Washington University in St. Louis

INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION FOR ADULTS AND CHILDREN WHO REACH THE AGE OF MAJORITY

RECIPIENT CONSENT

Sponsor / Study Title:	**Washington University School of Medicine / "Cytokine Induced Memory-like NK Cell Adoptive Therapy for Relapsed AML after Allogeneic Hematopoietic Cell Transplant in Children and Adults"**
Protocol Number:	**201709041**
HRPO #:	**202206197**
Principal Investigator: (Study Doctor)	**Amanda Cashen, MD**
Telephone:	**(314) 454-8304 (24 hours)**
Address:	**St. Louis Children's Hospital One Children's Place St. Louis, MO 63110** **Barnes-Jewish Hospital One Barnes-Jewish Hospital Plaza St. Louis, MO 63110**

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant. By signing this form you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you have been diagnosed with relapsed acute myeloid leukemia (AML) that was previously treated with a

stem cell transplant and your doctor is planning to treat your AML relapse with a donor lymphocyte infusion (DLI).

A DLI is an approved form of treatment for patients who have relapsed after stem cell transplant. In a DLI, lymphocytes (a kind of white blood cell) are collected from the person who originally donated stem cells for your transplant so they can be given to you to treat the relapsed AML. The goal of a DLI is to put the AML back into remission.

In this study, the white blood cells collected from your donor during apheresis will be separated. Some will be used for the DLI, while others will be used to generate cytokine induced memory-like (CIML) natural killer (NK) cells. NK cells are cells found in your bloodstream whose function is to fight infection and tumor cells. The type of NK cells you will receive if you participate in this study (CIML NK cells) have been selected because they are activated to better fight leukemia cells. They will be processed after collection from your donor to make them ready to fight the leukemia before they are infused into your bloodstream. This process includes exposing them to protein signals called "cytokines" overnight. The reason for treating you with CIML NK cells after DLI is to enhance the graft-versus-leukemia effect, allowing the graft to be more successful and reduce the risk of graft rejection.

The purpose of this research study is to see whether we can generate and use CIML NK cells from the white blood cells collected from your donor for the purpose of DLI.

The use of CIML NK cells is considered investigational, which means that they have not been approved by the U.S. Food and Drug Administration (FDA).

You will also receive study drugs called fludarabine or cladribine, cyclophosphamide, and IL-2. These drugs have not been approved by the FDA to be used the way they are being used in this study, which means they are considered investigational. However, they are approved to be used in other ways, and they are regularly used by physicians the way they are being used in this study.

WHAT WILL HAPPEN DURING THIS STUDY?

All study treatment will be given in the inpatient setting at Siteman Cancer Center. We feel it is important to remind you that any procedures regardless of whether they are tests you would have if you did not take part in the research or are research-related will require you to remain at the Siteman Cancer Center up to several hours to complete the necessary testing. There may also be a wide variability in the length of clinic visits due to the unique characteristics of your medical history and health condition as well as due to clinic factors such as physician availability, staffing shortages, and weather delays. This will also vary depending upon your needs at the visit as determined by your physician. It is important that you are able to be available to complete the procedures at each visit to ensure that your safety and treatment needs are met.

Before you begin study treatment:

You will need to have the following screening exams, tests, or procedures to find out if you can continue to be in the study. Most of these procedures are part of regular cancer care and may be

done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Physical exam, including taking of vital signs, reviewing your medical history, and talking about any symptoms or health problems you're having
- Blood tests (approximately 2 tablespoons of blood) for the following reasons:
    - To check your blood counts and organ function
    - Virology screen (to make sure you don't test positive for hepatitis or HIV)
    - Baseline chimerism testing, which allows researchers to compare your blood cells before you receive the transplant to your blood cells after the transplant
    - Pregnancy test (if you are a woman who is able to become pregnant) (approximately 1 additional teaspoon of blood will be drawn, if necessary)
- Bone marrow aspirate and biopsy to check on the status of your disease; this is a procedure during which a few teaspoons of your bone marrow and a little of the tissue will be removed using a hollow needle
- Chest X-ray or CT (computerized tomography) scan of the chest if you haven't had one done in the last 90 days. A CT scan uses X-rays to create a picture of the bones and soft tissues in your body, and in some cases a contrast medium will be used and you must not eat or drink anything for 4 hours before the test (the study doctor will tell you if this is the case). A "contrast medium" is a liquid or solid that helps make a sharper image from the scan. Before the scan, you will need to remove all jewelry. During the scan, you will lie on your back on an X-ray table. A strap may be placed across your body to prevent movement so that the X-ray will be clear. The table will then slide into a large tunnel-shaped machine.
- Pulmonary function tests to look at how your lungs are functioning if these tests haven't been done in the last 90 days; these tests involve breathing into a sensor to help measure the amount of air that can be inhaled and exhaled as well as the speed with which it can be inhaled and exhaled
    - If you are too young to complete a pulmonary function test, you may undergo a pulse oximetry test instead. This test involves a clip-like device placed on a body part, such as a finger or ear, and uses light to measure how much oxygen is in the blood.
- Electrocardiogram (ECG) to look at how your heart is functioning if this test hasn't been done in the last 90 days; this test involves putting sticky pads on your skin while the electrical activity of the heart is recorded
- Echocardiogram (ECHO) or MUGA (multiple gated acquisition) scan to look at how your heart is functioning if either of these tests haven't been done in the last 90 days; an echocardiogram uses a transducer (an instrument that transmits high-frequency sound waves) placed on your ribs near your breastbone to create a moving picture of your heart, and a MUGA uses a low-level radioactive substance (tracer) to label your red blood cells, after which your heart is scanned by a camera which can "see" the labeled blood cells and produces a moving image of your beating heart

It is possible that after your medical history, tests, and procedures are reviewed, you will not be able to continue in this study. If this occurs, your study doctor will go over the reasons with you.

Procedures throughout the study:
You will be admitted to the hospital.

You will then undergo treatment with fludarabine or cladribine and cyclophosphamide chemotherapy before the CIML NK cell and donor lymphocyte infusions. This will start 7 days before the CIML NK cell infusion (Day -7) and will continue through Day -3. The therapy regimen consists of:

- Fludarabine or cladribine, given daily for a total of 5 doses as an IV infusion over one hour
- Cyclophosphamide, given on two consecutive days as an IV infusion over 2 hours

On Day 0, you will receive the CIML NK cell infusion. The CIML NK cells will be infused into your body through your central line. Your vital signs will be monitored every 15 minutes during the infusion, then every 30 minutes for one hour after the end of infusion; this is to watch for a reaction to the infusion so that appropriate treatment can be given if needed. You will be pre-medicated with acetaminophen (Tylenol), diphenhydramine (Benadryl), and meperidine (Demerol) to help prevent a reaction to the cells.

After the cell infusions, you may receive injections of G-CSF to help your white blood cell count recover. You will continue to receive it as part of your routine until your white blood cell count is high enough.

Additionally, on Day 0 (approximately 4 hours after your CIML NK cell infusion), you will begin receiving injections of a protein called IL-2, which will help the NK cells fight the leukemia cells by supporting their survival and activating a more effective anti-leukemia immune response. You will receive IL-2 every other day for 12 days (total of 7 injections).

Thirty days after your CIML NK cell infusion, you will receive the DLI, which includes T cells from your donor to help fight off the relapsed AML cells. The DLI will be given through your central line. You will likely be pre-medicated with acetaminophen, diphenhydramine, and meperidine as well as intravenous fluids immediately before you receive the donor lymphocytes in order to decrease any side effects you may have from the infusion.

