THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Phase II Study of Blinatumomab in Patients with B-cell Lineage Acute Lymphocytic Leukemia with Positive Minimal Residual Disease 2014-0844

Subtitle: Supporter: Amgen

Study Chair: Elias Jabbour

_____ _____
Participant's Name Medical Record Number

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

STUDY SUMMARY

The goal of this clinical research study is to learn if Blinacyto (blinatumomab) can help to control ALL with positive MRD. The safety of this drug will also be studied.

This is an investigational study. Blinatumomab is FDA approved and commercially available for the treatment of ALL. It is considered investigational to use blinatumomab to treat ALL patients with MRD. The study doctor can explain how the study drug is designed to work.

The study drug may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, hospitalization, potential expenses, the availability of other standard treatment options, and prolonged stay out of town/time commitment.

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

The study drug may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Blinatumomab will be provided at no cost to you while you are on study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Visit

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

Within 21 days before the start of the study:

- You will have a bone marrow biopsy and/or aspiration performed to check the status of the disease. To collect a bone marrow biopsy/aspiration, an area of the hip or other site is numbed with anesthetic, and a small amount of bone marrow and/or bone is withdrawn through a large needle.
- You will have a lumbar puncture (spinal tap) to check the status of the disease. A spinal tap is when fluid surrounding the spinal cord is removed by inserting a needle into the lower back. The affected area is numbed with local anesthetic during the procedure.

Within 14 days before the start of the study:

- You will have a physical exam, including a neurological exam (tests to check the functioning of your nerves, including tests of your balance and reflexes).
- Blood (about 2-3 tablespoons) will be drawn for routine tests.
- If the doctor thinks it is needed, you will have a positron emission tomography-computed tomography (PET-CT) scan or x-ray of your body to check the status of the disease.
- If you can become pregnant, blood (about 1 teaspoon) or urine will be collected for a pregnancy test. To take part in this study, you must not be pregnant.

If some of these tests have been done recently, they may not need to be repeated. The study staff will discuss this possibility with you.

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

Up to 40 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration
Each study cycle is 6 weeks.

If you are found to be eligible to take part in this study, you will receive blinatumomab by a central venous catheter (CVC) continuously for Weeks 1-4 of each cycle. A CVC is a sterile flexible tube that will be placed into a large vein while you are under local anesthesia. Your doctor will explain this to you in more detail, and you will be required to sign a separate consent form for this procedure.

Blinatumomab will be delivered by a small pump, which you will carry with you for the whole time you receive the drug. You will be given a shoulder or belt bag to hold the pump and infusion bag. You will be able to wear regular clothes, walk around, and perform daily living activities. You will be given instructions for taking a shower and other activities. There will be some things that you should not do, such as go swimming. The study staff will give you more information on activities you should not do while receiving the drug.
Depending on the availability of the infusion bags, you will need to come to MD Anderson to have the infusion bags changed either every 48 hours or 7 days. The study staff will let you know when you need to return to the clinic.
You will receive dexamethasone by vein over 30 minutes within 1 hour before the start of each treatment cycle and at the time of any increase in dose to prevent side effects associated with blinatumomab treatment. If side effects do occur, you will receive dexamethasone by mouth or by vein for 3 to 7 days.

If you have severe side effects, your study doctor may decide to stop treatment permanently or temporarily. If you recover or if the symptoms have improved, the treatment may be continued. If the doctor thinks it is needed, you will have a magnetic resonance imaging (MRI) before you restart treatment.

Length of Study
You may receive blinatumomab for up to 5 cycles of induction and consolidation therapy, and then 1 cycle every 3 months for up to 4 cycles during maintenance therapy. You will no longer be able to take the study drug if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

You participation on this study will be over after you have completed follow-up.

Study Visits

At the **beginning of every cycle**, you will have a physical exam.

One (1) time each week during Cycles 1-5 and before each cycle during maintenance therapy, blood (about 2-3 teaspoons) will be drawn for routine tests.

O**n Day 42 of Cycle 1 and then every cycle that you receive blinatumomab until the doctor no longer thinks it is needed and then every 2-3 cycles after that,** you will have a bone marrow biopsy and/or aspiration to check the status of disease.

Follow-Up
After the last dose of study drugs, you will be called by the study staff every 6 months and asked about your health periodically. The phone call should last about 10 minutes.

Other Instructions
While taking part in this study, you should not take part in any other research study without checking with the study doctors of each study.

It is very important that you tell your study doctor what prescription and non-prescription drugs, vitamins, nutritional, and herbal supplements you are taking. The study doctor will review these drugs with you before you start the study.

You should not drive or engage in hazardous occupations or activities such as operating heavy or potentially dangerous machinery while you are receiving blinatumomab due to the risk of loss of consciousness and/or seizures.

2. POSSIBLE RISKS

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

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drug/procedures.

Blinatumomab Side Effects

Common (occurring in more than 20% of patients)

• swelling (arms/legs) • nervous system damage (possible seizures) • headache • fever • skin rash	• abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure)	• nausea • infection

Blinatumomab may cause low white blood cell counts:

- A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Occasional (occurring in 3-20% of patients)

• chest pain • fast heartbeat • low blood pressure (possible dizziness/fainting) • high blood pressure • fatigue • chills • difficulty sleeping • dizziness • confusion • inability to speak • abnormal sensation (such as pins and needles) • high blood sugar (possible diabetes)	• decrease in antibodies that fight infections and viruses (possible frequent infections, diarrhea, failure to thrive, and inability to process food) • weight gain • constipation • diarrhea • abdominal pain • vomiting • loss of appetite • abnormal liver test (possible liver damage or yellowing of the eyes/skin)	• tremors • pain • cough • difficulty breathing • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Blinatumomab may cause cytokine release syndrome. This involves a release of a large amount of proteins into the blood stream. This may cause changes in blood pressure and heartbeat, flu-like symptoms (nausea, fever, and chills), and/or affect your lung/liver/kidney function. It may also cause certain brain-related symptoms, such as dizziness, weakness, confusion, difficulty speaking, and/or decreased brain function (possible paralysis and/or coma).

Blinatumomab may cause low blood cell counts (red blood cells and/or platelets):

- A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.
- A low platelet count increases your risk of bleeding (such as nosebleeds, bruising, stroke, and/or digestive system bleeding). You may need a platelet transfusion.

Rare but serious (occurring in fewer than 3% of patients)

• seizures • decreased brain function (possible paralysis and/or coma) • memory loss • mental status change (such as memory loss and impaired thinking)	• loss of consciousness • difficulty speaking and understanding words • increase in infection-fighting cells • difficulty breathing due to narrowing of the airways	• leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing) • allergic reaction • cytokine storm (possible fever and/or low blood pressure)

Other Risks

Having **bone marrow biopsies and/or aspirations** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site. An allergic reaction to the anesthetic may occur. A scar may form at the site.

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

Spinal taps may cause headaches, sensitivity of the eyes to light, nausea, vomiting, confusion, drowsiness and/or pain at the injection site. They may cause fever, infection, and/or bleeding. Spinal taps may cause inflammation/bleeding around the brain and/or the covering of the spinal cord, which can lead to nerve damage. In rare instances, spinal taps may cause seizures, leakage of spinal fluid, and/or blockage of spinal fluid, which can lead to brain swelling. Severe infections of the spinal fluid or bleeding within the brain can result in coma and/or death. Repeated spinal taps may result in learning or memory difficulties.

This study may involve unpredictable risks to the participants.

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

Birth Control Specifications: If you can become pregnant or father a child, you must use acceptable birth control methods while on study, such as birth control pills or injections, intrauterine devices (IUDs), or double-barrier methods (for example, a condom in combination with spermicide).

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

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

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Amgen Inc. for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

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

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

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

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

Additional Information

4. You may ask the study chair (Dr. Elias Jabbour, at 713-792-4764) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

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

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

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

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

9. This study is sponsored and/or supported by: Amgen Inc.,

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

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

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover material that is stored at MD Anderson in future research. Leftover material stored by Amgen Inc., will not be used for future research.

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

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

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

Genetic Research
Research samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment.

Conflict of Interest

Elias Jabbour (Study Chair) has received compensation from Amgen as a consultant. The financial interests are within the limits of the conflict of interest policy.

Farhad Ravandi-Kashani (Co-Chair) has received compensation from Amgen as a scientific advisor. The financial interests are within the limits of the conflict of interest policy.

Hagop Kantarjian (Co-Chair) has received compensation from Amgen as a consultant. The financial interests are within the limits of the conflict of interest policy.

Jorge Cortes (Collaborator) has received compensation from Amgen as a consultant. The financial interests are within the limits of the conflict of interest policy.

Farhad Ravandi-Kashani (Collaborator) has received compensation from Amgen as a scientific advisor. The financial interests are within the limits of the conflict of interest policy.

Dr. Naval Daver (Collaborator) has received compensation from Amgen as a Scientific Advisor. The financial interests are within the limits of the conflict of interest policy.

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

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Amgen Inc., who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
   - Individuals with medical backgrounds who determine the effect that the treatment procedures may have on the disease
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

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

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

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

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

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

CONSENT/AUTHORIZATION

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

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2014-0844.

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

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

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

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

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

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

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

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

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

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION