THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Phase I/II Study of Recombinant Human Interleukin-7 to Promote T-Cell Recovery after Haploidentical and Cord Blood Stem Cell Transplantation
2018-0674

Study Chair: Gheath Al-Atrash

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

You are being asked to take part in this study because you received a haploidentical or umbilical cord blood stem cell transplant as part of your standard treatment. Umbilical cord blood is a source of blood-forming cells that can be used for transplantation, also known as a graft. A haploidentical transplant is a transplant that uses stem cells from a donor that is partially (at least 50%) matched to you.

The problem with this type of transplant is the small number of blood-forming cells available in haploidentical or cord blood transplants, which may delay the "take" of the graft in the transplant recipient.

The goal of this clinical research study is to find the highest tolerable dose of the study drug CYT107 that can be given to patients who have received a haploidentical or cord blood stem cell transplant. The safety and effects of this drug will also be studied. Researchers also want to learn if CYT107 affects the "take" of the graft and the recovery of certain blood cells related to the immune system (called T-cells, NK cells, and B cells) in patients who have had a haploidentical or cord blood transplant.

CYT107 is not FDA approved or commercially available. It is currently being used for research purposes only. Its use in this study is investigational.

The study doctor can explain how CYT107 is designed to work.

CYT107 may lower your chances of developing certain infections after your transplant. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, there may be an increased risk of developing GVHD or other complications after your transplant. You may also experience side effects, including fever, chills, or an allergic reaction.

You can read a full list of potential side effects below in the Possible Risks section of this consent.

You may receive 3 injections of CYT107. CYT107 will be provided at no cost to you while you are on this study.

You may choose not to take part in this study.

Instead of taking part in this study, you may choose to receive the standard-of-care treatment for the disease. You may choose to receive other investigational therapy, if available. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following tests and procedures will be performed to help the doctor decide if you are eligible:

- Blood (about 2 teaspoons) will be drawn for routine tests, to check your kidney and liver function, and to check for the BK virus (BKV), Epstein-Barr virus (EBV), and cytomegalovirus (CMV). BKV, EBV, and CMV are viruses commonly seen in transplant patients.
- You will have an EKG to check your heart function.
- You will have a physical exam.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Study Groups
You will be assigned to a dose level of CYT107 based on when you join this study. Up to 3 dose levels of CYT107 will be tested. Up to 7 participants will be enrolled at the first 2 dose levels. Three (3) participants will be enrolled at the third dose level, and if they tolerate their dose, all following patients will be enrolled at that dose level. The first group of participants will receive the lowest dose level. Each new group will receive a higher dose than the group before it, if no intolerable side effects were seen. This will continue until the highest tolerable dose of CYT107 is found.

Up to 21 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration
You will receive your first injection of CYT107 about 60 to 180 days after you receive your transplant.

You will be given one (1) injection of CYT107 directly into the muscle 1 time each week for 3 weeks. If the doctor thinks it is needed, you may be able to receive CYT107 as an injection under the skin instead of the muscle.

You will be given standard drugs like Benadryl and topical steroids to help decrease the risk of side effects. You may ask the study staff for information about how the drugs are given and their risks.

Length of Study Participation
You may receive 3 injections of CYT107. You will no longer be able to take the study drug if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Your participation in this study will be over about 1 year after the last injection.

Study Visits

Within 2 weeks before your first dose of CYT107 you will have the following. If these were done recently, they may not need to be repeated:
- Blood (about 2 teaspoons) will be drawn for routine tests and to check for the BKV, EBV, and CMV viruses.
- You will have an EKG.
- You will have a physical exam.

One (1) time each week until Day 42:
- Blood (about 1 teaspoon) will be drawn for routine tests.
- You will have a physical exam.

The study staff will also check for certain viruses at the following time points:
- Blood (about 1 teaspoon) will be drawn **1 time a week for Days 1-180** to check for CMV.

- Blood (about 1 teaspoon) will be drawn **every 2 weeks for Days 60-100**, then **monthly for Days 100-180**, to check for EBV.
- If you show symptoms of BKV, blood (about 1 teaspoon) and urine will be collected to check for BKV.