You will be seen frequently through Day +100, generally daily throughout hospitalization and at least once every week after that. After Day +100, your study doctor will decide how often your visits are and what tests to obtain for you based on your clinical situation. The tests and procedures outlined below are mandatory:

- Physical exam (daily beginning on Day -3 through Day +14, weekly through Day +42, then on Day +60, Day +100, Month 6, Month 9, and Month 12)
    - Beginning on Day +14, the study team will also assess you to see if you have any signs of graft-versus-host disease (GVHD), which occurs when some of the cells from the donor attack the recipient's tissues, resulting in mild, moderate, or even life-threatening side effects to the recipient's skin, stomach, intestines, and liver
- Blood tests to check your counts (daily beginning on Day -3 until your white blood cell count has recovered, weekly through Day +42, then on Day +60, Day +100, Month 6, Month 9, and Month 12)

- Blood tests to check your kidney function and electrolytes (daily on Day -3 through Day +14, weekly through Day +42, then on Day +60, Day +100, Month 6, Month 9, and Month 12)
- Blood test to check your liver function (weekly beginning on Day -3 through Day +42 (and on Days +1 and +2), then on Day +60, Day +100, Month 6, Month 9, and Month 12)
- Blood test for chimerism testing (Day +28 and Day +100)
- Bone marrow aspirate and biopsy to check on the status of your disease (Day +14, Day +28, Day +60, Day +100, and 6 months)

On the days listed below, you will have blood drawn for research purposes. This research includes testing which will allow researchers to compare your blood cells before you receive the CIML NK cells to your blood cells afterwards. It also includes some genetic research to see whether you and your donor are matched or mismatched for a certain gene and whether a match or mismatch affects how you respond to study treatment.

- Screening
- Day -3
- Day 0 before the CIML NK cell infusion
- Day +7
- Day +14
- Day +28
- Day +60
- Day +100
- 6 months
- 9 months
- 12 months

If you are aged 18 or older, 14 teaspoons (a little over ¼ of a cup) will be drawn at each time point. If you are under 18, the amount of blood drawn will depend on how much you weigh: if you are under 45 pounds, 4 teaspoons will be drawn; if you are 45 to 130 pounds, 8 teaspoons will be drawn; and if you are more than 130 pounds, the full 14 teaspoons will be drawn.

You will also have up to 1 teaspoon of bone marrow collected for research purposes on the following days:

- Screening
- Day +7
- Day +14
- Day +28
- Day +60
- Day +100
- 6 months
- At the time of any other routine bone marrow collection

If the first cycle of study treatment does not eliminate your AML, you can have a second course of study treatment with chemotherapy, CIML NK cell infusion, and DLI. If you have a second course of study treatment, the day of your second CIML NK cell infusion will be considered a

second "Day 0." All of the assessments listed above will occur again on the same schedule. This includes the routine procedures such as physical exams and blood draws for safety tests (such as checking your counts and organ function) as well as the blood draws for research purposes. You will not have additional bone marrow collected for research purposes during the second course of study treatment, however, and bone marrow biopsies will be performed only as needed to check the status of your disease.

After your 12-month visit, you will begin long-term follow-up. This will consist of either an annual physical exam or a telephone call from a member of the study team to check on your health status.

Will you save my samples or research data to use in future research studies?

As part of this study, we are obtaining blood, bone marrow, and data from you. We would like to use this blood, bone marrow, and data for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding AML or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your blood, bone marrow, and data you give up any property rights you may have in the blood, bone marrow, and data.

Future research with your donated blood and bone marrow may include the study of genetic factors relating to AML. This future research may focus on one or more genes to study the differences in specific genes or small groups of genes in people who have AML when compared to people who do not have AML. Future research with your blood and bone marrow may also attempt to sequence large parts of your genome or even your entire genome. These types of sequencing provide detailed descriptions of your DNA and result in the creation of information that is as unique to you as your fingerprint.

We will share your blood, bone marrow, and data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at Washington University, at other research centers and institutions, or industry sponsors of research. We may also share your research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

If you change your mind and do not want us to store and use your blood, bone marrow, and data for future research you should contact the research team member identified at the top of this document. The blood, bone marrow, and data will no longer be used for research purposes. However, if some research with your blood, bone marrow, and data has already been completed, the information from that research may still be used. Also, if the blood, bone marrow, and data has been shared with other researchers it might not be possible to withdraw the blood, bone marrow, and data to the extent it has been shared.

Please place your initials in the blank next to Yes or No for each of the questions below:

My blood, bone marrow, and data may be stored and used for future research as described above.

_____ Yes _____ No
Initials Initials

My blood, bone marrow, and data may be shared with other researchers and used by these researchers for the future research as described above.

_____ Yes _____ No
Initials Initials

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 45 donor-recipient pairs (90 people total) will take part in this study conducted by study doctors at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for up to 4 years (including follow-up), although only the first 4 months will require intensive participation. The length of time for each visit will vary due to the unique characteristics of your health condition. During the DLI and CIML NK infusion period, you will be admitted to the hospital (inpatient). After those study treatments, you will remain admitted until your physician feels that you are able to safely return home. Your post-transplant visits may vary from 2 to 8 hours in length, depending on what procedures are being performed at each individual visit.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Some risks described in this consent document, if severe, may cause death.

Risks of Fludarabine

Likely

- Infection, especially when white blood cell count is low
- Vomiting
- Loss of appetite
- Tiredness
- Fever
- Pain
- Bruising, bleeding
- Cough
- Increased risk of unusual infections lasting more than 6 months

Less likely

- Anemia (low red blood cell count) and kidney problems which may cause tiredness, bruising, or swelling
- Nausea
- Chills
- Feeling of pins & needles in arms and legs
- Damage to organs which may cause tiredness, changes in thinking, or shortness of breath
- Confusion

Rare

- Kidney damage which may require dialysis

Risks of Cladribine

Likely

- Anemia which may require blood transfusions
- Infection, especially when white blood cell count is low
- Cold symptoms such as stuffy nose, sneezing, sore throat
- Nausea
- Fever
- Tiredness
- Headache

Less likely

- Heart failure which may cause shortness of breath, swelling of ankles, and tiredness
- Bruising, bleeding
- Damage to the liver, which may cause belly pain, bleeding
- Damage to Kidney, which may cause swelling, may require dialysis
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Reaction during or following infusion of the drug which may cause chills, low blood pressure
- A new cancer resulting from treatment of a prior cancer
- Severe skin rash with blisters and can involve inside of the mouth and other parts of the body
- Rash

Rare

- Damage to the brain which may cause tiredness, changes in thinking
- Prior viral infection that returns which may cause sores and pain
- Confusion

Risks of Cyclophosphamide

Likely

- Hair loss
- Skin changes, rash, change in nails
- Nausea/vomiting
- Diarrhea
- Loss of appetite
- Pain in belly
- Sores in mouth
- Infection, especially when white blood cell count is low
- Absence of menstrual period which may decrease the ability to have children
- Blood in urine

Less Likely

- Damage to the bone marrow (irreversible) which may cause infection and bleeding and which may require transfusions
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, and swelling of the face or throat
- Loss or absence of sperm which may lead to an inability to father children
- Stuffy nose
- Scarring of the lungs which may cause shortness of breath
- Fluid around the heart

Rare

- Severe skin rash with blisters and peeling which can involve the mouth and other parts of the body
- Damage to the heart or heart failure which may cause shortness of breath, swelling of ankles, cough, or tiredness
- A new cancer including cancer of the bone marrow (leukemia) caused by chemotherapy
- Swelling of the body including the brain which may cause dizziness or confusion

Risks of IL-2

Less Likely

- Fever and chills
- Skin rash
- Fatigue
- Low platelet count with increased risk of bleeding
- Nausea
- Vomiting
- Fluid retention and weight gain
- Hypothyroidism (underactive thyroid gland, which can cause weight gain, heart failure, and/or constipation)
- Infection
- Abnormal kidney function, which could indicate kidney damage resulting in the need for dialysis

- Abnormal liver function, which means the liver is not functioning properly, and can cause fatigue and yellowing of the skin and eyes

Rare

- Capillary leak syndrome (CLS) in combination with NK cell therapy (leaky blood vessels that can result in low blood pressure, breathing issues, heart problems, kidney problems and difficulties with thinking that can be severe enough to result in death).

