6 months after treatment to avoid pregnancy. We also do not know if there may be unknown long-term effects to your future children.

If it is determined that you are eligible to proceed on to the treatment phase of this study there will be additional risks that will be described in further detail in the Treatment Phase consent. These risks would include those that are associated with receiving cells that have been genetically modified, including but not limited to: false positive testing for HIV, allergic and/or inflammatory reactions (fever, chills, difficulty breathing, hives, skin rashes, low blood pressure), infection, risks associated with chemotherapy, developing another cancer or an autoimmune disease, or death.

9. What are the possible benefits of the study?

We do not know if you will benefit from receiving SJCAR19. It is possible that this study treatment may help to put your disease in remission or keep it in remission. However, there is no guarantee that this will work. You may benefit from knowing that the information learned from this study may be able to help future patients with a cancer such as yours that may be difficult to treat. Additionally, even if you consent to the Collection Phase of this study, it is possible that you will not be eligible to continue with the subsequent phases of treatment (either the Manufacturing and/or the Treatment Phase).

10. Can I stop taking part in this study?

You can stop or withdraw from this study at any time. If you decide to withdraw from the study, you should talk to your doctor first. Your doctor can recommend other treatment options if you stop the study treatment or if the treatment is stopped without your consent.

11. Can I be taken out of the study without my consent?

You may be taken off the treatment without your consent for the following reasons:

- Your doctor decides that continuing in this study would be harmful.
- You need a treatment not allowed on this study.
- You are unable to keep appointments or take medicines as instructed.
- Your condition gets worse.
- You are pregnant.
- New information is learned that a better treatment is available, or that the study is not in your best interest.
- Your cell collection is low and is not enough to allow for study continuation.
- You are not eligible to continue to the next phase of this study (Manufacturing phase).

12. Will I be paid for my time or expenses?

You will not be paid to take part in this study.

13. How will new findings from this research study be shared with me?

We will tell you anything we learn during the study that might change your mind about staying in the study. If you are interested in learning more about this treatment, you may contact Dr. Aimee Talleur or Dr. Stephen Gottschalk at 901/595-3300.

14. How will I find out the results of this study?

The researcher will give you information about the overall results of this study. St. Jude researchers share information with people in studies in many ways, including:

- Articles on www.stjude.org
- In newsletters
- In medical or scientific journals
- In the media

Published research results will only describe groups of people who took part in the study. Information that points out a single person will not be in research journals or other reports.

15. What if all of my cells are not used?

If some or all of your cell product(s) is not used, the remainder will be frozen in a very low-temperature, secured freezer located at St. Jude Children's Research Hospital. Storage will be for a period of not more than five years. Cell product(s) will not be stored past the end of life of the intended recipient. Before we end storage of your cell product(s), we will contact you in writing, using certified mail or equivalent, so that you may instruct us about what to do with your frozen cells. For this reason, it is very important that you tell the St. Jude staff if your address or phone number changes. You should notify St. Jude of any changes by calling or by sending a letter about the change to:

St. Jude Children's Research Hospital
Patient Registration
262 Danny Thomas Place
Mail Stop #114
Memphis, TN 38105
901-595-3707

Before disposing of the frozen cells, we will make three attempts to contact you by mail as described above. In our letter to you we will offer the following choices:

(1) You may request to have the cells moved to an independent storage facility that is accredited for long-term cell storage to continue storage at your own expense. We will provide you with contact information for one or more such facilities, or you may locate your own, so that you may arrange for the transfer and continued storage of the cells;

(2) You may request to have the cells destroyed outright; or

(3) You may request to have all information that identifies the cells as yours removed and then have the cells transferred to a special storage facility within St. Jude Children's Research Hospital. These cells may be used as needed for research purposes. In the event you select this option, a consent for that purpose will be sent to you before the staff removes your identity from the cells and the transfer is done.

16. Will any genetic tests be done and what are the risks of genetic testing?

As discussed above, we will obtain samples of your immune cells and other cells including tumor cells during this study. Research performed on your apheresis collection, CAR T-cell product, and immune cells obtained from research blood draws will include some genetic testing. Genetic testing on material obtained from these samples should help us learn how well CAR T-cells work, and ways to improve T-cell therapies in the future.

The genetic tests are required and considered research only tests. Results are not reported to you or placed in your electronic medical records. The genetic tests include a partial analysis of genetic material obtained from the samples, and may include whole genome sequencing of tumor cells or normal cells from your body. No direct benefits to participants are expected from these genetic tests.

Risks of Genetic/Genomic Testing

There may be risks to your privacy and the privacy of your relatives from storing your information in a database. Although measures are taken to protect your privacy, we do not know how likely it is that your identity could become re-connected with your genetic and health information, and confidentiality cannot be guaranteed. If your genetic information were re-identified, personal information about you, your health, and your risk of disease could become known to others, and potentially be used to discriminate against or stigmatize you, your family, or your groups. This could also present unknown risks. We believe the chance that this will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us; we will make every effort to protect them.

17. What about privacy and confidentiality?

Privacy

We will keep your medical records private to the degree allowed by law. St. Jude may give your health data, without identifiers, to other researchers or use it for other research projects not listed in this form. St. Jude, Dr. Aimee Talleur, Dr. Stephen Gottschalk, and their staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

We will not identify you personally in any text published about this study. Your personal information will not be in any text published about this study.

Your study results will be kept in your research records for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will also be kept for an unknown length of time.

Government agencies such as the Food and Drug Administration (FDA) oversee medical treatment of people as required by state or federal regulations. Therefore, it may be necessary for these government agencies to review parts of your medical record.

The Transplant Program at St. Jude Children's Research Hospital is required by the United States federal government to report all cellular therapy follow up information to the Center for International Blood and Marrow Transplant Research (CIBMTR). The CIBMTR is a worldwide research organization of scientists and doctors who study important issues in transplantation and cellular therapy.

Your donor blood cell collection related information will also be sent to and reviewed by representatives from the Foundation for the Accreditation of Cellular Therapies (FACT). FACT is an international oversight group responsible for monitoring the clinical and laboratory activities of institutions that provide research and treatment with certain blood cell products including blood progenitor cells (blood cells similar to stem cells). These representatives may review your laboratory and medical records to verify institutional compliance with federal regulations regarding these blood cell products.

Data sent to the CIBMTR and FACT will not include your St. Jude record number. A unique identification number will be assigned to your information. However, some of the information sent may possibly be linked to you. This information includes but is not limited to the following:

- Your date of birth and primary country (and state) of residence;
- Type of cancer, prior cancer related therapy, dates of and results for all immune system and infectious disease related blood tests;
- Medications, doses used during study treatment, infusion date, side effects of the treatment;

- How your immune system, blood system and disease have responded to the study treatment.

Because this information may be linked to you, absolute privacy cannot be guaranteed.

By signing this consent form, you are allowing your data and/or biological sample to be sent to and medical records to be reviewed by these persons.

- Government agencies such as the FDA and the National Cancer Institute (NCI).
- A regulatory agency called FACT.
- A research organization called the CIBMTR.
- A research safety and ethics review committee, called the St. Jude Institutional Review Board (IRB).
- The St. Jude Institutional Biosafety Committee (IBC), an internal committee that oversees all aspects of investigational biologic products (which includes blood cell products processed through the use of an investigational device such as the CliniMACS) as well as all laboratory and clinical related safety issues.

Confidentiality

Health information and research data obtained from tumor and normal specimens, such as genetic data, are often shared with the research community using various databases, including those maintained by St. Jude and the federal government. Your data may be stored, shared broadly, and used for future research through the St. Jude Cloud run by St. Jude, and the Database for Genotypes and Phenotypes (dbGaP) and the Gene Expression Omnibus (GEO) both run by the National Institutes of Health, and the Sequence Read Archive (SRA). This is to advance scientific discovery and satisfy requirements of organizations that fund research and journals that publish that research. Prior to submitting your data to these databases, it will be de-identified by removing any information that could identify you, such as your name, date of birth, medical record number, and any other information that could link your identity to your data. The only health information included will be your age, solid tumor diagnosis, how long CAR T-cells remain in your blood, and response to CAR T-cell treatment. There are two types of databases used for sharing research data. One is a controlled access database, and the other is a public, unrestricted access database. Each is described below.

Controlled access database: Your individual genomic data and health information may be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the database must agree not to attempt to identify you.

Unrestricted access databases: De-identified summary level information from research studies using your samples, genetic information and health information may be freely available in a public, unrestricted database that anyone can use. Summary-level information about all participants included in a dataset, including you, but not genetic data for each individual, may be shared. This public information will not be labeled with your name or other information that could be used to easily identify you, and the risk of anyone identifying you with this information is very low.

You will not be notified every time your genomic information is used for research. We also do not know what types of future research will be done with genomic data from this study.

SUMMARY OF RESEARCH AND PRIVACY RIGHTS

The following statement describes your rights as a research participant in this study:

1) You may refuse to be in this research study or stop at any time. This decision will not affect your care or your relationship with your doctor or St. Jude. If available, you may receive routine medical care at St. Jude Children's Research Hospital.
2) If you have insurance, TennCare or Medicaid, or other health care coverage such as an employer-sponsored benefit plan, they will be billed for many of the services we provide. However, we do not bill patients or their families for the cost of medical care not covered by their health plans. This includes research costs.
3) Your samples and information may be used to develop a new product or medical test, which may be sold. If this happens, you will not receive any payments for these new products.
4) If you have any questions about this study or if you are injured as a result of this study, contact Dr. Aimee Talleur or Dr. Stephen Gottschalk**,** at 901-595-3300 immediately. If you are injured from being in this research study, St. Jude will provide reasonable and necessary care for that injury. If you need more care than St. Jude can provide, we will help you find medical care somewhere else. It is not the hospital's policy to provide payment if you are injured from being in this study; however, you are not giving up any of your rights by signing this consent form.
5) A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most the Website will include a summary of the results. You can search this Website at any time.
6) A decision to take part in this research means that you agree to let the research team use and share with other researchers your health information also called protected health information (PHI) for the study explained above. This information will be kept indefinitely. You have the right to see, copy, and ask for changes to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.
7) When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI may be used or given to someone outside the hospital. You have the right to read the Notice of Privacy Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude Internet website: *www.stjude.org*.
8) Federal agencies such as the Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP) or the National Institutes of Health (NIH), St. Jude Children's Research Hospital Institutional Review Board (IRB), your insurance company or other health benefits plans (if charges are billed to these plans), as well as other regulatory agencies, committees, or persons involved in overseeing research studies may review your research and medical record.

9) Information about you that may be given out includes your complete medical records, including details about diagnosis, illness, treatment, and information that may be recorded about past diagnosis or treatment and information taken as a part of this research study as explained in this informed consent.

10) After your records are given to or used by others, St. Jude Children's Research Hospital cannot promise that information will not be given out again. Also, the information given out may no longer be protected by federal privacy laws.

11) St. Jude uses reasonable safeguards and means to protect your private information. However, St. Jude cannot guarantee the security and confidentiality of e-mail, text messages, fax communications or mail.

12) Researchers and study staff are required by law to report suspected child abuse, threat of harm to self or others, and certain diseases that spread from person to person.

13) Your permission to use and give out your child's protected health information will end when your child turns 18 years of age. At that time, we may contact your child for his or her permission to continue using it.

14) You may take back permission for your records to be used or given out at any time, for any reason, except when that information has already been given out or used for the study based on your permission. To take back your permission, please fill out a form called a Revocation of Release of Authorization. You may ask for this form by calling the St. Jude Privacy Officer at 901-595-6141. You must mail the form or hand it to:

    HIPAA Privacy Officer
    St. Jude Children's Research Hospital
    262 Danny Thomas Place, Mail Stop 280
    Memphis, TN 38105

15) You can get more details about your rights as a research participant by calling the St. Jude Institutional Review Board at 901-595-4357 or the Research Participant Advocate at 901-595-4644. If you are outside of the Memphis area, please call toll-free 1-866-583-3472 (1-866-JUDE IRB).

16) The St. Jude Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns, and questions. The Advocate can help you obtain information and can relay any input you may have concerning the research to the research study team. You can reach the Advocate by calling 901-595-4644, or if you are outside of the Memphis area, call toll free at 1-866-583-3472 (1-866-JUDE-IRB)

17) You will be given a copy of this signed consent form.

PARENT/GUARDIAN STATEMENT (Required for patients younger than 18 years):

I have read this document or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give permission for my child to be in this research study.

______________________	____________	________ AM/PM
Parent/Legal Guardian Signature	Date	Time (circle one)

ASSENT DISCUSSION (Required for participants 7–13 years old)

☐ The research was explained to the minor participant in age-appropriate terms and the minor verbally agreed to take part in the study.

☐ Minor declined to take part in the study. The minor declined for the following reason(s):

____

☐ An assent discussion was not initiated with the minor for the following reason(s):

- ☐ Minor is under 7 years of age.
- ☐ Minor is incapacitated.
- ☐ Minor refused to take part in the discussion.
- ☐ Other____

RESEARCH PARTICIPANT'S STATEMENT (14–17 years old and Adult Participants 18 years old or older):

I have read this document or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this research study.

______________________	____________	________ AM/PM
Research Participant Signature/LAR	Date	Time (circle one)

RESEARCHER/DESIGNEE STATEMENT:

I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

______________________	____________	________ AM/PM
Researcher/Designee Signature	Date	Time (circle one)

____
Print Name

RESEARCH PARTICIPANT ADVOCATE STATEMENT:

I observed the informed consent process. The research study, intervention/observation, risks, benefits, and alternatives were presented to the research participant and/or legal guardian(s). They were encouraged to ask questions, and research team members answered all their questions. The participant/parent(s) indicated that they: 1) understood the information presented; and 2) voluntarily consented /agreed to take part in the research.

______________________________	________________	____________ AM/PM
Research Participant Advocate	Date	Time (circle one)
______________________________	________________	____________ AM/PM
Interpreter (if needed)	Date	Time (circle one)

PLEASE SEND COMPLETED CONSENT FORM TO CLINICAL TRIALS OPERATIONS:

- **SCAN and E-MAIL to:** protocoleligibilityoffice@stjude.org
- **Or FAX to:** (901) 595-6265

Informed Consent for Research

SJCAR19: A PHASE I/II STUDY EVALUATING SJCAR19 (CD19-SPECIFIC CAR ENGINEERED AUTOLOGOUS T-CELLS) IN PEDIATRIC AND YOUNG ADULT PATIENTS ≤ 21 YEARS OF AGE WITH RELAPSED OR REFRACTORY CD19$^+$ ACUTE LYMPHOBLASTIC LEUKEMIA

NOTE*: When we say "you" in this document, we mean "you or your child."*

1. Why am I being asked to take part in this research study?

You are being asked to volunteer for this research study because you have a type of cancer, acute lymphoblastic leukemia (ALL), which has been difficult to treat (refractory) or has returned (relapsed) even after very intensive therapy with chemotherapy and/or stem cell transplant. This consent form gives you information about the study, which will be discussed with you in detail. Please take your time making a decision and feel free to discuss it with your friends and family. Before agreeing to take part in this research study, it is important that you read this consent form that describes the study. After you understand the study, and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep.

2. Why is this study being done?

SJCAR19 is a research study evaluating the use of chimeric antigen receptor (CAR) T cell therapy, a type of cellular therapy, for the treatment of your type of cancer. The body has different ways of fighting infection and disease. CAR therapy combines two of the body's basic disease fighters: antibodies and T Cells. For this type of therapy, peripheral (circulating) immune cells are collected and then undergo a manufacturing process to engineer them to more effectively kill cancer cells. SJCAR19 is a CAR therapy cellular product which is created in the lab by genetically modifying your T cells in such a way that allows the T cells to recognize cancer cells and attack them like an antibody would. The SJCAR19 product will be manufactured at the St. Jude Children's Research Hospital's Good Manufacturing Practice (GMP) facility, using a viral vector (derived from a modified human immunodeficiency virus (HIV)) to deliver the antibody-gene (derived using a modified mouse protein) to the immune cells.

The main purpose of this study is to determine:

1. The largest dose of SJCAR19 that is safe to give,
2. How long SJCAR19 cells last in the body,
3. The side effects of SJCAR19, and
4. Whether or not treatment with SJCAR19 is effective in treating people with refractory or relapsed ALL.

3. What are my rights in this study?

Before you learn about the study, it is also important that you know the following:

- Whether or not you take part in this study is entirely up to you.
- You may leave the study at any time.
- You may take time to consider whether or not you would like to take part in this study and any options that are available to you.
- The persons in charge of this study (called the principal investigator and researcher) are Dr. Aimee Talleur and Dr. Stephen Gottschalk. They can be reached by phone at 901-595-3300. Please feel free to call her if you have questions at any time.
- If you choose not to be in the study, or to leave the study at any time, you may still be able to get routine medical care at St Jude.
- This study is sponsored by and done at St. Jude Children's Research Hospital.

4. What will be done in this study?

This study contains 3 phases. The first part is called the "Collection Phase," the second the "Manufacturing Phase" and the third the "Treatment Phase." Each phase of the study will be explained to you in detail, and will each have a separate consent.

Each treatment phase is briefly outlined below:

- The Collection Phase refers to your blood cells being collected via a process called apheresis. The cells are for use in the Manufacturing and Treatment phases of the study at a later time.
- The **Manufacturing Phase** refers to your blood cells being engineered to improve their ability to recognize and kill cancer cells. This process occurs in the GMP facility using the cells that were previously collected. The final cell product is referred to as SJCAR19.
- The Treatment Phase refers to the portion of the study in which you receive an infusion of the SJCAR19 cells that were made in the Manufacturing Phase; chemotherapy is often given for several day prior to the cellular infusion. You are then monitored for any possible side effects as well as efficacy of the treatment. Although SJCAR19 is not yet approved by the FDA, similar cell products have been tested by other institutions.

