Children's Hospital of Wisconsin

INTRODUCTION TO THE INFORMED CONSENT

Title of Study: Blinatumomab Bridging Therapy in High-Risk B-Acute Lymphoblastic Leukemia: A Phase 2 Study

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Name of Subject: _____ Date of Birth:_____

Subject: You are invited to take part in this research. This form tells you why this project is being done, what will happen in the project, possible risks and benefits to you, your choices, and other important information. If there is anything that you do not understand, please ask questions. Then you can decide if you want to join this project or not. If you are under the age of 18, your parent or guardian also needs to give their permission for you to join this project.

Parent/Guardian: Your child is invited to take part in this research. This form tells you why this project is being done, what will happen in the project, and possible risks and benefits to your child. If there is anything you do not understand, please ask questions. Then you can decide if you want your child to join this study or not. The word "you" in this form refers to your child.

Definitions

ALL	acute lymphoblastic leukemia
CHW	Children's Hospital of Wisconsin
HCT	hematopoietic cell transplantation
HTS	High throughput sequencing
IRB	Institutional Review Board
MRD	minimal residual disease

Purpose

This project is being done to to assess the effectiveness of Blinatumomab as a bridging therapy to lower MRD in high risk ALL patients prior to receiving an HCT.

Length

- You will be in this research project and receiving treatment for up to 3 months depending on if you need 1 or 2 cycles of blinatumomab.
- We would also like to follow you for an additional 30 days to so we can monitor your side effects.

Procedures

You will receive blinatumomab for one or two 28 day cycles. All visits below are standard of care.

List of visits:

- Screening Visit
- Cycle 1
  - Day 1
  - Weekly visits
- Cycle 2 (if applicable)
  - Day 1
  - Weekly visits
- End of treatment
- Follow up
  - Weekly visits for 30 days or until HCT

Procedures that will occur at various visits:

Invasive Procedures

- Drug administration, blood draws, bone marrow aspirate/biopsy, lumbar puncture

-

Non-invasive Procedures

- Full medical history exam, physical exam, echocardiogram, electrocardiogram, urine collection

All procedures mentioned above are standard of care.

Risks

This is a brief list of the most commonly seen side effects. The ***full consent form*** after this introduction contains a more complete list of potential research risks.

There may be risks of participating in this study that are currently unforeseen

Blinatumomab risks:

- Anemia which may require blood transfusion
- Diarrhea, nausea
- Tiredness, fever
- Bruising, bleeding
- Headache
- Tremors

Benefits

This project may or may not help you, but we hope the information from this project will help us remove your MRD prior to going on to HCT.

Participation in this study is voluntary. You do not have to join this project. Your other options may include:

- Joining a different project

My Other Options

- Routine care for this condition such as another combination of drugs before HCT.
- Getting no treatment for this condition

If you have more questions about this project at any time, you can call Michael Burke, MD at 414-955-4170.

If you have questions about your rights as a participant, want to report any problems or complaints, or offer input, you can call the CHW IRB Office at 414-337-7133.

CONSENT TO PARTICIPATE IN RESEARCH

INTRODUCTION – WHY ARE WE ASKING YOU TO PARTICIPATE?

Acute lymphoblastic leukemia (ALL) remains the most common form of leukemia diagnosed in children, as well as one of the most common hematological diseases for which allogeneic hematopoietic cell transplantation (HCT) is currently used. There is mounting evidence to support that for patients in remission, the presence of very small amounts of leukemia (known as minimal residual disease (MRD), identified immediately prior to HCT is associated with higher rates of ALL relapse following HCT.

We are asking if you want to participate in a research study of a treatment that might reduce pre-transplant disease burden by achieving a pre-transplant MRD negative state. The drug is called Blinatumomab. If successful, this drug could reduce your chance of relapse after HCT. You are being asked to take part in this research study for the following reasons:

- You have been diagnosed with high risk, persistent or relapsed acute lymphoblastic leukemia (ALL); and
- Your planned treatment involves receiving an allogeneic hematopoietic cell transplantation (HCT).