Risks of G-CSF

Likely

- Nausea
- Vomiting
- Pain in bone

Less likely

- Anemia (low red blood cell count) which may cause tiredness or may require blood transfusions
- Damage to the lungs which may cause shortness of breath
- Internal bleeding which may cause coughing up blood
- Swelling or tenderness of vessels

Rare

- Rupture of the spleen leading to bleeding in the belly

Risks of donor lymphocyte infusion (DLI)

The side effects of donor lymphocyte infusions may include graft versus host disease (GVHD), as well as the development of low blood counts. GVHD is when the transplanted cells attack your own body. If you develop GVHD, you will be treated with steroids and other standard of care treatments for GVHD if necessary. If you develop low blood counts, you will be supported with blood transfusions, antibiotics and G-CSF (a growth factor for white blood cells) as necessary.

Altered immune function is common after bone marrow transplantation. You therefore have a significant risk of getting a variety of infections, including bacterial or fungal infections. Antibiotic or antifungal therapy will be given as medically indicated.

Participants who are not complete or mixed chimeras (not all blood and bone marrow cells are replaced with donor cells) are at risk of bone marrow failure (the bone marrow is unable to produce enough blood cells) after the infusion of donor lymphocytes. The bone marrow failure may be lethal if the bone marrow does not recover afterwards.

Risks of CIML NK Cell Infusion

Likely

- Fever
- Chills
- Headache

- Rash
- Muscle pain
- Vomiting
- Diarrhea
- Shortness of breath

Rare

- GVHD (more likely to happen with the DLI)

Risks of Central Line Placement

It is likely that you will experience bruising or discomfort at the insertion site, and there is a rare risk of lung collapse, deep vein thrombosis (serious blood clot), injury to an artery in your neck or chest, and abnormal heartbeat.

Risks of Blood Draw

Possible side effects from a blood draw include fainting, feeling dizzy, pain, swelling, bruising, or bleeding where the needle is inserted. There is also a slight possibility of infection where the needle is inserted.

Risks of Testing for Reportable Disease

If you decide to participate in this study, we will test you for HIV and hepatitis B and C. The results of the test could indicate that you have HIV or hepatitis B or C. If that happens, we will refer you to a doctor who specializes in treating HIV or hepatitis B and C. We will make every effort to keep your personal information confidential. However, we are required by law to report positive tests to the state of Missouri and/or local agencies. Becoming aware of a diagnosis of HIV or hepatitis B or C could have serious personal and/or social consequences, including difficulty obtaining health insurance or employment. For more information about the risks of HIV and hepatitis B and C testing, please talk to your study doctor.

Risks of Bone Marrow Aspirate and Biopsy

It is likely that you will experience discomfort or pain, redness, swelling, and bruising at the site of the needle insertion. It is less likely that you will experience bleeding from the site of the needle insertion. There is a rare chance (approximately less than 1/100) of developing a significant infection or bleeding from this procedure. An allergic reaction to the anesthetic may occur. A scar may form at the site of needle entry.

Risks of CT Scan or Chest X-Ray

If you are scheduled for a CT with contrast, the dye that is injected into a vein for the scan is usually well tolerated. Some people feel dizzy, queasy, or get a headache when given the dye or notice a cold feeling near the injection site. There is a rare chance of having an allergic reaction to the dye that very rarely can be serious or life threatening. You must tell your study doctor if you have had bad reactions to dyes before. There is also a rare chance that a CT scan may cause a malfunction of worn or implanted medical devices. If you have electronic medical devices implanted such as a pacemaker or a drug pump, please make sure you tell your study doctors and research team.

Risks of ECG
The risks can include skin irritation and a rash due to wearing and the removal of the electrodes. The electrodes only detect electrical impulses produced by the heart. No electricity passes through the body from the machine, and there is no danger of getting an electrical shock.

Risks of Echocardiogram
You should feel no pain with this test. You may experience discomfort from lying quietly for a long period of time.