This consent form gives you information about the second part of the study, the Manufacturing Phase. During this phase, you will not be required to provide any additional blood samples or undergo further testing. Blood collected during a previous apheresis procedure will be used to make the SJCAR19 cells. If you are eligible for the Treatment Phase, we will discuss the study and give you another consent that will describe the potential risks and benefits of participation, including the potential risks of gene transfer.

At this time you are only agreeing to have your previously collected blood cells undergo manufacturing of the SJCAR19 cellular product. The SJCAR19 product will be manufactured in the Good Manufacturing Process (GMP) facility at St. Jude Children's Research Hospital. Your blood cells will be "filtered" using the CliniMACs system. This will allow us to select the T cells to be used in the manufacturing of the SJCAR19 product. The CliniMACS has not been licensed for this use in the U.S. Therefore, using this machine for cell processing is considered experimental and may result in unknown complications. If new information becomes available during your participation in this study that could influence your willingness to continue in the study, you will be given such new information. The selected T cells will then be activated (stimulated) and undergo gene transfer to modify them to recognize your cancer cells. The modified cells will then be referred to as SJCAR19. The SJCAR19 cells will then be tested for quality assurance and immunologic content prior to them being released for use in the Treatment Phase, including research tests on the apheresis and final SJCAR19 cellular products. In addition, collected and manufactured cells that are not needed for you, might be used for research studies so that researchers learn more about cellular immunotherapy. These research tests will not require additional blood samples to be collected from you.

5. What are my other choices if I do not take part in this study?

Potential alternatives to taking part in this research study include:

- Treatment with an FDA approved CAR therapy (manufactured by Novartis).
- Continue to receive standard chemotherapy with or without stem cell transplant.
- Other experimental treatments using new drugs or methods, if available.
- Supportive therapy (such as transfusions for low blood counts, medications for pain, antibiotics for infections or hospice care).
- No further treatment.

The researcher in charge of the study can tell you about the disease and the benefits of other treatment options. Please feel free to ask the researcher about the disease and its outcomes. If you decide not to get more treatment, your disease will likely get worse.

6. How many people will take part in this study?

We expect that about 30 patients will take part in this study over the next few years.

7. How long will I be in the study?

The manufacturing phase of this study will be complete once the SJCAR19 product is made. We anticipate this to take approximately 10 to 14 days. After manufacturing, if the product meets minimum requirements and you are found to be eligible to continue with treatment with SJCAR19, you may be allowed to continue to the next phase of this study. The timing for proceeding to the treatment phase of this study will be dependent on your general clinical status and organ function, as well as the duration of any cancer directed therapy you may receive during the time that manufacturing is occurring. You will need to provide additional consent in order to continue.

The total length of the treatment and follow-up for the purposes of the entire study is about one year after you have received the SJCAR19 product on this study. Participants who receive the SJCAR19 treatment at St. Jude are asked to return to the Transplant Clinic, or their local physician, for doctor visits and follow-up evaluations at least once a year for at least 15 years. We want to see if any long term effects of this research treatment occur. After one year from your SJCAR19 treatment, you will be asked to enroll in a long-term follow-up study of children and young adults who have received a gene transfer product at St. Jude Children's Research Hospital to complete the 15 year follow-up. If you choose not to enroll on this long-term follow-up study, we will continue to monitor you on-study on SJCAR19, for up to 15 years post-infusion, per FDA guidance.

8. What risks can I expect from taking part in this study?

There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks. There is no other risk to you as the cell modification is done in the laboratory. If it is decided that you will be eligible to proceed with the treatment phase of this study you should also be aware of these additional risks, which will be discussed in detail at the time you consent for that phase of the study.

9. What are the possible benefits of the study?

You may or may not benefit from taking part in this study. However information learned from this study may help doctors learn more about your cancer which may help children and adolescents in the future. Additionally, even if you consent to the Manufacturing Phase of this study, it is possible that you will not be eligible to continue with the Treatment Phase.

10. Can I stop taking part in this study?

You can stop or withdraw from this study at any time. If you decide to leave the study, you should talk to your doctor first. She/he will talk to you about health and safety issues. If you leave this study, other treatments may still be given to control your disease. Your doctor can recommend other treatment options if you stop the study treatment or if the treatment is stopped without your consent.

11. Can I be taken out of the study without my consent?

You may be taken out of the study without your consent for these reasons:

- If the SJCAR19 cells do not meet laboratory defined safety measures (release criteria).
- If you do not meet the eligibility criteria for the SJCAR19 treatment phase.
- New information is learned that a better treatment is available, or that the study is not in your best interest.

12. Will I be paid for my time or expenses?

You will not be paid to take part in this study.

13. How will new findings related to this study be shared with me?

We will tell you anything we learn during the study that might change your mind about staying in the study. If you are interested in learning more about this treatment, contact Dr. Aimee Talleur or Dr. Stephen Gottschalk at 901-595-3300.

14. How will I find out the results of this study?

The researcher will give you information about the overall results of this study. St. Jude researchers share information with people in studies in many ways, including:

- Articles on www.stjude.org
- In newsletters
- In medical or scientific journals
- In the media

Published research results will only describe groups of people who took part in the study. Information that points out a single person will not be in research journals or other reports.

15. Will any genetic tests be done and what are the risks of genetic testing?

As discussed above, we will obtain samples of your immune cells and other cells including tumor cells during this study. Research performed on your apheresis collection, CAR T-cell product, and immune cells obtained from research blood draws will include some genetic testing. Genetic testing on material obtained from these samples should help us learn how well CAR T-cells work, and ways to improve T-cell therapies in the future.

The genetic tests are required and considered research only tests. Results are not reported to you or placed in your electronic medical records. The genetic tests include a partial analysis of genetic material obtained from the samples, and may include whole genome sequencing of tumor cells or normal cells from your body. No direct benefits to participants are expected from these genetic tests.

Risks of Genetic/Genomic Testing

There may be risks to your privacy and the privacy of your relatives from storing your information in a database. Although measures are taken to protect your privacy, we do not know how likely it is that your identity could become re-connected with your genetic and health information, and confidentiality cannot be guaranteed. If your genetic information were re-identified, personal information about you, your health, and your risk of disease could become known to others, and potentially be used to discriminate against or stigmatize you, your family, or your groups. This could also present unknown risks. We believe the chance that this will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us; we will make every effort to protect them.

16. What about privacy and confidentiality?

Privacy

We will keep your medical records private to the degree allowed by law. St. Jude may give your health data, without identifiers, to other researchers or use it for other research projects not listed in this form. St. Jude, Dr. Aimee Talleur, Dr. Stephen Gottschalk and their staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

We will not identify you personally in any text published about this study. Your personal information will not be in any text published about this study.

Your study results will be kept in your research records for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will also be kept for an unknown length of time.

Government agencies such as the Food and Drug Administration (FDA) oversee medical treatment of people as required by state or federal regulations. Therefore, it may be necessary for these government agencies to review parts of your medical record.

The Transplant Program at St. Jude Children's Research Hospital is required by the United States federal government to report all transplant and post-transplant follow up information to the Center for International Blood and Marrow Transplant Research (CIBMTR). The CIBMTR is a worldwide research organization of scientists and doctors who study important issues in transplantation.

Your donor blood cell collection related information will also be sent to and reviewed by representatives from the Foundation for the Accreditation of Cellular Therapies (FACT). FACT is an international oversight group responsible for monitoring the clinical and laboratory activities of institutions that provide research and treatment with certain blood cell products including blood progenitor cells (blood cells similar to stem cells). These representatives may review your laboratory and medical records to verify institutional compliance with federal regulations regarding these blood cell products.

Data sent to the CIBMTR and FACT will not include your St. Jude record number. A unique identification number will be assigned to your information. However, some of the information sent may possibly be linked to you. This information includes but is not limited to the following:

- Your date of birth and primary country (and state) of residence;
- Type of cancer, prior cancer related therapy, dates of and results for all immune system and infectious disease related blood tests;
- Medications, doses used during study treatment, infusion date, side effects of the treatment;
- How your immune system, blood system and disease have responded to the study treatment.

Because this information may be linked to you, absolute privacy cannot be guaranteed.

By signing this consent form, you are allowing your data and/or biological sample to be sent to and medical records to be reviewed by these persons.

- Government agencies such as the FDA and the National Cancer Institute (NCI).
- A regulatory agency called FACT.
- A research organization called the CIBMTR.
- A research safety and ethics review committee, called the St. Jude Institutional Review Board (IRB).
- The St. Jude Institutional Biosafety Committee (IBC), an internal committee that oversees all aspects of investigational biologic products (which includes blood cell products processed through the use of an investigational device such as the CliniMACS) as well as all laboratory and clinical related safety issues.

Confidentiality

Health information and research data obtained from tumor and normal specimens, such as genetic data, are often shared with the research community using various databases, including those maintained by St. Jude and the federal government. Your data may be stored, shared broadly, and used for future research through the St. Jude Cloud run by St. Jude, and the Database for Genotypes and Phenotypes (dbGaP) and the Gene Expression Omnibus (GEO) both run by the National Institutes of Health, and the Sequence Read Archive (SRA). This is to advance scientific discovery and satisfy requirements of organizations that fund research and journals that publish that research. Prior to submitting your data to these databases, it will be de-identified by removing any information that could identify you, such as your name, date of birth, medical record number, and any other information that could link your identity to your data. The only health information included will be your age, solid tumor diagnosis, how long CAR T-cells remain in your blood, and response to CAR T-cell treatment. There are two types of databases used for sharing research data. One is a controlled access database, and the other is a public, unrestricted access database. Each is described below.

Controlled access database: Your individual genomic data and health information may be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the database must agree not to attempt to identify you.

Unrestricted access databases: De-identified summary level information from research studies using your samples, genetic information and health information may be freely available in a public, unrestricted database that anyone can use. Summary-level information about all participants included in a dataset, including you, but not genetic data for each individual, may be shared. This public information will not be labeled with your name or other information that could be used to easily identify you, and the risk of anyone identifying you with this information is very low.

You will not be notified every time your genomic information is used for research. We also do not know what types of future research will be done with genomic data from this study.

SUMMARY OF RESEARCH AND PRIVACY RIGHTS

The following statement describes your rights as a research participant in this study:

1) You may refuse to be in this research study or stop at any time. This decision will not affect your care or your relationship with your doctor or St. Jude. If available, you may receive routine medical care at St. Jude Children's Research Hospital.
2) If you have insurance, TennCare or Medicaid, or other health care coverage such as an employer-sponsored benefit plan, they will be billed for many of the services we provide. However, we do not bill patients or their families for the cost of medical care not covered by their health plans. This includes research costs.
3) Your samples and information may be used to develop a new product or medical test, which may be sold. If this happens, you will not receive any payments for these new products.
4) If you have any questions about this study or if you are injured as a result of this study, contact Dr. Aimee Talleur or Stephen Gottschalk**,** at 901-595-3300 immediately. If you are injured from being in this research study, St. Jude will provide reasonable and necessary care for that injury. If you need more care than St. Jude can provide, we will help you find medical care somewhere else. It is not the hospital's policy to provide payment if you are injured from being in this study; however, you are not giving up any of your rights by signing this consent form.
5) A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most the Website will include a summary of the results. You can search this Website at any time.
6) A decision to take part in this research means that you agree to let the research team use and share with other researchers your health information also called protected health information (PHI) for the study explained above. This information will be kept indefinitely. You have the right to see, copy, and ask for changes to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.
7) When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI may be used or given to someone outside the hospital. You have the right to read the Notice of Privacy Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude Internet website: *www.stjude.org*.
8) Federal agencies such as the Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP) or the National Institutes of Health (NIH), St. Jude Children's Research Hospital Institutional Review Board (IRB), your insurance company or other health benefits plans (if charges are billed to these plans), as well as other regulatory agencies, committees, or persons involved in overseeing research studies may review your research and medical record.

9) Information about you that may be given out includes your complete medical records, including details about diagnosis, illness, treatment, and information that may be recorded about past diagnosis or treatment and information taken as a part of this research study as explained in this informed consent.

10) After your records are given to or used by others, St. Jude Children's Research Hospital cannot promise that information will not be given out again. Also, the information given out may no longer be protected by federal privacy laws.

11) St. Jude uses reasonable safeguards and means to protect your private information. However, St. Jude cannot guarantee the security and confidentiality of e-mail, text messages, fax communications or mail.

12) Researchers and study staff are required by law to report suspected child abuse, threat of harm to self or others, and certain diseases that spread from person to person.

13) Your permission to use and give out your child's protected health information will end when your child turns 18 years of age. At that time, we may contact your child for his or her permission to continue using it.

14) You may take back permission for your records to be used or given out at any time, for any reason, except when that information has already been given out or used for the study based on your permission. To take back your permission, please fill out a form called a Revocation of Release of Authorization. You may ask for this form by calling the St. Jude Privacy Officer at 901-595-6141. You must mail the form or hand it to:

    HIPAA Privacy Officer
    St. Jude Children's Research Hospital
    262 Danny Thomas Place, Mail Stop 280
    Memphis, TN 38105

15) You can get more details about your rights as a research participant by calling the St. Jude Institutional Review Board at 901-595-4357 or the Research Participant Advocate at 901-595-4644. If you are outside of the Memphis area, please call toll-free 1-866-583-3472 (1-866-JUDE IRB).

16) The St. Jude Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns, and questions. The Advocate can help you obtain information and can relay any input you may have concerning the research to the research study team. You can reach the Advocate by calling 901-595-4644, or if you are outside of the Memphis area, call toll free at 1-866-583-3472 (1-866-JUDE-IRB)

17) You will be given a copy of this signed consent form.

PARENT/GUARDIAN STATEMENT (Required for participants younger than 18 years):

I have read this document or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give permission for my child to be in this research study.

______________________________ _______________ __________ AM/PM
Parent/Legal Guardian Signature Date Time (circle one)

ASSENT DISCUSSION (Required for participants 7–13 years old)

☐ The research was explained to the minor participant in age-appropriate terms and the minor verbally agreed to take part in the study.
☐ Minor declined to take part in the study. The minor declined for the following reason(s):

____

☐ An assent discussion was not initiated with the minor for the following reason(s):
  ☐ Minor is under 7 years of age.
  ☐ Minor is incapacitated.
  ☐ Minor refused to take part in the discussion.

  ☐ Other____

RESEARCH PARTICIPANT STATEMENT (14–17 years old and Adult Participants 18 years and older):

I have read this document or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this research study.

______________________________ _______________ __________ AM/PM
Research Participant Signature/LAR Date Time (circle one)

RESEARCHER/DESIGNEE STATEMENT:

I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

______________________________ _______________ __________ AM/PM
Researcher/Designee Signature Date Time (circle one)

____
Print Name

RESEARCH PARTICIPANT ADVOCATE STATEMENT:

I observed the informed consent process. The research study, intervention/observation, risks, benefits, and alternatives were presented to the research participant and/or legal guardian(s). They were encouraged to ask questions, and research team members answered all their questions. The participant/parent(s) indicated that they: 1) understood the information presented; and 2) voluntarily consented /agreed to take part in the research.

______________________________	________________	__________ AM/PM
Research Participant Advocate	Date	Time (circle one)
______________________________	________________	__________ AM/PM
Interpreter (if needed)	Date	Time (circle one)

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- You may leave the study at any time.
- You may take time to consider whether or not you would like to take part in this study and any options that are available to you.
- The persons in charge of this study (called the principal investigators and researchers) are Dr. Aimee Talleur and Dr. Stephen Gottschalk. They can be reached by phone at 901-595-3300. Please feel free to call them if you have questions at any time.
- If you choose not to be in the study, or to leave the study at any time, you may still be able to get routine medical care at St Jude.
- This study is sponsored by and done at St. Jude Children's Research Hospital.

4. What will be done in this study?

This study contains 3 phases. The first part is called the "Collection Phase," the second the "Manufacturing Phase" and the third the "Treatment Phase." Each phase of the study will be explained to you in detail, and will each have a separate consent.

Each treatment phase is briefly outlined below:

- The Collection Phase refers to your blood cells being collected via a process called apheresis. The cells are for use in the Manufacturing and Treatment phases of the study at a later time.
- The Manufacturing Phase refers to your peripheral blood cells being changed to improve their ability to recognize and kill cancer cells. This process occurs in the GMP facility using the cells that were previously collected. The final cell product is referred to as SJCAR19.
- The **Treatment Phase** refers to the portion of the study in which you receive an infusion of the SJCAR19 cells that were made in the Manufacturing Phase; chemotherapy is often given for several days prior to the cellular infusion. You are then monitored for any possible side effects as well the effectiveness of the treatment. The use of SJCAR19 cells is experimental. Although this product is not yet been approved by the FDA, similar cell products have been tested by other institutions.

This consent form gives you information about the third part of the study, the Treatment Phase.

This phase contains the following parts:

- Chemotherapy
- SJCAR19 infusion (Phase I & II dosing)
- Follow-up evaluations

Chemotherapy

Chemotherapy is typically given to get your body ready to accept the SJCAR19 treatment. For this study, these drugs are not intended to treat your cancer directly, but instead to help SJCAR19 work by decreasing interference from the cells in your immune system. During this time, chemotherapy will temporarily decrease the number of your own T cells, allowing the infused SJCAR19 cells a greater ability to grow and work. On "day 0 or +1" you will receive the SJCAR19 infusion. The table below outlines the most common treatment patients will receive. However, some patients may receive no chemotherapy or a different chemotherapy regimen than that which is in the table below. The specific chemotherapy that will be given to you will be discussed in greater detail with you by your doctor.

Example Treatment Table:

Medication or Procedure Name	**Schedule**
Fludarabine (a chemotherapy)	Day -4, -3 and -2
Cyclophosphamide (a chemotherapy)	Day -2
Rest Day	Day -1
SJCAR19 Infusion	Day 0 or +1

The minus sign (-) means before SJCAR19 infusion. Day 0 is the day of SJCAR19 infusion. The plus sign (+) means after SJCAR19 infusion.

The chemotherapy cyclophosphamide can have a bad side effect causing bleeding and clots in the urine and bladder. You will receive a medicine called mesna to help prevent these effects. You will be monitored closely during treatment. You will be given other medicines to help lessen the side effects as much as possible. The days and length of these treatments may vary depending on how your body responds to the treatment and if there are any side effects from the medicines or treatment. Your doctor will discuss any needed changes in your treatment and related medicines with you.

If you have previously experienced severe side effects from one or both of these chemotherapies that would prevent you from receiving them again, you may receive a different chemotherapy regimen or no chemotherapy at all. Your doctor will discuss these options with you at that time. If your treatment team decides that you should receive an alternative chemotherapy regimen, that therapy will be discussed with you in a separate consent.

SJCAR19 Dosing

The first part of this study is a Phase I study, a dose escalation study. This means we do not know the highest dose of SJCAR19 cells that is safe. This means that on the Phase I study, the first group of patients enrolled on study will receive the lowest dose. If that dose level is found to be safe, we will raise the dose given to the next group of participants. The dose that you will get will depend on how many patients have been treated on the study before you. Your dose will not be changed during the course of the research study. Once a maximum tolerated dose (MTD), is determined the study will continue as a Phase II study, and further patients will be treated at the MTD.

SJCAR19 infusion

You will receive an infusion of SJCAR19 that was manufactured from cells that were collected from you in the previous phases of this study. Full descriptions of the apheresis and manufacturing procedures were given in separate consent forms for you to review and sign. SJCAR19 may be administered as a fresh product, directly after completing manufacturing and passing quality release criteria, but most often it will be thawed from a frozen product that also has been subjected to the same quality control testing. Sometimes the cell infusions need to be delayed (not given on the planned days) requiring that the cells remain frozen and stored in a St. Jude laboratory before infusing. However, this is rare.

You will receive the SJCAR19 cells by vein, through either an IV or a central line. This infusion will take place in the hospital. We anticipate that the cells will be given in one infusion, taking about 30 minutes each. The day of infusion is called Day 0 (or Day +1). Once in your bloodstream, the SJCAR19 cells will go through your blood and begin to multiply and attack the target cells, including cancer cells.

Follow-up evaluations

You will be in the hospital for a minimum of about 1 - 2 weeks. How long you are in the hospital will depend on any complications you may have. We will monitor you closely, both while the SJCAR19 cells expand and begin to work, and for the first year after the cellular infusion. You and an adult caregiver will need to stay in or near Memphis for frequent clinic visits even after discharge, for at least 1 month after infusion.

Before, during and after this treatment, tests and procedures such as blood tests, bone marrow tests and radiological scans will be done to evaluate your condition and the effects (good and bad) of the treatment on your body and disease. Some of these tests, like the tests completed before your infusion, are for your clinical care (routine tests) and would be done even if you were not in this study. At first these tests will be done often, but will then be done less often as your condition gets better.

You will also have blood tests that are experimental (research tests). These blood tests will look at how well the SJCAR19 cells are expanding and how long we are able to detect them after the infusion. If you are having a bone marrow or lumbar puncture performed as part of your routine clinical care, then part of your sample may also be sent for some of this experimental testing. You will not be given the results of these research tests. They are described briefly in the table below.

Research Tests to be collected on this study	**Blood volume totals at the time of each collection**	**Frequency of sample collections during this study**
SJCAR19 Research Labs *(Cytokines, Persistence Studies, Function Studies)*	About 2 to 6 teaspoons *(Volume based on weight)*	Pre-chemotherapy, post chemotherapy but pre-infusion, day of infusion, and weeks 1, 2, 3, 4, 8, months 3, 6, 9, 12 after infusion (*optional 1-2 teaspoon sample 3-4 days post infusion)*
Human Anti-mouse Antibody (HAMA)	Less than 1 teaspoon	Pre-infusion and week 4 after infusion
Replication Competent Lentivirus (RCL)	About 1 teaspoon	Pre-chemotherapy and months 3, 6 and 12 after infusion

We will also be doing testing on the apheresis and final SJCAR19 cells to learn more about the cellular immunotherapy, and how the infused cells are interacting and changing once they have been infused; this testing will not require additional blood samples to be drawn and will be conducted on the cells that were previously collected during the collection phase and the SJCAR19 cells that were made during the manufacturing phase.

Quality of Life

The quality of life, hope, and well-being of children with cancer and their parents/caregivers can be greatly affected by their diagnosis and treatment. It is also an important part of each child's health. As part of this research study, we will ask parents/caregivers and patients to share with us how their cancer and this treatment is affecting their quality of life, hope, and well-being by completing a number of questionnaires and brief interviews with research staff. The questionnaires will be appropriate to the age of the patient. These questionnaires and brief interviews will take 40 to 60 minutes to complete and will be conducted before the study begins and at two weeks, four weeks, eight weeks, and three months after the cellular infusion.

Possible Reinfusion

We do not know how long the SJCAR19 cells will last in your body once they are infused. We do know that if CAR T-cells disappear within a few months after they are infused, there is a higher chance of your disease coming back (relapse). Reinfusion of the CAR T-cells may help to decrease that risk and/or may help with treatment of disease that has already comeback after prior infusion. Therefore, for patients treated on the Phase II study, there may be an option to receive additional courses of treatment with SJCAR19 for those participants in which the CAR T-cells disappear within 6 months of prior infusion, or leukemia returns within 12 months of prior infusion.

We will monitor for the SJCAR19 cells in your body by measuring the levels of your normal B-cells in your blood at specified time-points. We will also be following closely for the return of any leukemia cells. If normal B-cells or leukemia cells return after the treatment with

SJCAR19, patients may be able to receive another infusion of the SJCAR19 cells. Reinfusion of the SJCAR19 cells is not required as part of the study, and this option will be discussed with you if you meet criteria.

Reinfusion treatment would include chemotherapy as described above, as well an infusion of the SJCAR19 cells that were previously manufactured for you. Chemotherapy doses will be increased slightly compared to that which you received with initial infusion; this is meant to increase the chance that your immune system will accept the CAR T-cells. The dose of SJCAR19 cells will be the same dose you received with the initial infusion. After reinfusion of the SJCAR19 cells, you will continue to be monitored for any side effects, as well as the follow-up evaluations described in the previous section entitled "Follow-up evaluations"; this includes research studies.

5. What are my other choices if I do not take part in this study?

Potential alternatives to taking part in this research study include:

- Treatment with an FDA approved CAR therapy (manufactured by Novartis).
- Continue to receive standard chemotherapy with or without hematopoietic cell transplant.
- Other experimental treatments using new drugs or methods, if available.
- Supportive therapy (such as transfusions for low blood counts, medications for pain, antibiotics for infections or hospice care).
- No further treatment.

The researcher in charge of the study can tell you about the disease and the benefits of other treatment options. Please feel free to ask the researcher about the disease and its outcomes. If you decide not to get more treatment, your disease will likely get worse.

6. How many people will take part in this study?

We expect that about 30 patients will take part in this study over the next few years.

7. How long will I be in the study?

The total treatment and follow-up for this study is about one year. Participants who receive the SJCAR19 treatment at St. Jude are asked to return to the Transplant Clinic, or their local physician, for doctor visits and follow-up evaluations at least once a year for at least 15 years. We want to see if any long term effects of this research treatment occur. For the purpose of this study, you will need to be followed for 1 year after the last infusion. After one year from your last SJCAR19 infusion, you will be asked to enroll in a long-term follow-up study of children and young adults who have received a gene transfer product at St. Jude Children's Research Hospital to complete the 15 year follow-up. If you choose not to enroll on this long-term follow-up study, we will continue to monitor you on-study on SJCAR19, for up to 15 years post-infusion, per FDA guidance.

8. What risks can I expect from taking part in this study?

Both your disease and prior treatment may be associated with potentially life-threatening complications, side effects or death. SJCAR19 is an experimental therapy; therefore, all of the potential side effects of this treatment are unknown. The main risks of this treatment are the side effects of SJCAR19 (either from the gene modification process or from the cells after they are infused), and of the chemotherapy drugs used for conditioning before the infusion. You will be watched carefully for any side effects. Side effects may be mild or serious, and even life-threatening. Your health-care team may give you medications to lessen these side effects, and you may require care in the intensive care unit. Many side effects may be temporary, however some may cause long-lasting effects.

Risks related to SJCAR19 Manufacturing and Gene Modification

- **Filtering and processing of the donor cells using the CliniMACS device**:

  Because the use of the CliniMACS device for the blood cell processing is considered experimental, there may be risks including possible life-threatening reactions which we do not know about right now. Since only a small number of children and young adults in the world have received this study treatment, we cannot be certain about all the possible risks.

  Small amounts of mouse proteins and iron particles are added to the donated blood cells to help with the processing. If you are allergic to these materials, you could have a severe reaction when the donated cells are infused. This reaction could include fever, chills, wheezing, difficulty breathing, hives, skin rashes, severe low blood pressure, or death. Joint pain and fever often happen about 24 to 48 hours after the infusion. You should tell the doctors and nurses if you have a history of asthma, active inflammatory disease, allergies, or have ever had any exposure to mouse protein. It is possible that you could still have an allergic reaction when the donated cells are infused even if you do not have a history of allergies to these substances.

  There is a small chance that germs or yeast could get into the donated blood cells during CliniMACS processing. This could cause an infection in your body after the cells are given. We will make every effort to keep the donated cells free of germs and yeast, and we will test for germs or yeast in the cells. However, we cannot guarantee that all possible germs or yeast in the cells will be found. You will receive antibiotics and anti-yeast medicines as part of this therapy, if necessary. The risk of developing a severe infection from germs or yeast due to the donor cells is low.

Risk of Lentiviral Transduction

This study involves giving you cells that have been changed by a lentiviral vector. A lentiviral vector is a virus that can insert genetic material into cells. We use a vector to put SJCAR19 into your T cells to enhance their ability to fight your cancer more effectively.

- **RCL:** There is a chance that parts of the lentiviral vector could interact with natural lentiviruses in your body and cause an infectious virus to appear, called a "replication competent lentivirus (RCL)". The SJCAR19 product will be tested for RCL before it is administered to you. To monitor RCL after treatment with SJCAR19, you may be routinely tested per FDA guidance after gene transfer treatment. To date, no cases of humans developing lentivirus infections during gene transfer treatment have been reported.

- **Blood Cancer:** Another risk is that the gene transfer procedure could cause leukemia or another cancer of the blood cells. This can occur if the gene transfer vector disrupts normal genes present in your bone marrow stem cells. This type of complication has been seen in two European studies using a different type of retroviral vector. In these studies, the vector was not derived from the HIV virus but was instead derived from a mouse leukemia virus. To date, 5 out of 20 patients have developed a type of leukemia called T cell ALL. It is possible that more of these patients could develop this T cell ALL in the future. One of these patients has died of the leukemia; the other 4 patients have been treated and are in remission to the best of our knowledge. This is a very serious complication of gene transfer. Laboratory tests show that the lentiviral vector being used in this study may be less likely to disrupt normal genes and therefore may be less likely to cause leukemia or other blood disorders. The eight older children treated with this type of vector have not shown any signs of leukemia or side effects from the vector, however, it is still not known whether the lentiviral vector is indeed safer until it has been tested in patients and those patients have been followed carefully for 5 years or more. Therefore, it is possible that this lentiviral vector could cause leukemia or another blood disorder and if this were to happen, you could die from this complication. While tests in animals suggest that the lentiviral vector may be effective and safe, this has not yet been proven in humans.
- **Antibody Formation:** SJCAR19 was produced using foreign proteins. Strict procedures are in place to make sure that foreign proteins are completely removed prior to infusion, but it is possible that some of these proteins remain. Additionally, a small portion of the gene transfer product was derived using mouse proteins. These proteins are a permanent part of the SJCAR19 product. Your body could develop immune response against these proteins, resulting in an allergic reaction. This risk is thought to be minimal.

- **Autoimmune Disease:** The SJCAR19 cells could potentially result in autoimmune disease, where a person's immune system attacks itself by mistake and causes damage. Autoimmune diseases can affect many parts of your body, depending on what tissue is being attacked. This risk is thought to be minimal with SJCAR19.

- **"False Positive" HIV Test**: The lentiviral vector used in this study comes from the human immunodeficiency virus (also called HIV, a type of lentivirus). This virus can cause HIV infection in humans, which can lead to the acquired immunodeficiency syndrome (AIDS). Although the lentiviral vector used in this study is derived from HIV, it has been changed a lot so that it <u>cannot cause HIV/AIDS</u>. However, after receipt of the SJCAR19 product, you may develop a "false positive" HIV test.

  At the time you enroll in the study, you must have a negative HIV blood test to be sure that you are not infected with the human immunodeficiency virus that causes AIDS. After you receive the gene transfer, it is very likely that you will test positive for HIV RNA in some, but not all, brands of tests that detect HIV RNA using PCR. A positive test in a person who is not HIV infected is called a "false positive" test. If you do have a false positive HIV test caused by the gene transfer, it is unknown how long the test will be positive. You cannot pass the gene therapy vector to your partner.

There are social risks from having your HIV test appear positive. For this reason, you are advised to have all HIV testing done here in our clinic while you are on this study. Counseling about HIV tests, including social problems related to false positive results, is offered at all clinic visits. You may also call the clinic at other times if you have questions or concerns.

You may not ever be able to donate blood, bone marrow, or organs if you have a false positive HIV test when you try to donate. Please be sure to ask the study team to see if you have a negative HIV test before trying to donate blood, bone marrow, or organs.

If you have a false positive HIV test, you may also have difficulties with:

- Health insurance
- Life Insurance
- Medical or dental care
- Travel to other countries or immigration
- Employment
- Education
- Housing
- Military services or other government agencies
- Personal relationships

If you have problems like these, the staff at the clinic will try to help you work through them. If your blood tests look HIV positive because of the gene transfer, you will be offered a letter that shows you joined this study and that describes the response caused by the gene transfer. Even so, this letter or other help offered by the clinic may not solve a social problem caused by a false positive HIV test.

Risks of SJCAR19 infusion

The infusion of cells may cause blockages of the blood vessels in the lungs, kidney damage, trouble breathing, or failure of marrow to grow and make normal blood cells. There is also a small risk (less than 1 in 100) that the cells may contain a bacteria or virus that could cause an infection. The cell infusion will be checked for bacteria, and if there is any sign of infection, you will be treated with antibiotics.

- **Risks related to frozen cellular product infusion.**

  As noted before, sometimes the SJCAR19 product may need to be frozen and stored until the recipient is ready for the infusion. A frozen product is thawed (warmed at room temperature to "unfreeze") just before the infusion. When the donated cells are to be frozen, some fluids and a chemical called dimethyl sulfoxide (DMSO) must be added to protect the cells during the freezing process. If your cells are frozen before infusing, the DMSO that was added may cause you to have a temporary strange taste and smell. You may be able to eat candy, ice cream or popsicles to cover this taste during and/or after the infusion. DMSO may possibly cause your blood pressure to go up, nausea, and vomiting. In very rare cases it may cause your blood pressure to drop, cause changes in your heartbeat, or an allergic reaction. Your urine may have a red color for a few hours. This is from the lysed (broken up) red blood cells that are not protected during the freeze and thaw process. These effects usually last only a short time and almost always can be treated.

Risks after SJCAR19 Infusion

The risks listed below are based on commonly reported side effects that have been seen with similar cellular therapy products. Since SJCAR19 is an experimental treatment, there may be side effects that are not listed below as they are not yet known.

- **Risk of Infection:**

  B-Cell Aplasia: CD19 is a marker that can be found on the surface of both cancerous and normal B-cells. CAR engineered T-cells targeting CD19 cannot distinguish between these cancerous and normal B-cells. Therefore, B-cell aplasia (low numbers of B-cells or absent B-cells) is an expected side effect of treatment with this therapy. The absence of B-cells results in the decreased ability of a patient’s immune system to make antibodies that protect against infection. Intravenous immunoglobulin (antibody) replacement can be used to help prevent infection during this period of normal B-cell aplasia. It is not known how long the decreased number of B-cells persists; however no long-term side effects have been noted.

  Chemotherapy: The chemotherapy regimen you receive will temporarily weaken your immune system. During this time, you will be at risk of infection, which can be life-threatening in 5% to 10% of patients. Most infections can be treated with antibiotics. Sometimes an infection cannot be treated. In some cases, patients die of infection.

- **Tumor Lysis Syndrome**

  After infusion with SJCAR19, you may experience Tumor Lysis Syndrome. This can happen when large numbers of tumor cells are rapidly killed. This can result in electrolyte imbalances and kidney damage. You will be monitored closely for the development of tumor lysis syndrome, and may be given medication to treat it.

- **Cytokine-Release Syndrome (CRS)**

  CRS is a serious side effect associated with CAR therapy and is a result of activation of CAR T-cells after they are infused into the patient. Cytokines are chemical messengers that help immune cells perform their duties. When CAR cells encounter a target, they become activated and produce large amounts of cytokines. This can result in high fevers, chills, low blood pressure, liver and kidney problems, or poor lung oxygenation. These symptoms may make you quite ill and require intensive treatment support such as mechanical ventilation or dialysis. The onset of these symptoms is typically within the first few weeks of treatment. These symptoms are typically reversible. However, CRS can be extremely serious and even life- threatening. Medications such as corticosteroids or those that block cytokines can be used to treat CRS.

- **Neurotoxicity**

  Patients receiving CAR therapy have experienced a variety of neurologic symptoms, including delirium, confusion, stupor, somnolence and seizure while undergoing treatment. These symptoms generally occur in the setting of concurrent cytokine release syndrome, but not always. The onset of these symptoms is typically within the first few weeks of treatment. These symptoms are typically reversible. However, neurotoxicity can be extremely serious and even life-threatening. Medications such as corticosteroids or those that block cytokines can be used to treat neurotoxicity.

- **Reproductive risks**

  The risks of this study treatment on reproduction (ability to have a baby or father a baby) in the future are unknown. The effects of this treatment on an unborn or nursing child are also unknown. Females must not be pregnant or nursing (breast- feeding a baby) when starting treatment and must not get pregnant during treatment. Females of childbearing age must have a negative pregnancy test before starting the treatment. If you think you may have become pregnant during the treatment, you must notify your doctor immediately. If you become pregnant, the treatment may be stopped.

  There may be risks associated with male participants fathering a child while receiving this transplant treatment. Some medications cause DNA damage. This may be passed on to children through sperm resulting in possible birth defects or babies with abnormalities.

  Participants who are able to have a child or father a child must use an effective form of birth control while receiving this treatment. Effective forms of birth control include oral contraceptive pills, condoms, and abstinence (not having sexual intercourse). The study doctor will discuss effective forms of birth control with you. Birth control methods should be continued for at least 6 months after treatment to avoid pregnancy. We also do not know if there may be unknown long-term effects to your future children.

- **Graft-vs-host Disease**

  The risk of graft-vs-host disease (GVHD) only applies to those patients that have previously received an allogeneic hematopoietic cell transplant (cells from another person). If you have not previously had an allogeneic transplant, there is no risk of GVHD in this study. However, if you have previously had an allogeneic hematopoietic cell transplant, then the T cells used to manufacture SJCAR19 likely include T cells from your previous donor. As you may recall, GVHD occurs when donor T cells attack normal host tissues. The severity of GVHD ranges from mild to severe and life-threatening. Treatment for GVHD may include corticosteroids or other immunosuppressive medications. In this study, the T cells have been gene-modified to attack your cancer cells. However, it is possible that they could attack normal tissues. Based on the experiences of other institutions using similar cell products in those previously treated with a transplant, we feel that this risk of the SJCAR19 cells causing GVHD is very low.

- **Loss of privacy**

  Very rarely, personal information from your records could be given out by accident. This might make you upset, embarrass you, or affect your ability to get insurance. To stop this from happening, we:

  - Store records apart from names or other personal information
  - Only allow members of the study team to see the records
  - Store electronic data only on computers protected with a password and encryption software
  - Report study results on the whole group and never identify one single person in any reports

Chemotherapy and other agent related risks:

Common side effects of chemotherapy include nausea, vomiting, hair loss, mouth sores, stomach ulcers, and low blood counts. Low blood counts can mean that you are at a higher risk for infection (which may require antibiotics and hospitalizations), bleeding, and anemia (weakness and pale skin). This may require blood and/or platelet transfusions. Allergic reactions may occur with any medicine.

A possible late side effect of this study treatment and related medications is therapy-related cancer. The exact risk is not known but is thought to be less than 1% in the first 20 years of follow-up.

The following pages describe possible side effects specific to each of the agents that will be most commonly given as part of this research study. However, unknown side effects may occur. The symbol # before any side effect means that this problem is rare. If it is determined that you do not need to receive chemotherapy, or that a different chemotherapy regimen will be used, the details of this will be discussed with you by your doctor prior to signing consent to proceed with treatment with SJCAR19.

CYCLOPHOSPHAMIDE (Cytoxan®)

- Nausea and vomiting
- Hair loss
- Low blood counts with higher risk for infection, bleeding, and anemia
- Bladder problems that cause pain when urinating or cause blood in the urine. (May be prevented by giving extra fluids by mouth or by vein, or by a drug called MESNA.)
- Sterility (unable to have children)

Second cancers (very rare)
Lung damage (pulmonary fibrosis)
Blurred vision
Abnormal heart beats (at high doses)
Heart damage
Mouth sores
Problems with body fluids and electrolytes (SIADH)

MESNA (Mesnex®)

Stomach pain
Diarrhea and/or loose stools
Headache
Limb and joint pain
Tiredness
Allergic reactions
Low blood pressure

FLUDARABINE (Fludara®)

- Low blood counts with higher risk for infection, bleeding and anemia
- Mild nausea and vomiting
- Loss of appetite
- Tiredness, feeling bad, weakness, fever, chills
- Nerve pain, decreased feeling in hands and feet (21-60 days after therapy), eye problems, and hearing problems
- Cough or difficulty breathing
- Nerve damage with high doses

Redness, swelling or sores in the mouth or throat

9. What are the possible benefits of the study?

We do not know if you will benefit from being treated with SJCAR19. It is possible that this study treatment may help to put your disease in remission or keep it in remission. However, there is no guarantee that this will work. You may benefit from knowing that the information learned from this study may help future patients with a cancer such as yours that may be difficult to treat.

10. Can I stop taking part in this study?

You can stop or withdraw from this study at any time. If you decide to leave the study, you should talk to your doctor first. She/he will talk to you about health and safety issues. If you leave this study, other treatments may still be given to control your disease. Your doctor can recommend other treatment options if you stop the study treatment or if the treatment is stopped without your consent.

11. Can I be taken out of the study without my consent?

You may be taken out of the study without your consent for these reasons:

- Your doctor decides that continuing in this study would be harmful.
- You need a treatment not allowed on this study.
- You are unable to keep appointments or take medicines as instructed.
- Your condition gets worse.
- You have a positive pregnancy test.
- New information is learned that a better treatment is available, or that the study is not in your best interest.

12. Will I be paid for my time or expenses?

You will not be paid to take part in this study

13. How will new findings related to this study be shared with me?

We will tell you anything we learn during the study that might change your mind about staying in the study. If you are interested in learning more about this treatment, contact Dr. Aimee Talleur or Dr. Stephen Gottschalk at 901-595-3300.

14. How will I find out the results of this study?

The researcher will give you information about the overall results of this study. St. Jude researchers share information with people in studies in many ways, including:

- Articles on www.stjude.org
- In newsletters
- In medical or scientific journals
- In the media

Published research results will only describe groups of people who took part in the study. Information that points out a single person will not be in research journals or other reports.

15. Will any genetic tests be done and what are the risks of genetic testing?

As discussed above, we will obtain samples of your immune cells and other cells including tumor cells during this study. Research performed on your apheresis collection, CAR T-cell product, and immune cells obtained from research blood draws will include some genetic testing. Genetic testing on material obtained from these samples should help us learn how well CAR T-cells work, and ways to improve T-cell therapies in the future.

The genetic tests are required and considered research only tests. Results are not reported to you or placed in your electronic medical records. The genetic tests include a partial analysis of genetic material obtained from the samples, and may include whole genome sequencing of tumor cells or normal cells from your body. No direct benefits to participants are expected from these genetic tests.

Risks of Genetic/Genomic Testing

There may be risks to your privacy and the privacy of your relatives from storing your information in a database. Although measures are taken to protect your privacy, we do not know how likely it is that your identity could become re-connected with your genetic and health information, and confidentiality cannot be guaranteed. If your genetic information were re-identified, personal information about you, your health, and your risk of disease could become known to others, and potentially be used to discriminate against or stigmatize you, your family, or your groups. This could also present unknown risks. We believe the chance that this will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us; we will make every effort to protect them.

16. What about privacy and confidentiality?

Privacy

We will keep your medical records private to the degree allowed by law. St. Jude may give your health data, without identifiers, to other researchers or use it for other research projects not listed in this form. St. Jude, Dr. Aimee Talleur, Dr. Stephen Gottschalk and their staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

We will not identify you personally in any text published about this study. Your personal information will not be in any text published about this study.

Your study results will be kept in your research records for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will also be kept for an unknown length of time.

Government agencies such as the Food and Drug Administration (FDA) oversee medical treatment of people as required by state or federal regulations. Therefore, it may be necessary for these government agencies to review parts of your medical record.

The Transplant Program at St. Jude Children's Research Hospital is required by the United States federal government to report all transplant and post-transplant follow up information to the Center for International Blood and Marrow Transplant Research (CIBMTR). The CIBMTR is a worldwide research organization of scientists and doctors who study important issues in transplantation.