A total of about 35 people are expected to participate in this research at the following institutions

- Children's Wisconsin, Milwaukee, WI
- American Family children's Hospital, Madison, WI

The Director of the project is Michael Burke, MD in the Department of Pediatric Oncology, Hematology and Bone Marrow Transplant. A research team works with Dr. Burke. You can ask who these people are.

DO I HAVE TO PARTICIPATE?

You can decide whether to take part in this research or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this project, you do not have to stay in it. You may stop at any time.

A research project is different from routine medical care in three ways: 1) there are extra risks that we will tell you about in this form; 2) you may have some extra medical tests and visits; 3) the research procedures, tests and visits follow a set plan that must be kept.

WHY IS THIS PROJECT BEING DONE?

The purpose of this project is to assess the effectiveness of Blinatumomab as a bridging therapy to lower MRD in high risk ALL patients prior to receiving an HCT. We also want to learn if this treatment will prevent relapse and whether it will help high risk ALL patients with MRD prior to HCT to live longer.

Everyone in this study will receive Blinatumomab, which is approved by the U.S. Food and Drug Administration for use in patients with your condition. We don't know if this study will help you. Your condition may get better, but it could stay the same or even get worse. We hope the

information from this study will help us develop a better treatment for patients with MRD prior to HCT in the future.

This protocol is part of a planned two-phase treatment designed for patients who are moving onto treatment with HCT. The two-phase treatment consists of 2 separate protocols. This protocol is Part 1 in which treatment is designed to help the patient get into MRD negative status and then those patients will move onto the 2nd protocol, which is designed for patients who are in MRD negative status and are going to have treatment with HCT.

Your research team will discuss this Part 1 treatment with you along with the HCT treatment which will be offered as Part 2 of the two-phase treatment if you are able to achieve MRD negative status as discussed above.

WHAT WILL HAPPEN IF I PARTICIPATE?

Screening procedures:

If you decide to join the study, you will need to have the following exams, tests, or procedures to find out if you can be in the study. These exams, tests or 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.

- A medical history
- Physical exam including height and weight
- Vital signs (blood pressure, pulse, temperature)
- Blood tests to check blood counts, blood chemistries, prior viral exposure, and various organ functions
- Urine tests
- Echocardiogram/MUGA
- Electrocardiogram
- Pregnancy test (if you are a woman who could have children)
- Performance status (Karnofsky or Lansky)
- Bone marrow aspirate
- Lumbar puncture

Results of your blood test will be released only to authorized persons as governed by Wisconsin law. A list of persons to be notified and reasons that will cause release of your blood test is available upon request.

Please note that because of Wisconsin law and your child's age, the researchers may not be able to share your child's pregnancy test results with you during the study without your child's permission.

Summary of Procedures:

During the Study: If the exams, tests, and procedures show that you can be in the study, and you choose to take part; the administration of the study drugs will follow institutional drug and supportive care guidelines.

Treatment Plan: A treatment cycle lasts about 28 days with Blinatumomab given every day as a continuous infusion. Hospitalization is recommended for the first 3 days of Cycle 1 and the first 2 days of Cycle 2 (if needed).

The treatment is summarized in the following table:

Cycle	Day	How The Drug Will Be Given?
1	1-28	Continuous Blinatumomab infusion; pretreatment with prednisone or dexamethasone
1	29-42	14- day treatment free interval
2	1-28	Continuous Blinatumomab infusion
2	29-42	14- day treatment free interval

If you are ≥ 18 years of age, you will be pre-medicated with prednisone intravenously 1 hour prior to the first dose of blinatumomab in each cycle.

If you are <18 years of age, you will be pre-medicated with dexamethasone prior to the first dose of blinatumomab in Cycle 1 and when restarting an infusion after an interruption of 4 or more hours in the first cycle.

Prednisone or dexamethasone are given to prevent Cytokine release syndrome (CRS), which can be a side effect of blinatumomab.

Medical Tests During Treatment: While you are on study treatment the following standard medical tests will be done to monitor for response to therapy as well as side effects related to treatment. These include the following and may be done more frequently because you are in the study.

