Washington University in St. Louis



# INFORMED CONSENT DOCUMENT

**Project Title: A Phase 2 Trial Evaluating the Efficacy of Flotetuzumab for Relapsed Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome (MDS) Following Allogeneic Hematopoietic Cell Transplantation (allo-HCT)**

**Principal Investigator:** Matthew Christopher, MD, PhD

**Research Team Contact:** Matthew Christopher 314-454-7551

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.

## KEY INFORMATION

The first section of this document contains some key points that the research team thought you would find important. The research study is described in more detail after this section.

This is a research study conducted by Dr. Matthew Christopher looking at the effects, good and bad, of a drug called flotetuzumab when used to treat acute myeloid leukemia (AML) that has come back after treatment. You should carefully consider the information in this consent document and discuss it with the research team. Be sure you understand why you might want to participate, or why you might not want to participate. You may choose to participate or not.

If you agree and sign this consent, you will be volunteering to participate in the research study. All of the information below will be explained and is listed in more detail in the consent document below. The research team must give you a copy of this signed consent document.

**How will this study affect me?**

- The purpose of this study is to learn more about the safety and effectiveness of flotetuzumab in treating AML.
- As a voluntary participant, you will be asked to spend approximately 2 months receiving treatment and about 2 years being followed after treatment is finished. You will spend the first month of treatment in the hospital.
    - Before the first time you receive flotetuzumab, a tube for intravenous infusion known as a “central line” may be placed in a vein in your neck or chest. Having a central line will mean that you can get the drug many times without repeated needle sticks. The central line may also be used to draw blood samples.
    - During the first week, you will receive flotetuzumab in multiple doses that increase each day. Each dose will be given for approximately 24 hours until you reach the target dose.
    - Once you reach the target dose, you will continue to receive that dose every day for 4 weeks.
    - You will have a bone marrow biopsy at the end of the first cycle of treatment (Day 28), which will determine whether you receive a second cycle of treatment. If your bone marrow biopsy shows you are benefiting from the treatment, you will continue

flotetzumab. If your bone marrow biopsy shows you are having a partial benefit from the treatment, you may continue flotetzumab for Cycle 2 with permission of the study doctor, and you may also receive a standard treatment for AML, donor lymphocyte infusion. You can receive this donor lymphocyte infusion at either or both cycles. If your bone marrow biopsy shows that you are not receiving benefit from the study drug, you will discontinue flotetuzumab and receive standard treatment, which may include more chemotherapy or a donor lymphocyte infusion.
    - You will have daily blood draws while you are receiving treatment.
    - You will also have bone marrow biopsies at screening, on Day 14 of the first cycle (this biopsy may or may not be completed at the discretion of the Principal Investigator),Day 28 of the second cycle (if you receive a second cycle), and if you relapse again.
- You were selected because you are have AML that has recurred after previous treatment.
- The main risks to you are infusion-related reactions, including cytokine release syndrome. This is a temporary reaction that occurs during or after the infusion and involves a release of a large amount of proteins known as cytokines into the blood stream. This may cause fever, vomiting, rash, itching, muscle stiffness, chills, low blood pressure, difficulty breathing, increased heart rate and kidney damage. Other risks include swelling in the arms or legs, diarrhea, joing pain, fatigue, loss of appetite, and fever with low white blood cell count. More detail about risks is provided below.
- You will be not be paid for participating 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.
    - Macrogenics (the drug manufacturer) is providing flotetuzumab at no cost to you.
- If you withdraw from the study, the research team may continue to use information already collected about you in 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 acute myeloid leukemia (AML), which has recurred after treatment.

The purpose of this research study is to learn more about the safety and effectiveness of flotetuzumab in the treatment of patients with AML. Flotetuzumab is considered investigational, which means that it has

not been approved by the U.S. Food and Drug Administration.

## WHAT WILL HAPPEN DURING THIS STUDY?

All treatment will be given in either the outpatient or 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. There may also be a wide variability in the length of clinic visits. 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, measuring your height and weight, reviewing your medical history, and talking about any symptoms or health problems you're having
- Blood tests to check your blood counts and organ function (approximately 1 tablespoon of blood will be drawn from a vein in your arm)
- Blood will be drawn for a pregnancy test if you are a woman of childbearing potential (about ½ teaspoon of blood will be drawn from a vein in your arm)
- Blood will be drawn for research purposes. We will be using blood samples to test your immune cells at different points throughout the study, to see how you are responding to the treatment (approximately 1-2 tablespoons)
- Blood will be drawn (about 2 teaspoons of blood) to ensure you are not infected with hepatitis B or C, or HIV. If you have had these tests within the last 6 months, they may not need to be repeated. If you are determined to be positive for hepatitis B or C, or HIV, you will not be eligible for participation in the study. We will also refer you to another doctor in the Infectious Disease department to ensure you receive appropriate care for hepatitis or HIV.
- Bone marrow aspirate and biopsy specimen: These tests are used to tell whether leukemia is present. The doctor will use a long, thin needle to put medicine near the back of the hipbone to numb it.
    - In bone marrow aspiration, a thin needle and syringe is used to take out a small amount of liquid bone marrow. The sucking out of the marrow often hurts for a moment.
    - During a bone marrow biopsy, a small core of bone and marrow (about ½ inch long) is removed. After placing medicine to numb the area, the doctor will make a small cut in the skin in order to put in a wider needle. The needle is pushed into the bone with a twisting motion. Sometimes the needle going into the bone hurts, but it generally only lasts a short time.
- Electrocardiogram (ECG) test to see how your heart is working. You will be asked to lie flat and several small electrode pads (like stickers) will be placed on the body. This test takes about 10 minutes.
- An echocardiogram (sonogram of the heart) will also be performed. A hand-held wand will be placed on your chest to see moving images of your heart, while you are lying down. This test takes about 30 to 60 minutes.

- Pulmonary function tests (PFTs) to show how well your lungs are working. You will be asked to breathe in and out of a tube connected to a machine that measures the functions of your lungs.
- A sample of your cerebral spinal fluid (CSF) may be removed through a lumbar puncture, if the doctor needs to check your diagnosis. A lumbar puncture, also called a spinal tap, is done by inserting a needle through your lower back into your spine. You will receive pain medication during this procedure. The procedure will take approximately 1 hour, and you may need to rest afterwards.

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

**Procedures throughout the study:**
If you continue in the study, you will be admitted to the hospital for treatment with flotetzumab. You will need to remain in the hospital for at least one month, while you are receiving treatment. Flotetuzumab will be given by intravenous infusion, which means it will be delivered directly into your blood through a small plastic tube. Before the first time you receive flotetuzumab, a central line may be placed in a vein in your neck or chest.

Before the first time you receive flotetuzumab, you will be given medications and fluids to help prevent side effects. During the first week you will receive flotetuzumab in multiple doses that increase each day. Each dose will be given for approximately 24 hours until you reach 500 ng/kg/day.

Once you reach the 500 ng/kg/day dose, you will continue to receive that dose every day for up to two cycles or 8 weeks (one cycle is 4 weeks). You will have a bone marrow biopsy on Day 28 of Cycle 1, which will determine whether you should continue on to Cycle 2. If your bone marrow biopsy shows you are benefiting from the treatment and in remission from leukemia, you will continue flotetzumab for Cycle 2. If your bone marrow biopsy shows you are having a partial benefit from the treatment, you may continue flotetzumab for Cycle 2 with permission of the study doctor, and you may also receive a standard treatment for AML, donor lymphocyte infusion. You can receive this donor lymphocyte infusion at either or both cycles. If your bone marrow biopsy shows that you are not receiving benefit from the study drug, you will discontinue flotetuzumab and receive standard treatment, which may include more chemotherapy or a donor lymphocyte infusion. We will also continue to monitor your progress over the next 30 days.

You may take a break of up to two weeks in between Cycle 1 and Cycle 2. Note that if you take a break in between Cycle 1 and Cycle 2 of treatment with flotetuzumab, your dose will be increased each day during the first week of treatment, until you reach the target dose of 500 ng/kg/day.

While you are receiving study treatment and/or donor lymphocyte infusion, you will have the following tests and procedures:

- Daily, while you are in the hospital, you will have your vital signs (pulse, blood pressure, and temperature) checked. You will also have a physical exam and your weight, breathing, and oxygen saturation will be checked. You will be asked about any side effects or symptoms you might be having.

- Daily, while you are in the hospital, you will have blood tests to check your blood counts and organ function.
- Once a week, you will have blood tests to check your thyroid and liver function.
- Blood will be drawn for research purposes (to check your immune system) once a week.
- A bone marrow biopsy will be done on Cycle 1 Day 14 (this biopsy may or may not be collected and is up to the discretion of the Principal Investigator), Cycle 1 Day 28, and Cycle 2 Day 28.
- You will have an electrocardiogram (ECG) on Day 1 of Cycle 1 (before you begin treatment) and on Day 1 of Cycle 2.

Investigational drugs may interact with other drugs during this study. It is important to notify your physician of all drugs, including over the counter drugs, herbal supplements, and vitamins taken while you are participating in this study.

**At the end of treatment:**
When you have finished treatment with the study drugs, you will have the following procedures done:

- Physical exam
- Blood tests to check your blood counts and organ function
- Bone marrow biopsy
- Blood drawn for research purposes

**Follow-up procedures:**
Follow-up will take place every 6 months for up to 2 years after the end of treatment on the study. You will need to return to the clinic for routine post-transplant visits during the first 6 months. After the first 6 months, information about your health and well-being will be collected every 6 months, either through an in-person visit or phone call. The study team may also continue to access your medical record to check on your medical care and health.

**Genetic Research**
Genes are a unique combination of molecules (called DNA) that we inherit from our parents. There are millions of tiny differences in our genes. These differences may make us more or less likely to develop certain diseases or conditions or to have certain characteristics. Genetic research involves studying the differences in genes and DNA between individuals. This type of testing creates information that is as unique to you as your fingerprint.

As part of this study, we are obtaining blood and bone marrow tissue from you. These may be used for commercial profit (even if we remove your identifiable information.) There are no plans to provide financial compensation to you should this occur. By allowing us to use your blood and bone marrow tissue you give up any property rights you may have in the blood and bone marrow tissue.

**Will you save my research information and/or biospecimens to use in future research studies?**
As part of this study, we are obtaining data and samples (blood and bone marrow tissue) from you. We would like to use these data and samples for studies going on right now as well as studies that may be conducted in the future. Your data and samples may also be used for broad sharing throughout the research community. This means your data and samples may be used for any sort of research and not just research related to your current condition including research to develop investigational tests,

treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. These researchers may be at Washington University, at other research centers and institutions, or commercial sponsors of research. 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 for use of your data and samples. By allowing us to use your data and samples you give up any property rights you may have in the data and samples.

One way in which we may share your data with others is by putting it into a large database of information, called a data repository. If your data is placed in one of these repositories it will be placed in the "controlled-access" portion of the repository. This means that only qualified researchers, who have received permission from individuals that monitor the access to and use of the data, will be able to look at and use your information. Before we put it in this repository, we will remove any information, such as your name and birthdate, that might easily identify you. Even though these data will not have your name or other identifying information associated with it, it is still possible that someone may be able to trace these data back to you because genetic information is unique. Although your individual data will only be in the controlled access database certain summary information may be available to the general public.

This future research may include genetic research. Genes are a unique combination of molecules (called DNA) that we inherit from our parents. There are millions of tiny differences in our genes that determine things like our height or the color of our eyes. Some of these differences may make some people more or less likely to develop certain diseases or conditions or to have certain characteristics. The future genetic research may include looking at the difference in genes between different groups of people or it may include studying your entire DNA sequence. Studying your entire DNA sequence will provide a detailed description of your DNA and is sometimes called whole genome sequencing.

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

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

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

**_____ Yes** **_____ No**
**Initials** **Initials**

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

**_____ Yes** **_____ No**
**Initials** **Initials**

- Identifiers may be removed from your private information, including your data, blood, and bone marrow tissue and used for future research or shared with others. If this occurs, we will not ask you for additional consent.

## HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 30 people will take part in this study conducted by investigators 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 approximately 2 months, with 2 years of follow-up.

## 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 Flotetuzumab

The main side effect observed in 154 of 174 patients (88.5%) is:

- **Infusion-related reaction, including cytokine release syndrome (CRS).** This is a temporary reaction that occurs during or after the infusion and involves a release of a large amount of proteins known as cytokines into the blood stream. This may cause fever, vomiting, rash, itching, muscle stiffness, chills, low blood pressure, difficulty breathing, increased heart rate and kidney damage. This can be life threatening and in rare cases may cause death. You will be given medications before your infusions to help minimize the probability of this type of reaction. Majority of infusion-related reactions (including CRS) that happened in patients that received flotetuzumab were mild to moderate, 141/174 (81%), while 12/174 (7%) experienced severe reactions. One event was life-threatening and no event was considered fatal. If you experience an infusion-related reaction (including CRS) you will be given medications to treat the symptoms.

Additional side effects attributed to the administration of flotetuzumab observed in more than 1 in 10 patients (≥ 10%) include:

- Fever
- Nausea
- Peripheral edema (swelling in arms or legs)
- Diarrhea

- Arthralgia (joint pain)
- Fatigue
- Alanine aminotransferase increased and aspartate aminotransferase increased (abnormal liver tests)
- Loss of appetite
- Rash maculo-papular (skin rash)
- Myalgia (muscle pain)
- Low blood pressure
- Vomiting
- Difficulty breathing
- Febrile neutropenia (fever with low white blood cell counts)

These events, in addition to infusion-related reactions, were not experienced by all patients and all have been clinically manageable. Your study doctor will monitor you for side effects.

Patients in this study have experienced pericardial effusion which is a build-up of fluid in the tissue around the heart; in one patient this event was considered life threatening. Collection of fluid around the heart could cause a life-threatening condition where the heart is unable to pump correctly due to the external pressure. This may require medical intervention to drain the fluid and remove the pressure. Call your doctor immediately if you have any signs of shortness of breath, chest discomfort or fullness, or abnormally low blood pressure.

Patients have experienced respiratory events of dyspnea (shortness of breath), pulmonary edema (fluid in the lung that may be associated with difficulty breathing) and pleural effusion (collection of fluid around the lungs in the chest cavity which can cause shortness of breath and may require treatment). One patient experienced life-threatening dyspnea and subsequently expired from cardiac arrest. Additionally, one patient experienced severe event of pneumonitis (lung inflammation with possible difficulty in breathing). Call your doctor if you have difficulty breathing or worsening shortness of breath.

Patients have exhibited events of fast weight gain, drop in albumin (low levels of a blood protein) and build-up of fluid in the body or extremities causing swelling. These events could quickly become life-threatening and may require quick medical intervention. Call your doctor immediately if you have any of the following: fast weight gain, swelling of your face, arms, hands, legs, or feet, difficulty breathing or shortness of breath, low blood pressure.

Patients have experienced a type of herpes virus reactivation known as Epstein-Barr virus (EBV). Symptoms may include fever and fatigue. Rituximab (anti-CD20 antibody) is an effective treatment option in patients with EBV-reactivation.

Based on the studies of flotetuzumab in laboratory studies and in animals, and based on studies in humans with other, similar types of drugs, there is a chance that flotetuzumab will also cause these types of symptoms to happen:

- **Swelling** around your eyes and/or your face

- **Low levels of a blood protein called albumin**. This can cause swelling, weakness, and/or fatigue.
- **Tumor lysis syndrome (TLS)**. TLS is caused by the sudden, rapid death of cancer cells in response to treatment. When cancer cells die they may spill their inner contents, which build up faster than your body can get rid of them. This can change the balance of the chemistry of the body and cause severe nausea and vomiting, shortness of breath, an irregular heartbeat, kidney failure, urine abnormalities, severe fatigue and/or joint pain.
- **Infection**. Flotetuzumab may alter the normal levels of some of your immune cells, the cells in your body that fight infection, and may make it more likely for you to get an infection. It is possible that such infections could become severe or life-threatening and possibly fatal. Your doctor will monitor you carefully for signs of infection and you should report any signs of infections (for example, fever or chills) to your doctor immediately.
- **Immune-related side effects**. Flotetuzumab is designed to help your immune system target and kill cancerous cells. A possible side effect of flotetuzumab is that the changes in immune cells may result in your immune system also attacking other, healthy parts of your body. When your immune system attacks healthy parts of your body, you are considered to have an autoimmune disease. Autoimmunity can be directed against specific organs such as your lungs, colon, liver, thyroid, pituitary gland, joints, kidney, heart muscle, or organs that are hormone-responsive.
- **Neurotoxicity**. Neurotoxicity refers to problems with the brain or nervous system which may result in symptoms such as seizure, fainting, headaches, trouble sleeping, confusion or disorientation, dizziness, memory loss, trouble speaking, loss of balance, physical tremors, or changes in mood. Neurotoxicity has been reported with other drugs that work in a similar way to flotetuzumab. In the study so far, about one third of patients who received flotetuzumab had symptoms that may suggest neurotoxicity that were attributed to flotetuzumab, although most cases were mild to moderate in severity. The most common treatment related events seen in 5% or more of patients were headache and confusion. Severe events attributed to flotetuzumab included delirium (loss of contact with reality), mental status changes, confusion, aphasia (inability to speak), depressed level of consciousness (sleepiness), dizziness, fainting, encephalopathy (decreased brain function), and headache, and, to date, these have occurred in 7% of patients. Overall, these events have generally been of short duration and patients recovered fully, although some patients have experienced intermittent symptoms over an extended period of time. Your doctor will monitor you for symptoms of neurotoxicity.
- Due to the risk of possible neurotoxicity, you should not drive or operate heavy machinery while receiving flotetuzumab and for 30 days after you receive your last dose of flotetuzumab.

<u>Risks of Central Line Placement</u>

- Pain
- Bruising, bleeding
- Infection
- Blood clot

<u>Risks of Bone Marrow Aspirate/Biopsy</u>

Serious problems from a bone marrow aspiration or biopsy are not common. Side effects may include pain, infection of the test site (redness and feeling of warmth in the area) and bleeding or bruising at the test site. You may feel some tenderness for a week or more after your bone marrow aspirate/biopsy.

Risks of Electrocardiogram (ECG)
Placement of the leads may cause skin irritation, itching, redness, or burning of the skin at the sites where the leads were attached.

Risks of Blood Drawing
The blood draw may cause bleeding, bruising, or pain. Some people become dizzy or feel faint. There is also a rare risk of infection.

Risks of Lumbar Puncture

- Post-lumbar puncture headache. Up to 25 percent of people who have undergone a lumbar puncture develop a headache afterward due to a leak of fluid into nearby tissues.
- The headache typically starts several hours up to two days after the procedure and may be accompanied by nausea, vomiting and dizziness. The headaches are usually present when sitting or standing and resolve after lying down. Post-lumbar puncture headaches can last from a few hours to a week or more.
- Back discomfort or pain. You may feel pain or tenderness in your lower back after the procedure. The pain might radiate down the back of your legs.
- Bleeding. Bleeding may occur near the puncture site or, rarely, into the epidural space.
- Brainstem herniation. Increased pressure within the skull (intracranial), due to a brain tumor or other space-occupying lesion, can lead to compression of the brainstem after a sample of cerebrospinal fluid is removed. A computerized tomography (CT) scan or MRI prior to a lumbar puncture can be obtained to determine if there is evidence of a space-occupying lesion that results in increased intracranial pressure. This complication is rare.

Risks of Computed Tomography (CT) scan
*Rare:* Malfunction of worn or implanted electronic 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 staff. The CT scan may cause a malfunction of electronic medical devices.

CT scans will expose you to doses of radiation. There is a small risk of cancer from radiation exposure. A liquid contrast material may be injected into your vein before your CT scan. In rare cases, people have an allergic reaction to the contrast material. This reaction can be serious and life-threatening. Tell your study doctor if you are taking Glucophage or metformin before you have contrast material.

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 12 weeks after your last dose of treatment. 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 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. 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 you not impregnate anyone or donate sperm during your participation in this study, and for 12 weeks after your last dose of treatment. There may be unknown risks to the unborn child or risks we did not anticipate. If pregnancy is a possibility, you must agree to use birth control if you want to take part in this study. If you believe or know that you have impregnated anyone, donated sperm or otherwise fathered a child during your participation in this study, please contact the research team member identified at the top of the document as soon as possible.

Risks of Genetic Research

There may be information obtained from the genetic testing that indicates that you, or potentially a family member (since we inherit genes from our parents, and pass genes on to our children) are at risk for a particular disease or condition. For example, genetic sequencing may indicate that an individual is more prone to develop certain types of cancer or other types of diseases, (e.g. Alzheimer's or other inherited diseases).

If made available to persons or agencies outside of our research group, information about genetic test results could affect your employment or insurance. For instance, employers, insurers, or others may use this information when making decisions about you or your family members regarding employment, insurance, or other benefits.

Risk of 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. Because your DNA is unique to you, it is possible that someone could look at the information in the DNA database and compare it to information in another database, and use that to identify you. This is difficult to do and is very unlikely to happen.

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.

Risks of Testing for Reportable Diseases

If you decide to participate in this study, we will test you for hepatitis B or C, or HIV. The results of these tests could indicate that you have one of these conditions. If that happens, we will refer you to a doctor who specializes in treating your condition. We will make every effort to keep your personal information confidential. However, we are required by law to report certain positive tests to the state of Missouri and/or local agencies. The test results could also be reported to the Centers for Disease Control. You may be contacted by these agencies for more information. Becoming aware of a new diagnosis could have serious health, personal and/or social consequences. For more information about the risks of this testing, please talk to your study doctor.

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 we are trying to find better treatments for people with your disease.

## WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your 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 palliative care, also called comfort care.

Be sure to ask any questions you have about all of your options

## WHO IS FUNDING THIS STUDY?

MacroGenics, Inc., the manufacturer of flotetuzumab, and the National Institute of Health are funding this research study. This means that Washington University is receiving payments from MacroGenics, Inc. and the National Institute of Health to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from MacroGenics, Inc. or the National Institute of Health for conducting this study.

## 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, Matthew Christopher at 314-454-7551, 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 and MacroGenics, Inc. 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 indicated 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. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- MacroGenics, Inc.
- The National Institute of Health
- Your primary care physician if a medical condition that needs urgent attention is discovered
- Hospital or University representatives to complete Hospital or University 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.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.
- The Siteman Cancer Center Clinical Trials Office
- The Quality Assurance and Safety Monitoring Committee, to monitor the conduct of 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.

To help protect your confidentiality, we will make sure that your study information is kept secure. We will keep study information in a secure database that requires a username and password. To help protect your confidentiality, no identifying information such as your name, birth date, or social security number will be made available to researchers who receive your health information. Furthermore, the study team will keep the master code list that links your unique study number with your name and other identifying information in locked storage in a locked office (for paper copies) or on a secured network on a password-protected computer (for electronic copies). Access to either paper or electronic copies will be limited to the Principal Investigator and members of the study team.