Your donor blood cell collection related information will also be sent to and reviewed by representatives from the Foundation for the Accreditation of Cellular Therapies (FACT).

FACT is an international oversight group responsible for monitoring the clinical and laboratory activities of institutions that provide research and treatment with certain blood cell products including blood progenitor cells (blood cells similar to stem cells). These representatives may review your laboratory and medical records to verify institutional compliance with federal regulations regarding these blood cell products.

Data sent to the CIBMTR and FACT will not include your St. Jude record number. A unique identification number will be assigned to your information. However, some of the information sent may possibly be linked to you. This information includes but is not limited to the following:

- Your date of birth and primary country (and state) of residence;
- Type of cancer, prior cancer related therapy, dates of and results for all immune system and infectious disease related blood tests;
- Medications, doses used during study treatment, infusion date, side effects of the treatment;
- How your immune system, blood system and disease have responded to the study treatment.

Because this information may be linked to you, absolute privacy cannot be guaranteed.

By signing this consent form, you are allowing your data and/or biological sample to be sent to and medical records to be reviewed by these persons.

- Government agencies such as the FDA and the National Cancer Institute (NCI).
- A regulatory agency called FACT.
- A research organization called the CIBMTR.
- A research safety and ethics review committee, called the St. Jude Institutional Review Board (IRB).
- The St. Jude Institutional Biosafety Committee (IBC), an internal committee that oversees all aspects of investigational biologic products (which includes blood cell products processed through the use of an investigational device such as the CliniMACS) as well as all laboratory and clinical related safety issues.

Confidentiality

Health information and research data obtained from tumor and normal specimens, such as genetic data, are often shared with the research community using various databases, including those maintained by St. Jude and the federal government. Your data may be stored, shared broadly, and used for future research through the St. Jude Cloud run by St. Jude, and the Database for Genotypes and Phenotypes (dbGaP) and the Gene Expression Omnibus (GEO) both run by the National Institutes of Health, and the Sequence Read Archive (SRA). This is to advance scientific discovery and satisfy requirements of organizations that fund research and journals that publish that research. Prior to submitting your data to these databases, it will be de-identified by removing any information that could identify you, such as your name, date of birth, medical record number, and any other information that could link your identity to your data. The only health information included will be your age, solid tumor diagnosis, how long CAR T-cells remain in your blood, and response to CAR T-cell treatment. There are two types of databases used for sharing research data. One is a controlled access database, and the other is a public, unrestricted access database. Each is described below.

Controlled access database: Your individual genomic data and health information may be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the database must agree not to attempt to identify you.

Unrestricted access databases: De-identified summary level information from research studies using your samples, genetic information and health information may be freely available in a public, unrestricted database that anyone can use. Summary-level information about all participants included in a dataset, including you, but not genetic data for each individual, may be shared. This public information will not be labeled with your name or other information that could be used to easily identify you, and the risk of anyone identifying you with this information is very low.

You will not be notified every time your genomic information is used for research. We also do not know what types of future research will be done with genomic data from this study.

SUMMARY OF RESEARCH AND PRIVACY RIGHTS

The following statement describes your rights as a research participant in this study:

1) You may refuse to be in this research study or stop at any time. This decision will not affect your care or your relationship with your doctor or St. Jude. If available, you may receive routine medical care at St. Jude Children's Research Hospital.
2) If you have insurance, TennCare or Medicaid, or other health care coverage such as an employer-sponsored benefit plan, they will be billed for many of the services we provide. However, we do not bill patients or their families for the cost of medical care not covered by their health plans. This includes research costs.
3) Your samples and information may be used to develop a new product or medical test, which may be sold. If this happens, you will not receive any payments for these new products.
4) If you have any questions about this study or if you are injured as a result of this study, contact Dr. Aimee Talleur or Dr. Stephen Gottschalk, at 901-595-3300 immediately. If you are injured from being in this research study, St. Jude will provide reasonable and necessary care for that injury. If you need more care than St. Jude can provide, we will help you find medical care somewhere else. It is not the hospital's policy to provide payment if you are injured from being in this study; however, you are not giving up any of your rights by signing this consent form.
5) A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most the Website will include a summary of the results. You can search this Website at any time.
6) A decision to take part in this research means that you agree to let the research team use and share with other researchers your health information also called protected health information (PHI) for the study explained above. This information will be kept indefinitely. You have the right to see, copy, and ask for changes to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.
7) When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI may be used or given to someone outside the hospital. You have the right to read the Notice of Privacy Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude Internet website: *www.stjude.org*.
8) Federal agencies such as the Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP) or the National Institutes of Health (NIH), St. Jude Children's Research Hospital Institutional Review Board (IRB), your insurance company or other health benefits plans (if charges are billed to these plans), as well as other regulatory agencies, committees, or persons involved in overseeing research studies may review your research and medical record.

9) Information about you that may be given out includes your complete medical records, including details about diagnosis, illness, treatment, and information that may be recorded about past diagnosis or treatment and information taken as a part of this research study as explained in this informed consent.

10) After your records are given to or used by others, St. Jude Children's Research Hospital cannot promise that information will not be given out again. Also, the information given out may no longer be protected by federal privacy laws.

11) St. Jude uses reasonable safeguards and means to protect your private information. However, St. Jude cannot guarantee the security and confidentiality of e-mail, text messages, fax communications or mail.

12) Researchers and study staff are required by law to report suspected child abuse, threat of harm to self or others, and certain diseases that spread from person to person.

13) Your permission to use and give out your child's protected health information will end when your child turns 18 years of age. At that time, we may contact your child for his or her permission to continue using it.

14) You may take back permission for your records to be used or given out at any time, for any reason, except when that information has already been given out or used for the study based on your permission. To take back your permission, please fill out a form called a Revocation of Release of Authorization. You may ask for this form by calling the St. Jude Privacy Officer at 901-595-6141. You must mail the form or hand it to:

    HIPAA Privacy Officer
    St. Jude Children's Research Hospital
    262 Danny Thomas Place, Mail Stop 280
    Memphis, TN 38105

15) You can get more details about your rights as a research participant by calling the St. Jude Institutional Review Board at 901-595-4357 or the Research Participant Advocate at 901-595-4644. If you are outside of the Memphis area, please call toll-free 1-866-583-3472 (1-866-JUDE IRB).

16) The St. Jude Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns, and questions. The Advocate can help you obtain information and can relay any input you may have concerning the research to the research study team. You can reach the Advocate by calling 901-595-4644, or if you are outside of the Memphis area, call toll free at 1-866-583-3472 (1-866-JUDE-IRB)

17) You will be given a copy of this signed consent form.

PARENT/GUARDIAN STATEMENT (Required for participants younger than 18 years):
I have read this document or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give permission for my child to be in this research study.

______________________________ ______________ ___________AM/PM
Parent/Legal Guardian Signature Date Time (circle one)

ASSENT DISCUSSION (Required for participants 7–13 years old)

☐ The research was explained to the minor participant in age-appropriate terms and the minor verbally agreed to take part in the study.
☐ Minor declined to take part in the study. The minor declined for the following reason(s):

____

☐ An assent discussion was not initiated with the minor for the following reason(s):
  ☐ Minor is under 7 years of age.
  ☐ Minor is incapacitated.
  ☐ Minor refused to take part in the discussion.

  ☐ Other____

RESEARCH PARTICIPANT STATEMENT (Patients 14–17 years old and Adult Participants 18 years and older):
I have read this document or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this research study.

______________________________ ______________ ___________AM/PM
Patient Research Participant Signature/LAR Date Time (circle one)

<u>Separate Caregiver Consent to participate in study for QOL:</u>
RESEARCH PARTICIPANT STATEMENT (Caregiver Adult Participants 18 years and older):
I have read this document or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this research study, including the QOL Studies.

______________________________ ______________ ___________AM/PM
Parent Research Participant Signature/LAR Date Time (circle one)

RESEARCHER/DESIGNEE STATEMENT:

I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

______________________________	_______________	__________ AM/PM
Researcher/Designee Signature	Date	Time (circle one)

____
Print Name

RESEARCH PARTICIPANT ADVOCATE STATEMENT:

I observed the informed consent process. The research study, intervention/observation, risks, benefits, and alternatives were presented to the research participant and/or legal guardian(s). They were encouraged to ask questions, and research team members answered all their questions. The participant/parent(s) indicated that they: 1) understood the information presented; and 2) voluntarily consented /agreed to take part in the research.

______________________________	________________	__________ AM/PM
Research Participant Advocate	Date	Time (circle one)
______________________________	________________	__________ AM/PM
Interpreter (if needed)	Date	Time (circle one)

PLEASE SEND COMPLETED CONSENT FORM TO CLINICAL TRIALS OPERATIONS:

- **SCAN and E-MAIL to:** protocoleligibilityoffice@stjude.org
- **Or FAX to:** (901) 595-6265