Informed Consent/Authorization for Participation in Research

Title of Research Study: Phase I/II Study of the Combination of Blinatumomab and Asciminib in Patients with Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia

Study Number: 2024-0054

Principal Investigator: Nicholas Short, MD

_____ _____
Participant's Name Medical Record Number

Key Information

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?

You are invited to take part in a research study because you have Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL).

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

There are 2 phases to this clinical research study: Phase I and Phase II.

The goal of Phase I is to find the recommended dose of asciminib that can be given in combination with blinatumomab to patients with Ph+ ALL.

The goal of Phase II is to learn if the combination of blinatumomab and asciminib can help to control Ph+ ALL.

The safety and effects of the drug combination will also be studied in both phases.

This is an investigational study. Blinatumomab is FDA approved and commercially available for the treatment of ALL. Asciminib is FDA approved and commercially available for the treatment of chronic myeloid leukemia, but not for the treatment of Ph+ ALL. It is considered investigational to give blinatumomab and asciminib together to patients with Ph+ ALL.

The study doctor can explain how the study drugs are designed to work.

How long will the research last and what will I need to do?

You will receive the study drugs for as long as the study doctor thinks it is in your best interest. You will receive 5 cycles of the combination of blinatumomab and asciminib, followed by asciminib alone for as long as it benefits you.

You will be asked to visit the clinic about 1-2 times every week during Cycle 1, every 1-3 weeks during Cycles 2-5, followed by every 4-8 weeks for up to 2 years and then 1 time every 3-6 months after that. At each visit, you will have tests and procedures for routine and research purposes, such as blood draws and bone marrow aspirates.

More detailed information about the study procedures can be found under ***"What happens if I agree to be in this research?"***

Is there any way being in this study could be bad for me?

Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment.

More detailed information about the risks of this study can be found under ***"Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

The study drugs may help to control the disease. Future patients may benefit from what is learned. However, it cannot be promised that there will be any benefits to you or others from your taking part in this research.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate, not participate, or stop participation at any time without penalty or loss of your regular benefits.

Instead of taking part in this study, you may choose to receive chemotherapy, a commercially available tyrosine kinase inhibitor (such as dasatinib or ponatinib), blinatumomab, or any combination of these agents. You may choose to receive other investigational therapy, if available. These alternative treatments have risks and benefits that may be the same or different than those in this research study. The study doctor can discuss these alternative treatments, including their possible risks and benefits, with you.

You may choose not to have treatment for cancer at all. If you decide that you don't want any more active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually, this care can be provided at home. If you think you might prefer comfort care, please discuss this with your family, friends, and your doctor.

In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

Detailed Information

The following is more detailed information about this study in addition to the information listed above.

Who can I talk to if I have questions or concerns?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the study doctor, Dr. Nicholas Short, at 713-563-4485 or 713-792-2121 (24 hours).

This research has been reviewed and approved by the MD Anderson Institutional Review Board (IRB – an ethics committee that reviews research studies). You may talk to them at 713-792-6477 or IRB_Help@mdanderson.org if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be in this study?

It is expected about 40 people at MD Anderson will be enrolled in this research study.

What happens if I agree to be in this research?

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

- You will have a physical exam.
- You will have an EKG and either an echocardiogram (ECHO) or MUGA scan to check your heart function.
- Blood (about 3½ tablespoons) will be drawn for routine tests and correlative studies. Correlative studies help researchers learn how the study drugs work together.
- You will have a bone marrow aspirate for correlative studies and genetic testing. Genetic testing includes studying DNA and RNA (the genetic material of cells) and identifying genetic mutations (changes). Genetic testing may help researchers better understand the disease and its response to the study drugs.
- If you can become pregnant, blood or urine will be collected for a pregnancy test. To take part in this study, you must not be pregnant.

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

Study Groups
If you are found to be eligible to take part in this study, you will be assigned to a study phase (Phase I or Phase II) based on when you join the study.

If you are assigned to Phase I, the dose of asciminib you receive will depend on when you join this study. Up to 3 dose levels of asciminib will be tested. At least 3 participants will be enrolled at each dose level. The first group of participants will receive the lowest dose level. Each new group will receive a higher dose than the group before it, if no intolerable side effects were seen. This will continue until the highest tolerable dose of asciminib is found.

If you are enrolled in Phase II, you will receive asciminib at the recommended dose that was found in Phase I.

All participants will receive the same dose level of blinatumomab.

Study Drug Administration

You will receive 5 cycles of blinatumomab and asciminib, followed by asciminib alone for as long as it benefits you.

You will receive **blinatumomab** as a continuous (non-stop) infusion on Days 4-31 of Cycle 1 and on Days 1-28 of Cycles 2-5. Cycle 1 is 45 days long, and Cycles 2-5 are 42 days. If the study doctor thinks it is needed, you may be able to receive up to another 4 cycles of blinatumomab. For each additional cycle, blinatumomab will be given as a continuous infusion over 4 weeks, followed by a 2-week break.

You will take **asciminib** by mouth 1 time every day during this study. Each dose should be taken at about the same time every day. You should fast (have nothing to eat or drink, except water) for at least 2 hours before taking asciminib and for 1 hour after taking asciminib. If you forget to take a dose or vomit a dose, tell the study doctor, and do not take another dose to make up for the missed/vomited dose unless the study doctor or research team tells you to do so. Take the next dose as scheduled.

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

You may be hospitalized for the first 6 days of Cycle 1 to be watched for side effects. You and/or your insurance provider will be responsible for the cost of this hospital stay.

Intrathecal Chemotherapy
You will also receive intrathecal chemotherapy to help prevent side effects. Intrathecally means the chemotherapy will be given directly into the cerebrospinal fluid (CSF—the fluid surrounding the brain and spinal cord). This may be done using an Ommaya reservoir if you have one placed or through a spinal tap (also called a lumbar puncture, in which your lower back will be numbed with an anesthetic and a needle will be inserted into the lower back). Intrathecal chemotherapy will consist of methotrexate and cytarabine.

If your disease is newly diagnosed, you will receive 15 intrathecal treatments. A total of 3 doses will be given with each course of blinatumomab on Days 1, 15, and 29 until a total of 15 doses have been completed.

If your disease is relapsed or refractory, intrathecal chemotherapy will be given based on your treating doctor's discretion. This may include 6-8 doses.

If you have CNS leukemia, intrathecal chemotherapy will be given per standard of care. This usually consists of intrathecal treatments 2 times a week for at least 2 weeks, then 1 time every week for 2 months, then 1 time every other week for 2 months, and then 1 time every month after that until you complete a total of 1 year of therapy.

Your intrathecal chemotherapy treatment plan will be discussed with you.

Study Visits

One (1) – 2 times every week during Cycle 1, every 1-3 weeks during Cycles 2-5, every 4-8 weeks after that for up to 2 years, and then every 3-6 months after that, blood (about 2-3 teaspoons) will be drawn for routine and/or genetic testing.

On Days 3 and 6 of Cycle 1, at the end of Cycles 1 and 3, and if the disease gets worse, blood (about 2-3 teaspoons) will be drawn for correlative studies.

On Day 28 of Cycle 1, at the end of Cycles 3 and 5, then every 3-6 months after that for up to 2 years, and if the disease gets worse, you will have a bone marrow aspirate to check the status of the disease, for genetic testing, and/or for correlative studies. Based on how the disease responds to the study drugs, you may have another bone marrow aspirate on Day 42 of Cycle 1 and/or at the end of additional study cycles. This will be discussed with you.

End-of-Dosing Visit
As soon as possible after your last dose of study drug(s), you will have an End-of-Dosing visit. At this visit, the study staff will ask you about any side effects you may have.

Follow-Up Visit
Thirty (30) days after your last dose of study drug(s), you will have a Follow-Up visit. At this visit, the study staff will ask you about any side effects you may have. This may be done over the phone. The call will last about 10 minutes.

Long-Term Follow-Up
Every 6 months until the study ends or you withdraw from the study (whichever happens first), the study staff will call you to check on how you are doing and ask about the status of the disease. Each call will take about 10 minutes.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for the following:

- Tell the study team about any symptoms or side effects you have, follow study directions, and come to all study appointments (or contact the study team to reschedule).
- Tell the study doctor/study staff about all medications that you are taking or plan to take, including prescription and over-the-counter medications, supplements, vitamins, and herbal remedies.
- Do not take part in other research studies to treat your leukemia.
- Do no drive or use heavy machinery while receiving blinatumomab.

What happens if I say yes, but I change my mind later?

You can leave the research at any time; it will not be held against you. You may withdraw from participation in this study without any penalty or loss of benefits. If you withdraw from this study, you can still choose to be treated at MD Anderson.

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 who can help you safely stop study treatment. It may be dangerous to suddenly stop study treatment. The study doctor will also decide if you need to have any visits or tests to check on your health.

If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Is there any way being in this study could be bad for me? (Detailed Risks)

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. 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.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Blinatumomab, asciminib, cytarabine, and methotrexate each may cause low blood cell counts (red blood cells, platelets, and white blood cells):

- 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.
- 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.

Blinatumomab Side Effects

Common (occurring in more than 20% of patients)

• high blood pressure that may be severe (possible stroke) • neurotoxicity (brain and nervous system-related effects) • headache • fever • chills • tremors	• low blood cell counts (red, white, platelets) • infection, possibly severe and life-threatening (possible low blood pressure, kidney failure, and/or heart failure)	• bacteria in the blood • infusion reaction (possible chills and/or hives)

Occasional (occurring in 3-20% of patients)

• swelling (arm/leg) • low blood pressure (possible dizziness and/or fainting) • irregular heartbeat • decreased brain function (possible paralysis and/or coma)	• inability to speak • difficulty sleeping • dizziness • skin rash • weight gain	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • back pain • cough

Blinatumomab may occasionally cause cytokine release syndrome (CRS). 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).

Exact frequency unknown but occurring in 2-10% of patients

• seizure

Frequency Unknown

• chest pain/discomfort • mental status change (such as memory loss and impaired thinking) • paralysis (face) • nerve pain (face) • confusion • loss of consciousness • depression	• memory loss • unresponsiveness • suicidal thoughts • flushing • hot flashes • hives • allergic skin reaction	• leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing) • tumor lysis syndrome (TLS)-- breakdown products of the cancer cells entering the blood

• fatigue • difficulty paying attention • difficulty walking • trouble with balance • numbness • decreased brain function (possible paralysis and/or coma) • abnormal sensation (such as pins and needles) • difficulty speaking	• decreased blood volume (possible organ failure) • increase in infection-fighting cells • difficulty breathing (possibly due to narrowing of the airways) • fast breathing • wheezing • pain (arm, leg, bone) • numbness • lymph node swelling • abnormal eye movement	stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • immune system reaction (possible fever, jaundice, liver/spleen enlargement, irritability, and/or seizures) • body-wide inflammation • shock • allergic reaction that may be life-threatening (such as difficulty breathing, low blood pressure, and/or organ failure)

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

• inflammation of the pancreas (possible abdominal pain)	• immune system response (possible loss of drug function)

Relapse of CD19 negative B-precursor ALL (meaning that the leukemia cells no longer have surface expression of the CD19 target needed for blinatumomab to work) and lineage switch from ALL to AML (meaning the type of leukemia cell causing the disease changes during treatment) have been observed in patients with ALL, during or following blinatumomab treatment, in clinical trials and the post-marketing setting (studies done after regulatory agency approval was obtained).

Asciminib Side Effects

Common (occurring in more than 20% of patients)

• fatigue • headache • high blood levels of fat (possible heart disease and/or stroke)	• high blood levels of uric acid (possible painful joints and/or kidney failure) • abnormal blood test (possible muscle disorders)	• abnormal liver test (possible liver damage) • muscle and/or bone pain

Occurring in fewer than 20% of patients

• high blood pressure • irregular heartbeat • swelling • heart failure • abnormal EKG • fever • dizziness • skin rash • itching • hives • 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)	• underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • abdominal pain • diarrhea • abnormal blood test (possible pancreas inflammation or damage) • nausea • constipation • loss of appetite • vomiting	• nerve damage (possible numbness, pain, and/or loss of motor function) • joint pain • abnormal kidney test (possible kidney damage) • blurry vision • dry eyes • flu • cough • difficulty breathing • build-up of fluid around the lungs • allergic reaction

Frequency Unknown
Asciminib may cause additional heart problems, such as:

- decreased blood supply to the brain caused by stroke
- decreased blood supply to the heart
- blood clots in an artery (possible organ damage such as stroke and/or heart attack)
- blood clot in a vein (possible pain, swelling, and/or redness)

Cytarabine Side Effects

Frequent:

• fever • skin rash • anal and/or rectal inflammation • anal sores • loss of appetite	• diarrhea • mouth sores and/or blisters • nausea • vomiting • low blood cell counts (red, white, platelet)	• abnormal liver tests (possible liver damage and/or yellowing of the skin and/or eyes) • blood clots in a vein (possible pain, swelling, and/or redness)

Less Frequent:

• chest pain • inflammation of the tissue around the heart (possible chest pain) • dizziness • headache • nerve damage (possible dizziness and/or headache) • inflammation of nerves (possible pain and/or loss of motor or sensory function) • hair loss (partial or total) • itching • skin freckling	• skin sores • hives • abdominal pain • death of tissue in the intestines • esophageal sore • throat inflammation • inflammation of the pancreas (possible abdominal pain) • sore throat • inability to urinate • jaundice (yellowing of skin and/or eyes) • painful red eyes • decreased kidney function	• difficulty breathing • injection site swelling • allergic reaction (swelling of face, mouth, and/or tongue) • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure)

Infrequent:

• chest pain due to heart trouble • stoppage of heart and lung function • inflammation of the membranes around the spinal cord and brain (possible headache and/or coma) • brain injury that may be reversible (possible headache, confusion, seizures, and/or vision loss)	• mental status change • paralysis • enlarged bowel (possible abdominal pain) • high blood levels of uric acid (possible painful joints and/or kidney failure) • abnormal blood test (possible pancreas inflammation and/or damage) • liver damage due to blood clots	• breakdown of muscle tissue (possible kidney failure) • lung inflammation (possible difficulty breathing) • injection site pain and/or swelling • cytarabine syndrome (bone/chest/muscle pain, painful red eyes, fever, skin rash, and/or fatigue/lack of energy)

Additional side effects seen only in high dose cytarabine:

It is not well known how often the following side effects may occur.

• enlarged heart • decreased brain function affecting movement • coma • nervous system damage (possible seizure and/or coma) • nerve damage (possible numbness, pain, and/or loss of motor function) • personality change • sleepiness • skin peeling	• stomach and/or small intestine ulcer • abdominal wall inflammation • inflammation of the pancreas (possible abdominal pain) • air-filled cysts in the intestines • decreased blood flow to part of the bowel (possibly causing death of tissue)	• pus-filled areas in the liver • liver damage • damage to the surface of the eye • bleeding in the eye • difficulty breathing • fluid in the lung (possible difficulty breathing)

When cytarabine is given directly into the spine, it may also cause the following side effects:

• decreased brain function (possible paralysis and/or coma) • fever • nausea/vomiting	• paralysis (possibly of the nerves in the neck and/or both legs) • difficulty swallowing • blindness	• double vision • cough • hoarseness • voice loss

<u>Methotrexate Side Effects</u>

Occurring in more than 10% of patients:

• dizziness • mouth blisters/sores • headache	• fatigue • diarrhea • nausea	• abnormal liver test (possible liver damage) • cough

Occurring in between 1 and 10% of patients:

• hair loss (partial or total) • skin rash and/or itching • skin sensitivity to sunlight or lamps	• weight loss • loss of appetite • low blood cell counts (red/white/platelets)	• blurred vision • sore throat • difficulty breathing

Frequency Unknown

• chest pain • low blood pressure (possible dizziness/fainting)	• very severe blistering skin disease (loss of large portion of skin)	• birth defects • miscarriage • impotence • inability to have children

• blood clots in an artery (possible organ damage such as stroke and/or heart attack) • blood clots in a vein (possible pain, swelling, and/or redness) • blood clots in the brain • inflammation of and/or build-up of fluid in the tissue around the heart (possible chest pain) • blood clot inside the eye (possible blindness) • blood vessel inflammation (possible bleeding and/or bruising) • dilated red blood vessels • blockage in the lung (possible pain and/or shortness of breath) • inflammation of the membrane around the spinal cord and brain (possible headache, vomiting, and fever) • damage to the spinal cord (possible paralysis, weakness, and/or abnormal sensation) • fever • chills • abnormal sensation on the scalp • brain damage that may be reversible (possible headache, confusion, seizures, and/or vision loss) • mental status change (such as memory loss and impaired thinking) • fatigue/lack of energy	• shedding and scaling of the skin (possible fatal loss of bodily fluids) • red, dry, scaly patches of thickened skin (psoriasis) • allergic skin reaction • lightening or darkening of skin • skin rash • acne-like rash • severe sunburn-like rash at site of previous radiation (called radiation recall) • death of skin • skin redness • hives • decreased sex drive • enlarged breasts in males • failure of the ovaries to produce hormones (possible stopped menstrual cycle) • low blood level of albumin (possible swelling, weakness, and/or fatigue) • diabetes • abdominal pain • loss of appetite • gum disease • stomach ulcer • inflammation of the intestines • digestive system bleeding • hole in the intestines (possibly leaking contents into the abdomen)	• low sperm count • decreased egg production • vaginal discharge • liver damage due to scarring • liver failure • liver damage due to inflammation • bone destruction and soft tissue death of tissue (with radiotherapy) • broken bone(s) • loss of bone strength (possible broken bones) • joint/muscle pain • blurry vision • temporary blindness • painful red eyes • eye pain • blindness • ringing in the ears • abnormal kidney test (possible kidney damage) • decreased kidney function • kidney failure • difficulty breathing • lung inflammation (possible difficulty breathing) • difficulty breathing due to lung damage • increase in infection-fighting cells • infection • life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure) • sore throat

• decreased brain function (possible paralysis and/or coma) • mood swings • confusion • weakness on one side of the body • inability to speak • difficulty forming or speaking words • seizures • coma • sweating • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• inflammation of the pancreas (possible abdominal pain) • vomiting of blood • tarry or coffee ground-like blood in the stool • build-up of bodily waste products in the blood (possible kidney damage) • bladder inflammation (possible pain and/or urge to urinate) • difficult and/or painful urination • blood in the urine	• severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • breakdown products of the cancer cells entering the blood stream (possible weakness, low blood pressure, muscle cramps, kidney damage, and/or other organ damage) • cough

Methotrexate may rarely cause you to develop another type of cancer (such as lymphoma, a type of lymph node cancer).

When given intrathecally, methotrexate may cause inflammation of the membrane around the spinal cord and brain (possible headache).

Study Drug Combination Side Effects

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects listed above.

Other Risks

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

MUGA scans may cause allergic reactions to the radioactive tracer, injection site soreness, and/or swelling. They may cause damage to cells or tissue from being exposed to the radiation used in the scan. These side effects may occur in less than 10% of patients.

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

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

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.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

You will be told about any new information that may affect your health, welfare, or choice to stay in the research.

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.

Birth Control Requirements: If you can become pregnant or father a child and you are sexually active, you must use highly effective birth control during the study and for at least 4 months after your last dose of study drug(s). Talk to the study doctor about the birth control method(s) you and/or your partner should use.

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.

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

Will it cost anything to be in this study? Will I be paid to be in this study?

Asciminib will be provided at no cost to you during this study. You and/or your insurance provider will be responsible for the cost of blinatumomab.

You and/or your insurance provider will not have to pay for certain research exams and procedures done that are covered by the study.

You and/or your insurance provider will be responsible for the costs of routine clinical services (such as diagnostic/therapeutic procedures, drugs, devices, laboratory assays, and other services that would ordinarily be ordered for medical care, regardless of whether or not you are participating in a study). There may be extra costs that are not covered by your medical plan that you will have to pay yourself.

Taking part in this study may result in added costs to you (such as transportation, parking, meals, or unpaid leave from work). You may have to pay for medication prescribed to treat or prevent side effects, and you may have to visit the clinic/hospital more often than if you were not participating in this study.

If you have insurance, talk to your insurance provider and make sure that you understand what your insurance pays for and what it does not pay for if you take part in this study. Also, find out if you need approval from your plan before you can take part in the study.

You may ask that a financial counselor be made available to you to talk about the costs of this study.

You will not receive any compensation for taking part in this study.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who need to review this information. Complete secrecy cannot be promised. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

A participant study number will be assigned to you once you have been enrolled in the study. This participant study number will be used to identify your data in the study report and when reporting any data from the study.

Any personal information that could identify you will be removed or changed before data are shared with other researchers or results are made public.

The results of this research may be published in scientific journals or presented at medical meetings. However, your identity will not be disclosed. Your name and other identifying information will be kept confidential.

The sponsor, monitors, auditors, the IRB, and the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access.

Federal law provides additional protections of your medical records and related health information. These are described below.

Will my data or samples be used for future research?

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

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

If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or shared with another researcher for future research studies without your additional informed consent.

Can I be removed from the research study without my permission?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include if the disease gets worse, if intolerable side effects occur, if you are unable to follow study directions, or if the study is stopped.

What happens if I get hurt from being in this study?

If you get sick or hurt and it is related to your participation in this study, you will be given care at MD Anderson (if you are at the clinic when you are sick or hurt). If you get hurt or sick and you are not at the clinic (for example, you are at home or at another doctor's office):

- call your personal doctor right away (or in an emergency, call 911)
- tell your personal doctor or ER staff that you are in this study (try to give them a copy of this consent form or show them your participant card)

- call the study doctor (Dr. Nicholas Short, at 713-563-4485) or 713-792-2121 (24 hours)

You will not be reimbursed for expenses or compensated financially by MD Anderson or Novartis for this injury. Costs of treatment received because you were hurt or sick will be billed to you or your insurance company. No other form of payment is available.

You may also contact the MD Anderson 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.

What else do I need to know?

This research is being supported by Novartis.

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

Outside relationships are disclosed to and approved by the Conflict of Interest Committee, which reviews these relationships for compliance with institutional policy. This review helps the IRB to assure that financial relationships do not have an impact on the conduct of this study. The following members of the study staff have disclosed compensation from the funding source(s) of this study:

- Prithviraj Bose (co-investigator)

Your information and samples (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will not contact you to let you know what they have found.

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

The Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection

for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Please contact the study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

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

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

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Novartis, who is a supporter of this study, and/or any future sponsors/supporters of the study, and/or licensees of the study technology
   - 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 do its best to protect the privacy of your records, but it is possible that once information is shared with people listed on this form, it may be released to others. If this happens, your information may no longer be protected by federal law.

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

E. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify

you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONSENT/AUTHORIZATION

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

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under this protocol.

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

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
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.)