The following tests will be done weekly during each cycle:

- Physical exam
- Vital signs
- Performance status (Karnofsky or Lansky)
- Evaluation of side effects
- Blood tests to check blood counts, blood chemistries and various organ functions
- Urine tests

End of Treatment tests: at the end of the treatment cycle Day 28 +/- 2 days, a bone marrow aspirate and/or biopsy and lumbar puncture will be done to evaluate your disease status.

Tests on the Bone Marrow: Examinations of the bone marrow will be performed when you are screened for the study and at the end of each treatment cycle. You have already had many tests of your bone marrow for your previous treatment of ALL. Many children receive some form of sedation or anesthesia during this procedure. A small area over your hip bone on the back will be cleaned and numbed with lidocaine and/or with an anesthetic cream. The test is painful, especially when the bone marrow is withdrawn. There is also a small risk of bleeding or infection from this procedure. Approximately 2 teaspoons of bone marrow will be withdrawn through a needle inserted into the bone Your doctor will use your bone marrow sample to evaluate your disease status and test for MRD using flow cytometry and high throughput sequencing (HTS).

HTS technologies can sequence multiple DNA molecules in parallel, enabling hundreds of millions of DNA molecules to be sequenced at a time.

Follow up Visits: If you begin protocol therapy, you will be followed for safety monitoring until the start of a new therapy (i.e. transplant preparative regimen) or until Day 30, whichever occurs earlier. Your doctor will need to check to see how you are doing. The doctor will ask you how you feel, if you have trouble doing your daily routine, and what drugs you are taking. You will also have the following tests done:

- Physical examination
- Vital signs
- Performance status
- Evaluation of side effects
- Blood tests to check your organ function

If you go on to have a transplant as per Part 2 of the two-phase treatment, routine outcomes and health information will be collected as per the Part 2 protocol of this two-phase treatment plan.

HOW LONG WILL I BE IN THE PROJECT?

You will receive treatment for up to 3 months depending on if you need 1 or 2 cycles of Blinatumomab. After treatment, you will be followed for additional 30 days to so we can monitor your side effects.

If you have a transplant, you will be monitored as per the transplant protocol you are treated on.

CAN I STOP BEING IN THE PROJECT?

You are free to withdraw from the project at any time. If you leave, your regular medical care will not change. If you are thinking about leaving, please tell the research doctor.

You can stop taking part in the study at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular doctor first. They will help you stop safely.

The research doctor may take you out of this project at any time. This would happen if:

- They think it is in your best interest.
- You do not follow the project rules.
- The whole project is stopped.

If this happens, the research doctor will tell you.

WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE PROJECT?

There are risks to taking part in any research project. There is a risk that the treatment plan will not help your condition or may make it worse. There also may be problems (side effects) we do not know about yet, from Blinatumomab itself, or how it combines with other drugs you are taking. If we learn about new important side effects, we will tell you.

We watch everyone in the project for problems (side effects). **You need to tell the research doctor or a member of the research team immediately if you experience any problems, side effects, or changes in your health.** If you experience any neurologic symptoms, call Dr. Burke immediately at 414-955-4170. In an emergency, call 911.

RISKS OF BLINATUMOMAB

Blinatumomab may cause problems (side effects). Side effects may be mild or very serious. Some can last a long time or never go away.

Although blinatumomab is FDA approved, it may still cause side effects.

Do not drive, operate heavy machinery, or do other dangerous activities while you are receiving Blinatumomab because Blinatumomab can cause neurological symptoms, such as dizziness, seizures, and confusion.

Call your doctor or Dr. Burke, a member of the research team, or get emergency medical help right away if you develop any of the following symptoms:

- **Cytokine Release Syndrome (CRS) and Infusion Reactions.** Symptoms of CRS and infusion reactions may include:
  - Fever, vomiting, tiredness or weakness, chills, dizziness, face swelling, headache, wheezing or trouble breathing, low blood pressure, skin rash, and nausea
- **Neurological problems**
  - Seizures, loss of balance, difficulty in speaking or slurred speech, headache, loss of consciousness, difficulty with facial movements, hearing, vision, or swallowing, trouble sleeping, confusion and disorientation.
- **Infections**
  - Blinatumomab may cause life-threatening infections that may lead to death. Tell your healthcare provider right away if you develop any signs or symptoms of an infection.

As 02 June 2020 approximately 1389 people have received blinatumomab in research studies. Since it was first approved for sale in December 2014 through 02 June 2020, approximately 10,461 people have been prescribed blinatumomab (Blincyto®) for treatment.

Side effects related to drugs occur in people at different rates or frequencies. The following tables (drug monographs) provide details of the known and expected side effects associated with the drugs given in this therapy.

The side effects that other people have experienced so far with the drug are:

Known Risks and Side Effects Related to Blinatumomab Include Those Which Are:		
Very Common (In 100 people receiving blinatumomab, more than 10 and up to 100 people may have)	**Common** (In 100 people receiving blinatumomab, between 1 and 10 people may have)	**Uncommon** (In 1000 people receiving blinatumomab, between 1 and 10 people may have)
• Anemia (decreased red blood cells) which may require blood transfusion • Thrombocytopenia (decreased platelets, for clotting blood) • Leukopenia (decreased white blood cells) • Pyrexia (fever) • Infusion related reactions • Weight increased • Hypertension (high blood pressure) • Neutropenia (decreased neutrophils with fever • Increased hepatic enzymes (in the blood, which may be due to inflammation or damage to liver cells) • Tachycardia (rapid heart rate) • Edema (swelling of hands, legs, ankles, feet, face, or trunk) • Back pain • Bone pain • Headache • Insomnia (difficulty falling and/or staying asleep) • Cough • Rash • Hypotension (low blood pressure) • Infections in the blood	• Leukopenia, Lymphopenia (decreased types of white blood cells) • Leukocytosis (increased white blood cells) • Lymphadenopathy (swelling in lymph nodes) • Hyperbilirubinemia (high levels of bilirubin in the blood) • Decreased immunoglobulins (in the blood, proteins made by the body's immune system to fight against infections and foreign substances) • Increased alkaline phosphatase (in the blood can be due problems in your liver or in your bones) • Chills • Chest pain • Pain in the arms, legs and hands • Overdose, Accidental overdose • Weight increased • Hypertension (high blood pressure) • Flushing • Dyspnea (difficulty breathing, wheezing or respiratory failure) • Hypersensitivity, allergic reactions to blinatumomab, including hypersensitivity, have been reported. Signs and symptoms of allergic reactions can be very similar	• Speech disorder • Cytokine storm, is a severe form of cytokine release syndrome which is described under the "Very Common" column. • Pancreatitis, inflammation of the pancreas that can be life-threatening or may even lead to death. Symptoms can include severe and persistent stomach pain, with or without nausea and vomiting. • Leukoencephalopathy, a rare, serious disorder of the white matter in the brain that can lead to severe disability and death and for which there is no known prevention, treatment, or cure. Symptoms can include difficulty thinking, loss of balance, changes in speech or walking, weakness on one side of your body, or blurred or lost vision. • Capillary leak syndrome (leakage of fluid from small blood vessels into other

Known Risks and Side Effects Related to Blinatumomab Include Those Which Are:		
Very Common (In 100 people receiving blinatumomab, more than 10 and up to 100 people may have)	**Common** (In 100 people receiving blinatumomab, between 1 and 10 people may have)	**Uncommon** (In 1000 people receiving blinatumomab, between 1 and 10 people may have)
including bacteria, fungi, viruses or infections in other organs. Serious infections can happen during and after treatment and can lead to death. Serious infections such as sepsis (infection in the bloodstream), and pneumonia (severe lung infection) have been reported in patients treated with blinatumomab. Your doctor may give you antibiotics to treat the infection or stop your treatment with blinatumomab • Infusion related reactions occur during or after the drug is given through the vein. Symptoms of infusion reaction may include headache, rash, itching, flushing, swelling, shortness of breath, nausea and sometimes vomiting. Severe infusion reactions can cause dizziness, severe skin reactions, difficulty breathing or swallowing, a decrease in blood pressure, and could be life	to infusion reaction. If you have symptoms of an allergic reaction, you should contact the study doctor or his/her study staff immediately. • Hematophagocytic histiocytosis can occur with cytokine release syndrome, described under the "Very Common" column. It is a life- threatening overactivity of your immune system caused by releasing large amounts of inflammatory cytokines. Your doctor may give you medications such as steroids and/or other medications to prevent or treat cytokine release syndrome. • Tumor lysis syndrome (a group of complications from release of large amounts of potassium, phosphate, and nucleic acid caused by the breakdown of tumor cells after cancer treatment). Tumor lysis syndrome may cause kidney failure, abnormal heart rhythm, and can even lead to death. Patients with moderate kidney failure showed an increased rate of tumor lysis syndrome compared with patients with mild kidney failure or normal kidney function. However, this did not lead to permanent discontinuation of treatment with blinatumomab. Your	body spaces that could cause swelling of the trunk, arms and legs)

Known Risks and Side Effects Related to Blinatumomab Include Those Which Are:		
Very Common (In 100 people receiving blinatumomab, more than 10 and up to 100 people may have)	**Common** (In 100 people receiving blinatumomab, between 1 and 10 people may have)	**Uncommon** (In 1000 people receiving blinatumomab, between 1 and 10 people may have)
threatening. Signs and symptoms of infusion reaction can be very similar to cytokine release syndrome. • Cytokine release syndrome is when your body releases substances called cytokines during the blinatumomab infusion. This can cause fever, chills, headache, decreased blood pressure, increased liver enzymes, nausea, and vomiting. Cytokine release syndrome symptoms generally are mild to moderate but occasionally can be serious or life-threatening or may even lead to death. Your doctor may give you medications such as steroids and/or other medications to prevent or treat cytokine release syndrome.	doctor may give you medicines before your treatment to help prevent tumor lysis syndrome. • Nervous system problems such as tremor (shaking), dizziness, seizures, somnolence (changes in alertness), paresthesia (abnormal skin sensation such as burning, prickling, tingling), hypoaesthesia (numbness), aphasia (difficulty speaking or slurred speech), cognitive disorder (difficulty understanding words), encephalopathy (loss of consciousness, brain malfunction), memory impairment (memory loss), confusion and/or disorientation, or loss of balance. These nervous system problems can be serious, or life-threatening or may even lead to death. Patients with a medical history of neurologic signs and symptoms had a higher rate of neurologic events (such as tremor, dizziness, confusion, encephalopathy and poor coordination). Your doctor will be closely monitoring you and may give you medications such as steroids and/or other medications to treat nervous system problems or stop your	

Known Risks and Side Effects Related to Blinatumomab Include Those Which Are:		
Very Common (In 100 people receiving blinatumomab, more than 10 and up to 100 people may have)	**Common** (In 100 people receiving blinatumomab, between 1 and 10 people may have)	**Uncommon** (In 1000 people receiving blinatumomab, between 1 and 10 people may have)
	treatment with blinatumomab.	

Relapse of CD19 negative B-precursor ALL and lineage switch from ALL to AML have been observed in patients with ALL, during or following blinatumomab treatment, in clinical trials and the postmarketing setting.

Side effects in children and adolescents were similar to adults, except for the following common side effects that occurred more than 10% more frequently in children and adolescent patients:

Very Common side effects (which may affect more than 1 person in 10):

- **Anaemia** (decreased red blood cells)
- **Thrombocytopenia** (decreased platelets, for clotting blood)
- **Leukopenia** (decreased white blood cells)
- **Pyrexia** (fever)
- **Infusion related reactions**
- **Weight increased**
- **Hypertension** (high blood pressure)

After you start taking blinatumomab, it is possible that your body may make antibodies (proteins that may stop blinatumomab from working or may cause side effects). In clinical studies of patients treated with blinatumomab, less than 2% tested positive for anti-blinatumomab antibodies. Anti-blinatumomab antibody formation may affect the pharmacokinetics (how much blinatumomab is in your body). Blood tests will be used to check for antibodies during the study.

Tell your doctor if you think you may need any vaccinations in the near future, including those needed to travel to other countries. Some vaccines must not be given within 2 weeks before, at the same time as, or in the months after you receive treatment with blinatumomab. Your doctor will check if you should have the vaccination.

Tell the study doctor or the study staff about any drugs you are taking, have recently taken, or are planning to take, including herbal remedies, supplements, and drugs you take without a prescription. The side effects of using blinatumomab in combination with other drugs are unknown at this time. Please discuss any concerns you may have with the study doctor.

What are the risks associated with the device used to give blinatumomab during this study?

If you agree to participate in this study, you will be required to use an infusion pump to infuse blinatumomab into the blood stream.

While not expected to occur, it is possible that the infusion pump will not work properly during the infusion. If this occurs, it is possible that you could receive an incomplete dose, an overdose or even no dose at all of blinatumomab. Contact your study doctor immediately if you believe that your infusion pump did not work properly during the infusion.

RISKS of DEXAMETHASONE

Possible Side Effects of Dexamethasone
COMMON, SOME MAY BE SERIOUS In 100 people receiving dexamethasone, more than 20 and up to 100 may have:
• High blood pressure which may cause headaches, dizziness • Skin changes, rash, acne • Swelling of the body, tiredness, bruising • In children and adolescents: decreased height • Pain in belly • Infection • Damage to the bone which may cause joint pain or loss of motion • Difficulty sleeping • Mood swings • Diabetes • Increased appetite and weight gain in belly, face, back and shoulders • Loss of bone tissue

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving dexamethasone, from 4 to 20 may have:
• Blood clot which may cause swelling, pain, shortness of breath • Glaucoma • Cloudiness of the eye, visual disturbances, blurred vision • A tear or a hole in the bowels which may cause pain or that may require surgery • Numbness and tingling of the arms, legs and upper body • Muscle weakness • Non-healing wound • Heartburn • Kidney stones

RARE, AND SERIOUS In 100 people receiving dexamethasone, 3 or fewer may have:
• Bleeding from sores in stomach • Broken bones

OTHER RISKS OF THIS RESEARCH PROJECT

All procedures discussed below are considered standard of care. You would have these procedures done even if you decide not to join the study.

Other procedures that are part of the research also involve some risks:

Risks of Blood Drawing
Risks associated with drawing blood are slight, but some risks include: pain, excessive bleeding, and bruising around the needle stick site, fainting or feeling lightheaded, infection (a slight risk any time the skin is broken), and multiple punctures to locate veins. If you do not have an indwelling venous catheter (i.e. an IV), a topical anesthetic cream (numbing cream/lotion) can be used to decrease the discomfort of blood drawing. The procedure will be performed with sterile preparation (clean the skin with alcohol or iodine wipes) at the site of the blood draw and a bandaid will be applied at this site to prevent any additional bleeding.

Bone Marrow Examination Risks
The test may be painful. There is also a small risk of infection or bleeding. The pain normally lessens within minutes to hours.

Confidentiality
Another risk may be loss of confidentiality. Every effort will be made to keep your research records confidential, but we cannot guarantee it. Depending on the kind of information being collected, if your research information were accidentally seen, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the project director about whether this could apply to you.

The researcher is required by law to report child abuse or neglect (or suspicion of abuse or neglect) if you mention it to the researcher or if it is suspected.

REPRODUCTIVE RISKS

Risks to women who could become pregnant
The drug in this project might affect a baby, before or after the baby is born. We do not know if the drug causes harm to a baby, so we do not want anyone who might be pregnant to enter the project. You should not become pregnant or nurse a baby while in this project. You must tell the research doctor right away if you think you are pregnant. You will be asked to have a pregnancy test to be sure you are not pregnant at the start of the project.

If you become pregnant during the project, you will be dropped from participation for safety reasons. If you become pregnant while you are taking this drug or within 30 days after you have stopped taking it, we ask that you inform the research doctor immediately. The research doctor will ask you for written permission to obtain information from you or your obstetrician on your pregnancy and the health of the baby.

Risks of fathering a child
You should not father a baby while taking part in this project because it is unknown if drug could affect a baby. If your partner is able to become pregnant, one or both of you must use some form of effective birth control. You must tell the research doctor right away if you think your partner is pregnant.

If you think that you have fathered a baby while you are taking this drug or within 30 days after you have stopped taking it, we ask that you inform the research doctor immediately. At that time, the research doctor will ask permission of your partner for the use and disclosure of her health information regarding the pregnancy. She will be asked to sign a separate consent form. She can choose to do this or not. She will be asked to sign this form to allow your research doctor to contact her obstetrician to collect information on the progress of the pregnancy and its outcome. The research doctor will make this information available to the sponsor for safety monitoring.

Birth control methods for all subjects
Check with the research doctor about the birth control methods needed for this project and how long to use them. Some methods might not be good enough for this project. If you are having sex that could lead to pregnancy, you should use birth control while you are in this project. This may include:

- Not having vaginal sex (abstinence)
- Taking birth control pills orally
- Having birth control shots or patches such as Depo-Provera
- Surgical sterilization (hysterectomy or tubal ligation)
- Use of an intrauterine device (IUD)
- Use of diaphragm with contraceptive jelly
- Use of condoms with contraceptive foam
- Use of diaphragm with condoms ("double barrier")

You should continue using birth control for 1 month after stopping blinatumomab.

ARE THERE ANY BENEFITS TO TAKING PART IN THE PROJECT?

We don't know if this study will help you. Your condition may get better but it could stay the same or even get worse. We hope the information from this study will help us remove MRD prior to going on to HCT but this is not guaranteed. Your cancer may not have any response to the therapy received while participating in this study.

ARE THERE ANY COSTS TO BEING IN THE PROJECT?

Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment. Some third-party payers (insurance companies, HMOs, etc.) may not pay for hospitalization, treatments or procedures which are determined to be experimental or research related. The study has no plans to pay for medical treatment.

The health care costs during your participation in this study that are considered part of the standard treatment of your disease will be billed to your insurance or other third-party payer. This includes blood tests, hospitalizations, procedures that will be done, and medications. All costs not paid by your insurance will be your financial responsibility. Please ask about any expected added costs or insurance problems. Financial Counselors are available to discuss insurance, costs, and other issues.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at *http://www.cancer.gov/clinicaltrials/learningabout.* You can print a copy of the Clinical Trials and Insurance Coverage information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy of Clinical Trials and Insurance Coverage.

If you participate in this research, the costs of any necessary emergency medical treatment in the event of a research-related injury may be billed to you or your health insurance.

WILL I BE PAID FOR PARTICIPATING IN THE PROJECT?

There are no plans for you to receive payment for participating in this study.

WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this project. You are free to say yes or no. If you do not join this project, your research doctor can discuss other healthcare choices with you.

Most treatment plans have used drugs similar to those used in this protocol, although these drugs may be given in different combinations, and at different times. You can receive other combinations of chemotherapy without participating in this study.

As an alternative to this study, you may decide you do not want additional treatment for your relapsed leukemia. You will always receive medicines to help you feel more comfortable and deal with problems caused by your cancer or treatment whether you participate in this study or not.

Talk to your doctor about your choices before you decide if you will take part in this study.

The research doctor can explain both the possible benefits and the risks of other options that are available to you.

WILL I BE GIVEN NEW INFORMATION ABOUT THE PROJECT?

If we learn any important new information about the drug that might change your mind about being in the project, we will tell you about it right away. You can then decide if you want to stay in the project.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE PROJECT?

Emergency medical treatment for injuries caused by your participation in this research project will be arranged for you. You or your health insurance may be billed for the costs of this

emergency treatment. If your research-related injury requires medical care beyond this emergency treatment, you or your insurer may be responsible for the costs of this follow-up care.

At this time, there is no plan for any additional financial payments.

If you think that you have become ill or were harmed because of this study, let the study doctors know right away by calling the Principal Investigator or your doctor.

WHO CAN ANSWER MY QUESTIONS ABOUT THE PROJECT?

- If you have more questions about this project at any time, you can call Michael Burke, MD at 414-955-4170.
- If you have questions about your rights as a research participant, want to report any problems or complaints, or offer input, you can call the CHW IRB office at 414-337-7133.
- If you believe that you have been injured because of your participation in this project, contact the research doctors right away. Contact information: Michael Burke, MD, 414-955-4170

Nothing in this consent form affects any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

What health information will be collected and used for this study?

To be in this research project, the study team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the study. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the project.

The health information to be collected and used for this project is:

- Past and present treatment as an inpatient or as an outpatient in a clinic or physician office setting.
- The history and diagnosis of your disease.
- Other medical conditions that may affect your treatment.
- Laboratory, radiology and pathology test results
- Personal information such as race, gender, ethnicity, etc.

Who will see the health information collected for this project?

The only CHW/MCW employees allowed to handle your health information are those on the research team, those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

If the costs of any necessary emergency medical treatment in the event of a research-related injury are billed to your health insurance, your health information may need to be disclosed to the insurer for billing purposes.

Because this project involves the use of drugs and/or devices, the FDA also has the right to inspect all study records.

We may record your research information, including results of tests and procedures done for research, in your Children's Hospital of Wisconsin medical record. As a result, this research information may be seen by people allowed to see your medical records for healthcare operations or treatment, by those you allow to see your medical records by giving written permission, and by others when required by law.

A copy of this signed consent/assent and HIPAA authorization will be placed in your Children's Hospital medical record

We will not use your personal health information for a different project without your permission or the permission of the Institutional Review Board (IRB).

Your information and/or biospecimens will not be used or distributed for future research studies even if personal identifiers are removed.

What are the risks of sharing this health information?

One risk of taking part in a research project is that more people will handle your personal health information collected for this project. The research team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the research doctor about whether this could apply to you.

How long will you keep the health information for this project?

If you sign this form, we plan to keep your information until the research study ends in case we need to check it again for this project.

Can I cancel my permission to share this health information?

If you change your mind later and do not want us to collect or share your health information, you need to send a letter to Michael Burke, MD at 8701 Watertown Plank Rd MFRC 3018 Milwaukee, WI 53226. The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we may decide that you cannot continue to be part of the project. We may still use the information we have already collected.

FOR MORE INFORMATION ABOUT THE PROJECT

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.

You can look up this project by referring to the ClinicalTrials.gov number NCT04556084 or by asking the research team for a printed copy.

CONSENT/ASSENT TO PARTICIPATE

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document,
  All of my questions have been answered to my satisfaction.
- The project's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the research team use and share the health information and other information gathered for this project.
- I voluntarily agree to participate in this research project. I agree to follow the procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

You will be asked when you turn 18 years old if you would like to continue to participate in this study. If you do you will need to sign a new form.

Consent of Adult Subject (18 years or older)		
Subject's Name *please print*	**Subject's Signature**	**Date**

Assent of Minor Subject (17 years old or younger)		
Name of Minor Subject *please print*	**Signature of Minor Subject**	**Date**
If child's assent is **not** obtained above, please indicate reason below (check one): ☐Assent is documented on a separate IRB-approved assent form ☐ Child is under the required age range for assent ☐The IRB granted a waiver of assent, please specify:_____		

Consent of Parent(s)/Guardian(s) of Minor Subject		
Name of Parent/Guardian *please print*	**Signature of Parent/Guardian**	**Date**
Name of Parent/Guardian *please print*	**Signature of Parent/Guardian**	**Date**

Permission of the second parent not obtained because (*select all that apply*):

☐Not required by the IRB (Risk Level 46.404 or 46.405)
☐Other parent is deceased
☐Other parent is unknown
☐Other parent is not reasonably available: Specify

_____

☐Only one parent has legal responsibility for the care and custody of subject.

Name of Legally Authorized Representative (if applicable) *please print*	**Signature of Legally Authorized Representative**	**Date**
Name of Witness (if applicable**)** *please print* (for short form consent process, or consent of blind or illiterate subject)	**Signature of Witness**	**Date**

Name of Principal Investigator OR person* discussing/ obtaining consent *please print*	**Signature of Principal Investigator OR person* discussing/obtaining consent**	**Date**

** A member of the research team trained and authorized by the Principal Investigator to act on her/his behalf in obtaining informed consent according to the protocol. The Principal Investigator is responsible and accountable for the research project.*