Risks of MUGA Scan
Allergic reactions to the tracer are rare. Most of the tracer will be eliminated from your body within a day. You may have some pain or swelling where the tracer is injected into your vein.

Risks of Radiation Exposure
This research study involves radiation exposure from a single MUGA scan (if you have one instead of an echocardiogram) and a single CT scan or chest x-ray if you haven't had one within the last 90 days. Because the study allows some flexibility in the number of type of scanning procedures, we cannot give you an exact amount of the radiation exposure you will receive, but you will be exposed to more radiation than a person in the general population. Please be assured that modern scanners are designed and operated to keep your radiation exposure as low as possible. If you would like more information about radiation exposure, please see the "Radiation Fact Sheet" located at http://hrpo.wustl.edu or ask the research team for a copy.

Risks for Women Capable of Becoming Pregnant
If you are a woman capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You must use effective birth control methods and try not to become pregnant while participating in this study and for at least 100 days after your CIML NK cell infusion and at least one year after receiving cyclophosphamide. If you become pregnant, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. You must tell the study doctor if your birth control method fails while you are on the study. If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. All pregnancies will be followed to outcome. Please discuss with the research team how long you need to wait before becoming pregnant after completing the treatment or procedures on this study.

Risks of Radiation Exposure in Women Capable of Becoming Pregnant
You may not participate in this study if you are pregnant. If you are capable of becoming pregnant, we will perform a pregnancy test before exposing you to research-related radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

Risks for Sexually Active Males
If you are a sexually active male it is important that your partner not become pregnant during your participation in this study. There may be unknown risks to the unborn child or risks we did

not anticipate. You and your partner must agree to use birth control if you want to take part in this study and for at least 100 days after your CIML NK cell infusion and at least one year after receiving cyclophosphamide. If you believe or know that your partner has become pregnant during your participation in this study, please contact the research team member identified at the top of this document as soon as possible.

Risks of Genetic Research

There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans and employers with greater than 15 employees to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance or long term-care insurance.

Re-Identification from Genetic Sample

While the data developed for this study is being stored without traditional identifiers (stored only with coded ID numbers, no names), there may be ways of linking the genetic materials back to you. DNA does directly identify you, so it is possible that someone could compare information in our database with information from you in another database and be able to identify you.

Risk of Breach of Confidentiality

One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study. However, we hope that, in the future, other people might benefit from this study because it will help researchers learn more about how to maximize the benefits DLI by boosting its effectiveness with CIML NK cells in patients who have relapsed after allogeneic hematopoietic cell transplant.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your study doctor will discuss the other options that are available to you. Instead of being in this study, you could:

- Get treatment or care for your cancer without being in a study;
- Take part in another research study
- Get no treatment
- Get comfort care, also called palliative care, which helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer without treating the cancer directly

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

As part of this study you will receive tests and procedures that are similar to what you would receive during routine clinical care of your condition. Your health plan/insurance company will be billed for some or all of these costs, and you will be responsible for any co-pays and deductibles that are normally required by your health plan/insurance. Not all insurance plans cover the costs associated with being in a study. Even if they do, you may be responsible for

more out-of-pocket expenses, such as co-pays and deductibles, when there are more tests and procedures or more expensive tests and procedures involved in the study than if you were to receive routine clinical care outside the study.

If you wish to know whether there are more tests and procedures or more expensive tests and procedures in the study, you should ask your study doctor.

If you wish to know whether your insurance will pay, you should contact them directly, or speak with the study team about obtaining a financial pre-certification prior to enrolling in the study.

You will not have any additional costs for being in this research study.

WILL I BE PAID FOR PARTICIPATING?

You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?

WuGen and the National Cancer Institute, NCI are funding this research study. This means that Washington University is receiving payments from WuGen and the NCI to support the activities that are required to conduct the study. No one on the research team will receive direct payment or increase in salary from WuGen or the NCI for conducting this study.

Financial Disclosure: An investigator on this study has an ownership interest in WUGEN, which provides financial support for this research study. An investigator also has licensing/product development agreements or royalties for inventions/Investigational product. As a result, the investigator may benefit financially from a successful study. An investigator is also being paid by WUGEN for activities that are not part of the study. These activities may include, for instance, consulting, serving on advisory boards, or giving speeches. Additional steps have been taken to manage the potential conflict of interest that this financial arrangement may create. Please speak with your study doctor if you have questions about this.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator at (314) 454-8304 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

How will you keep my information confidential?

Other people such as those listed below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities

- The U.S. Food and Drug Administration
- Your primary care physician if a medical condition that needs urgent attention is discovered
- Public health agencies to complete public health reporting requirements.
- Siteman Cancer Center
- The National Cancer Institute, NCI
- The Quality Assurance and Safety Monitoring Committee, to monitor the conduct of this study
- Hospital or Washington University representatives to complete their responsibilities
- Information about your participation in this study may be documented in your health care records and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- Washington University's Institutional Review board (a committee that oversee the conduct of research involving human participants) and the Human Research Protection Office
- Advarra IRB **(**An Institutional Review Board has reviewed and approved this study).

Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed above.

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA and may further be shared without your permission.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- Your treatment or the care given by your health provider.
- Your insurance payment or enrollment in any health plans.

- Any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
    - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at http://hrpo.wustl.edu/participants//withdrawing-from-a-study/ or you may request that the investigator send you a copy of the letter.
        - **If you revoke your authorization:**
            - The research team may only use and share information already collected for the study.
            - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
            - You will not be allowed to continue to participate in the study.

Can we contact you by email or text message?

We would like to contact you by email or text message for the purposes listed below. Some of these emails may contain health information that identifies you.

- Patient education
- Prescription refills
- Appointment scheduling

Only the research team will have access to your email and text communications. We will only communicate in this method by email to send you the information listed above. If you have any questions or need to contact us for an urgent or emergent situation, please contact the research team member identified at the top of this document.

You should be aware that there are risks associated with sending your health information via email or text.

- Text messaging is not a secure communication method.
- There is always a risk that the message could be intercepted or sent to the wrong email address or phone number. To avoid sending messages to the wrong email address, the first email we send you will be this we will send a test message to ensure we have the correct email address or phone number.
- When using any computer you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.
- If you share a home computer or cell phone with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.
- Your employer will have access to any email communications sent or received on any electronic devices used for work or through a work server.

- If you lose your phone, others may be able to access the messages that we send.

Do you agree to allow us to send your health information via email?

_____ Yes _____ No
Initials Initials

Do you agree to allow us to send your health information via text?

_____ Yes _____ No
Initials Initials

myChart Required Language
If you have a MyChart account we may use this as a way to communicate with you about the treatment and/or medical care you are receiving as part of this study.

IS BEING IN THIS STUDY VOLUNTARY?
Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?
You may withdraw by telling the research team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under Withdrawing from a Research Study.

If you decide to leave the study early, we will ask you to tell the study doctor so any risks can be evaluated by your study doctor. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

Will I receive new information about the study while participating?
If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?
Under certain circumstances, the study doctor might decide to end your participation in this research study earlier than planned. This might happen for no reason or because staying in the study would be harmful, you need treatment that is not allowed while on the study, you fail to follow instructions, you become pregnant, you develop a major side effect, or the study is canceled.

WHOM TO CONTACT ABOUT THIS STUDY?

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a research participant;
- Eligibility to participate in the study;
- The study doctor's or study site's decision to withdraw you from participation;
- Results of tests and/or procedures;

Please contact the study doctor at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

- By **mail**:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00064866.

You may also contact the Human Research Protection Office at 660 South Euclid Avenue, Campus Box 8089, St. Louis, MO 63110, 1-(800)-438-0445, or email hrpo@wusm.wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

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 Form: Signatures

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Date
Conducting the Consent Discussion

FOR CHILDREN WHO BECOME ADULTS

I have been told that my parents/legal guardian agreed for me to participate in this research study as a minor. I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to continue to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date