The research team will send study results to MacroGenics, Inc. Information sent to MacroGenics, Inc. will be de-identified. The information will be used by MacroGenics, Inc. to learn more about the safety and side effects of flotetuzumab. In the future, MacroGenics, Inc. may continue to use your health information that is collected as part of this study. For example, MacroGenics, Inc. may combine

information from this study with the results of other studies to re-analyze the safety and effectiveness of the study drug**,** to evaluate other products or therapies, to develop a better understanding of a disease, or to improve the design of future research studies. MacroGenics, Inc. may also share information from the study with regulatory agencies in foreign countries.

If you receive Medicare benefits, are injured as part of your participation in this research study and medical treatment relating to this injury is paid by anyone other than you or your insurance company, that payer will need to collect personal information about you. This information includes your name, date of birth, gender, social security number, Medicare identification number and information related to this research study. The payer will report this information to the Centers for Medicare & Medicaid Services (CMS), the federal agency that oversees the Medicare program, during your participation in the study and for as long as the payer is required by CMS to report this information. If you do not want to release your personal or treatment related information you have the right to refuse reimbursement by the payer for any research injury. The payer will not use this information for any other purpose.

The Siteman Cancer Center at Washington University School of Medicine and Barnes-Jewish Hospital is supported by funding from the National Cancer Institute (NCI). To meet NCI requirements, your protected health information relating to your participation in this study (including your social security number) will be stored in a secure database at the Siteman Cancer Center. This database and also your health care records may be reviewed by Siteman Cancer Center personnel. All information will be securely and confidentially maintained.

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.

To further protect your privacy, this research is covered by a Certificate of Confidentiality from the federal government. This means that the researchers can refuse to disclose information that may identify you in any legal or court proceeding or to anyone who is not connected with the research except if:

- there is a law that requires disclosure, such as to report child abuse and neglect, or harm to self or others*;*
- you give permission to disclose your information, including as described in this consent form; or
- it is used for other scientific research allowed by federal law.

This Certificate may not be effective for information held in foreign countries.

You have the right to share your information or involvement in this study with anyone at any time. You may also give the research team permission to disclose your information to a third party or any other person not connected with the research.

If information about you or your involvement in this research is placed in your medical record the information may no longer be protected under the Certificate. However, information in your medical records is protected in other ways.

**Are there additional protections for my health information?**

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 under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

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 https://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?**
We would like to contact you by email for the purposes listed below. Some of these emails may contain health information that identifies you. We may want to email you to schedule appointments, check on your health, and send you reminders of upcoming visits.

Only the research team will have access to your email communications. We will only communicate 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.

- There is always a risk that the message could be intercepted or sent to the wrong email address. To avoid sending messages to the wrong email address, the first email we send you will be a test message to ensure we have the correct email address.
- 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 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.

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

**_____ Yes** **_____ No**
**Initials** **Initials**

**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 study 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 if you are thinking about stopping so any risks can be evaluated by your doctor. Another reason to tell your 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 investigator or MacroGenics, Inc., might decide to end your participation in this research study earlier than planned. This might happen for no reason or because in our judgment it would not be safe for you to continue, because your condition has become worse, because you are or became pregnant, because funding for the research study has ended, or because the sponsor has decided to stop the research.

**WHAT IF I HAVE QUESTIONS?**

We encourage you to ask questions. If you have any questions about the research study itself, please contact: **Dr. Matthew Christopher, at 314-454-7551.** If you experience a research-related injury, please contact: **Dr. Matthew Christopher, at 314-454-7551.** If you call after hours, you will be directed to the exchange number which will be covered by a nurse practitioner or fellow on call. Please tell this person that you are a research participant.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office 1-(800)-438-0445, or email hrpo@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.

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This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study.

As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

**Do not sign this form if today's date is after EXPIRATION DATE: 06/03/25.**

_____ _____

(Signature of Participant) (Date)

_____

(Participant's name – printed)

**Statement of Person Who Obtained Consent**

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)

_____

(Name of Person who Obtained Consent - printed)