Before and 1 day after each dose of CYT107, blood (about 1 tablespoon each time) will be drawn to check the effects of CYT107 on your body.

Before each dose of CYT107 and then about 21, 28, and 100 days after the first injection, blood (about 1 tablespoon each time) will be drawn to check your immune system function, to check for infections, and to check the effects of CYT107 on your body.

Please note that throughout this study, some study procedures (such as lab blood tests or physical exams) may be performed at a laboratory or clinic closer to your home. The study doctor will discuss this with you.

Research Testing
You will be asked to take part in LAB99-062 for additional research testing. If you consent to take part in LAB99-062, blood (about 1 teaspoon each time) will be drawn before the first CYT107 injection and on Day 42 to test for anti-CYT107 antibodies. Antibodies are created by the immune system and may attack foreign cells or substances, such as CYT107. If the test for antibodies on Day 42 is positive, blood (about 1 teaspoon) will be drawn on Day 100 and about 4-6 weeks after your last dose of CYT107 to check for CYT107 antibodies. These blood samples will be sent to the supplier of the study drug, Revimmune. After the samples are used for this antibody testing, the samples will be destroyed. You can still take part in this study if you do not take part in LAB99-062.

Follow-Up
After your last dose of CYT107, you will continue to have follow-up visits as part of your standard care (visits you would have even if you were not taking part in this study) for up to 3 years after your last dose. Information from these follow-up visits, such as results of any standard of care testing, will be collected.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases, side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Tell the study staff about any side effects you may have, even if you do not think

they are related to CYT107/the study procedures.

CYT107 Side Effects

This is an early study of CYT107 so the side effects are not well known. Based on early studies, CYT107 may cause:

• slow heartbeat • sudden stopping of the heart • fever • fatigue • skin rash • abnormal liver tests (possible liver damage) • abdominal pain • diarrhea • vomiting • bleeding in the rectum	• lymph node swelling • difficulty breathing • injection site reaction (possible chills and/or hives) • graft-versus-host-disease (when transplanted donor tissue attacks the tissues of the recipient's body) • kidney failure	• allergic reaction, possibly life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure) • immune reaction (possible loss of drug function)

CYT107 may cause you to develop another type of cancer (such as post-transplant lymphoproliferative disorder, a type of lymph node cancer).

CYT107 may cause secondary graft failure. Secondary graft failure is when the donor's stem cells may fail to grow and multiply in your body. If this occurs, you may have a high risk of infections and/or bleeding. You may need frequent blood transfusions.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

EKGs may cause discomfort while lying on the exam table, and the tape on the EKG pads may cause skin irritation.

Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. The researchers with this CoC may not disclose or use information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information protected by this CoC cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below).

The CoC cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation. You should understand that a CoC does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The CoC will not be used to prevent disclosure for any purpose you have consented to.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks

Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: Talk with the study doctor about acceptable birth control methods to use while on study.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Revimmune for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-2933 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Gheath Al-Atrash, at 713-792-8750) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-2933 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is supported by: Revimmune. Revimmune is supplying the study drug during this study.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study supporter. If you have any questions about this, you may call the IRB at 713-792-2933.

Future Research

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson or shared with other researchers and/or institutions for use in future research.

Before being shared for future research, every effort will be made to remove your identifying information from any data and/or samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or samples are used for future research. If this research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research

Any samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

Outside Care

Part of your care may be provided outside of MD Anderson by your home doctor(s).

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Revimmune, who is a supporter of the study and supplies the study drug, and/or any future sponsors/supporters of the study
   - Any future licensees of the study technology
   - Center for International Blood and Marrow Transplantation Research (CIBMTR) and National Marrow Donor Program (NMDP)
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Your name and personal information will be coded with a number to protect your privacy. Personal and coded information will be kept secure and inaccessible to other people. Any data reporting or publication will only use the coded number. Only the Principal Investigator and individuals chosen by the Principal investigator will have access to any personal information.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

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

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2018-0674.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION