Medical College of Wisconsin and Froedtert Hospital
CONSENT TO PARTICIPATE IN RESEARCH

Name of Study Subject: _____

X16016: Phase I Study Of Vincristine, Doxorubicin, And Dexamethasone (VXD) Plus Ixazomib In Adults With Relapsed Or Refractory Acute Lymphoblastic Leukemia/Lymphoma, Lymphoblastic Lymphoma Or Mixed Phenotype Acute Leukemia

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You are invited to take part in this research study. This form tells you why this research study is being done, what will happen in the research study, 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 study or not.

A1. INTRODUCTION – WHY ARE WE ASKING YOU ABOUT THIS STUDY?

You are being invited to participate in this research study because you have relapsed or refractory acute lymphoblastic leukemia/lymphoma or mixed phenotype acute leukemia.

A total of about 18 people are expected to participate in this study at the Medical College of Wisconsin/Froedtert Hospital.

The Director of the study is Ehab Atallah, MD in the Department of Medicine. A study team works with Dr. Atallah. You can ask who these people are.

Millennium Pharmaceuticals, Inc. provides financial support to the Medical College of Wisconsin, including Dr. Atallah and other key members of his/her study staff, for work on this study as well as others being conducted at the Medical College of Wisconsin. Previously a sub-investigator for this study reviewed safety data for another Millennium study. This sub-investigator received compensation for the work he did reviewing the safety data. Dr. Atallah is the sponsor of the study.

A2. DO I HAVE TO BE IN THIS STUDY?

You can decide whether to take part in this study 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 study, you do not have to stay in it. You may stop at any time.

A research study 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 study procedures, tests and visits follow a set plan that must be kept.

A3. WHY IS THIS RESEARCH STUDY BEING DONE?

Ixazomib is a new drug which so far has been mostly used in studies for multiple myeloma patients either alone or with other combination of drugs. To date approximately 300 patients have been treated with oral Ixazomib either alone or with other combinations of drugs.

In this study we want to find out more about the side effects (problems and symptoms) and what doses are safe using a new drug Ixazomib in combination with modified VXD (vincristine, doxorubicin, and dexamethasone) for relapsed or refractory acute lymphoblastic leukemia/lymphoma. Everyone in this study will receive Ixazomib which is still experimental and is not approved by the U.S. Food and Drug Administration.

B1. WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

STUDY DRUGS

The duration of your treatment will depend upon how you are feeling, how well you tolerate the study drug and how your disease responds to the study drug. If you are responding to therapy you could continue to receive the study treatment for up to two cycles (1 cycle = 28 days).

You will receive the following drugs while you are on the study:

Vincristine: You will be given 1.5 mg/m^2 to a maximum dose of 2 mg through a vein (IV) on days 1, 8, 15 and 22.

Dexamethasone: You will be given 10 mg/m^2 of Dexamethasone by mouth (orally) or through a vein (IV) on days 1-14.

Doxorubicin: You will be given 60 mg/m^2 of Doxorubicin on day 1 through a vein (IV).

Cytarabine and Methotrexate: A lumbar puncture (also known as a "spinal tap") to diagnose and treat any ALL cells that have infiltrated into the central nervous system (CNS) will be done. At that time you will be given:

For patients without CNS involvement:

Cytarabine: You will be given 100 mg by an injection into the spinal fluid (intrathecally) on day 1 (+/-1 day) (cytarabine dose should be reduced to 50 mg if given through a central ommaya reservoir).
Methotreaxte: You will be given 12 mg by an injection into the spinal fluid (intrathecally) on day 8 (+/-1 day).

For patients with CNS involvement:
Cytarabine: You will be given 100 mg by an injection into the spinal fluid (intrathecally) on day 1 (+/-1 day) (cytarabine dose should be reduced to 50 mg if given through a central ommaya reservoir).
Cytarabine: You will be given 30 mg an injection into the spinal fluid (intrathecally) on (Days,8, 15 and 22 (+/-1 day)).
Methotrexate: 15 mg an injection into the spinal fluid (intrathecally) on (Days,8, 15 and 22 (+/-1 day))
Hydrocortisone: 15 mg an injection into the spinal fluid (intrathecally) on (Days,8, 15 and 22 (+/-1 day)).

Ixazomib: You will be given Ixazomib by mouth (orally) on weekly on days 1, 8 and 15. There are 3 groups. Up to 6 patients will be enrolled in each group.

Group 1: Will receive 2.3 mg orally (dose level 1)
Group 2: Will receive 3.0 mg orally (dose level 2)
Group 3: Will receive 4.0 mg orally (dose level 3)

Your study doctor may decide to adjust your dose of any of the medications above if he/she feels this is necessary.

STUDY PROCEDURES

Before any tests or procedures are done, you will be asked to sign this consent form. The study doctor will discuss the study with you and answer your questions.
If you decide to join the study, some screening tests will be done first to see if you are eligible.

Some of these tests and procedures are considered 'standard of care' which means that they would be done even if you were not participating in this research study and some are considered for research purpose which means they are being done only because you have agreed to be in this research study.

At every visit, you will be asked what medications you are taking or have taken since your last visit. You will also be asked how you are feeling and if you are having or have had any symptoms or side effects from your last visit.

Below is a list of the tests and procedures which will be done during the study.

- **Complete Medical history & Demographics:** A complete medical history will be taken including any medications you have used or are currently using, and any therapies you have had.
- **Physical exam:** A physical exam will be done including your height and weight. Your height will only be measured during the screening period. This will also include an exam of your nervous system.
- **Vital signs:** This will include your heart rate, blood pressure and temperature.
- **Eastern Cooperative Oncology Group (ECOG) Performance Status:** This is a scale which will be used by your study doctor to assess how the disease affects your daily living abilities.
- **Blood samples (disease assessments, hematology, chemistry, coagulation):** Blood samples will be taken to determine the state of your disease and later to determine how well you are responding to the study treatment.
    - ***Hematology and Chemistry:*** These blood samples (about 2 ½ tablespoons) will be used to evaluate your blood counts and blood chemistry (this includes tests of liver and kidney function, blood sugar, minerals and proteins). These results will be used to see if you are well enough to receive the study drugs.
    - **Direct Bilirubin:** This blood sample will be used to see how your liver is functioning.
    - ***Fibrinogen:*** This blood sample (about ½ teaspoon) will test to see how well your blood clots.
    - **Serum or Urine Pregnancy test:** If you are a woman that is child bearing, a blood sample or urine sample will be taken to make sure you are not pregnant; you cannot be in this study if you are pregnant, or if you are planning to become pregnant.
- **Echocardiogram (ECHO) or MUGA:** These tests are to measure your heart's rhythm and the strength of your heart's contractions.
- **Bone marrow biopsy or aspirate:** These samples will be tested to look at your disease at the beginning of the study and measure the amount of disease you have and how your disease responds to treatment. For this procedure, a numbing drug is injected into the skin over one of your hipbones. A needle is then inserted into the hipbones and a small piece of bone and/or fluid is removed.

Optional Correlative Study Sample

Dr. Atallah would also like to keep a portion of your bone marrow or blood sample for future research studies in the institutional bank. These optional samples will be taken either from your bone marrow or blood at the same time that you get your other standard of care tests completed. **You will be asked to sign a separate consent that will detail how the samples are stored and when the samples are taken if you are**

interested in participating in these optional samples. Talk to a member of the study team if you are interested in hearing more about this option.

STUDY PERIODS

This study is split up into 4 different periods: Screening, Treatment, End of Treatment, Follow-up.

Screening:

After you have agreed to participate in the study and have signed this form, you will enter screening which can last up to 14 days before you receive the first dose of study drug. You will have tests and evaluations as listed below, to determine if you are eligible to participate in the study. If you have had some of the tests or procedures described below recently they may not need to be repeated.

- Medical History & Demographics
- Complete physical exam
- Vital signs
- Height and Weight
- ECOG Performance Status
- Blood samples (hematology, chemistry, direct bilirubin, fibrinogen)
- Pregnancy test (if female and child bearing)
- ECHO or MUGA
- Bone Marrow biopsy/aspirate within 4 weeks of week 1

If the screening information shows that you meet the requirements, then you will be able to start the study. If the screening information shows that you are not eligible for the study, the study doctors will discuss other options with you and/or refer you back to your regular doctor.

Treatment:

Once it has been determined that you are eligible to participate in this study, you will be enrolled and you will begin taking the study drug combination (Ixazomib with modified VXD).

The following are the procedures that will occur during the treatment period of the study. These may change slightly if your doctor feels it is in your best interest.

Cycles 1 and 2 Week 1

- Medical History
- Complete physical exam
- Vital signs

- Weight
- ECOG Performance Status
- Blood samples (hematology, chemistry, fibrinogen)

Weekly

- Blood samples (hematology, chemistry, direct bilirubin, fibrinogen)

Every 2 Weeks

- Complete physical exam
- ECOG Performance Status
- Vitals

Every 4 Weeks

- Bone Marrow biopsy/aspirate

End of Treatment or Early Termination

End of Study

The following will be performed when your participation in the study ends early or you complete the treatment phase of the study:

- Complete physical exam
- Vital signs
- Weight
- Blood samples (hematology, chemistry)
- Bone Marrow biopsy/aspirate

Follow-Up

Progression Free Survival (PFS) Follow-up

After the end of treatment, if you were removed from the study for any reason other than your disease getting worse, you will be asked to return to the clinic monthly to monitor your disease status. This will continue until your disease worsens.

Overall Survival (OS) Follow-up

If your study treatment was stopped because your disease got worse, then you will be contacted by the clinic yearly to monitor how you are doing.

B2. HOW LONG WILL I BE IN THE STUDY?

You will take the study medication for up to two cycles (1 cycle =28 days). When study treatment ends, you will be followed until the study completed.

B3. CAN I STOP BEING IN THE STUDY?

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

⇒ The doctor can tell you about the effects of stopping, and you and the doctor can talk about what follow-up care would help you the most.
⇒ You might be asked to come back for one more visit to check your health.

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

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

If this happens, the study doctor will tell you.

B4. ARE THERE ANY SPECIAL INSTRUCTIONS WHILE I AM IN THE STUDY?

- Your Ixazomib should be taken on an empty stomach (no food or drink) at least 1 hour before or 2 hours after a meal.
- Missed doses of Ixazomib can be taken as soon as you remember as long as the next scheduled dose is 72 hours or more away. If you vomit after ingestion, you should not take an additional dose, but should resume dosing at the time of the next scheduled dose.

C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE STUDY?

There are risks to taking part in any research study. There is a risk that you may get a drug, drug combination or dose of a drug that does not help your condition or may make it worse. There also may be problems (side effects) we do not know about yet, from drug 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 study for problems (side effects). **You need to tell the study doctor or a member of the study team immediately if you experience any problems, side effects, or changes in your health.** If you have problems, call Dr. Atallah immediately at 414-805-6800. In an emergency, call 911.

C2. RISKS OF TREATMENT

The research drug itself may cause problems (side effects). Side effects may be mild or very serious. Some can last a long time or never go away. Many go away soon after you stop taking the drug. Drugs can affect individuals in different ways. . Complications

of some of the side effects below may lead to life-threatening events such and possibly death.

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

Ixazomib

Based on studies of Ixazomib that are using both an intravenous (IV) liquid and an oral (pill), it is possible to predict some of the discomforts and risks. However, it is possible that Ixazomib may cause risks that have not yet been observed in patients. The following risks might be seen:

- Low platelet count which may increase the chance of bleeding
- Skin rash which may range from some red areas, small flat spots, or small raised bumps that may or may not be itchy in a few areas or all over the body
- Feeling tired or weak
- Nausea
- Vomiting
- Diarrhea
- Numbness or tingling or pain feelings in hands and feet
- Fever
- Constipation
- Lowered red cells or anemia which may make you feel tired;
- Lowered white blood cells called neturophils that may increase your risk of infection and may be associated with fever
- Distortion of the sense of taste i.e. an abnormal or impaired sense of taste.
- Trouble falling asleep, staying asleep or both

- Other discomforts and risks reported in studies with Ixazomib, which may have been due to the patient's disease, Ixazomib, other medications, or some combination of these include:
  - Not feeling like eating
  - Electrolyte imbalance (blood chemical imbalance)
  - Loss of water from the body (dehydration) because of vomiting and/or loose stools
  - High blood creatinine and renal failure, which means your kidneys are having trouble working well; Patients who had lost body water (dehydration) because of vomiting and/or loose stools have had high levels of creatinine indicating that the kidneys were failing to function adequately. In some severe situations, less kidney function may require temporary treatment with a machine that supports the function of the kidney (dialysis)
  - Headache

- Flu-like symptoms and other upper respiratory tract infections
- Feeling short of breath
- Lung infections including pneumonia or pneumonitis
- Cough
- Chills
- Pain in the abdomen or back
- Swelling or fluid buildup in the arms or legs
- General aches or pains in muscles, joints, bones, or arms and legs
- Feeling dizzy
- Lowered blood pressure that can commonly cause you to feel light headed, faint or pass out when you stand up
- Lowered white blood cells called lymphocytes
- Pain (muscular) in extremities

Some discomforts and risks that occur with lesser frequency (<1%) than those mentioned above, should be noted because they are severe, life-threatening or fatal. With limited experience, we do not know if Ixazomib causes such problems. Stevens Johnson's Syndrome, a severe, life-threatening or deadly condition that may involve rash, skin peeling and mouth sores has been reported in ongoing Ixazomib studies. Stevens Johnson Syndrome is a disorder of the immune system, which differs from a regular skin rash.

In addition posterior reversible encephalopathy syndrome has also been reported with Ixazomib with lesser frequency (<1%). This condition affects the brain and may cause headaches, changes in your vision, changes in your mental status, or seizures (fits), but is usually reversible.

Additionally, it is worth noting that:

- Ixazomib is similar to the drug known as VELCADE ® (bortezomib) for Injections, which is approved for the treatment of multiple myeloma (a cancer of the plasma cell), as well as mantle cell lymphoma (a cancer of the lymph nodes) in patients who have received at least one prior therapy.
- Ixazomib, like Velcade, should not be taken if you have ever had an allergic reaction to boron or boron containing products.

- The following side effects have been reported with VELCADE use and therefore may also be a risk with Ixazomib:

    - Reactivation of the herpes virus infection such as herpes zoster (shingles) that can sometimes cause local pain that may last after recovery from the skin rash and does not go away for some time; and
    - Rapid death of cancer cells that may let large amounts of the cells into the blood that injure organs, such as kidneys (this is referred to as tumor lysis

syndrome). Your study doctor can talk with you about other common side effects with VELCADE use.

- The more severe but rare side effects seen with VELCADE, include but are not limited to, worsening of your heart function (congestive heart failure), disorders that could affect the function of your lung that could be serious enough to result in death, and liver failure. Your doctor can talk to you further about the risks of VELCADE.

- Other drugs and supplements may affect the way Ixazomib works. Tell your doctor about all drugs and supplements you are taking while you are in this study.

Vincristine Side Effects:

- Hair loss that is often reversible
- Lowered white blood cells, that may increase the risk of infection
- Lowered platelets; that may increase the chance of bleeding
- Lowered red cells or anemia which may make you feel tired
- Damage to nerves that may result in numbness, tingling sensation, nerve pain, difficulty walking which may continue through the duration of treatment, and perhaps longer after treatment has stopped. These events may be worse if you have a pre-existing condition that affects the muscles or the nerves of the muscles
- Loss of muscle coordination, tremors, muscle weakness or muscle wasting, muscle aches
- Back pain, jaw pain, throat pain, bone pain, limb pain
- Weakness and loss of muscle tone
- Constipation, impaction of the colon bloating, bowel blockage, damage to the intestine, holes in the intestine or death of intestinal tissue
- Abdominal cramps, weight loss and loss of appetite
- Nausea, vomiting
- Ulcers or sores in the mouth and throat
- Diarrhea
- Increased or decrease in urination, difficulty urinating, burning upon urination or worsening of kidney function
- High blood pressure, or low blood pressure, development of heart disease if you have previously been treated with radiation therapy to the chest
- Shortness of breath, trouble breathing, which can start suddenly and be severe and require treatment
- Rash
- Severe headache
- Fast death of cancer cells that may let toxins into the blood and injure organs, such as the kidneys

Vincristine Rare Side Effects:

- Allergic reactions which include sudden serious reactions, rash, swelling, which can be life- threatening
- If vincristine leaks out of the vein into the surrounding tissue it may cause tissue irritation, damage or tissue death
- Convulsions that may occur with high blood pressure
- Loss of facial nerve control (or paralysis), for example, of the throat muscles, or the eye muscles
- Damage to the optic nerve resulting in blindness
- Paralysis, foot drop, change in gait
- Development of other cancers
- Change in the levels of certain drugs
- Changes in the level of sodium in the blood
- You should not receive vincristine if you have the demyelinating form of Charcot-Marie-Tooth syndrome (loss of muscle tissue and touch sensation,)

Doxorubicin Common Side Effects:

Common side effects are those that have occurred in greater than or equal to 30% of patients who have received Doxorubicin:

- Fatigue, weakness
- Temporary decrease in white blood cells that could cause increased your risk of infections
- Low platelets that may affect the ability of your blood to clot
- Nausea and vomiting shortly after dosing, which can be severe
- Thin hair, brittle hair, complete hair loss that is reversible
- Painful sores in the throat or mouth that may cause difficulty in swallowing
- Red discoloration of urine
- Blood clotting disorders and anemia (lack of red blood cells)

Doxorubicin Less Common Side Effects:

Less common side effects are those that have occurred in 10-29% of patients who have received Doxorubicin:

- Diarrhea, loss of appetite, dehydration, weight loss
- Injection site reactions including swelling, pain, redness or tissue damage. If doxorubicin leaks into the surrounding tissue it may lead to tissue death
- Flushing of the face
- Sensitivity to light
- Peeling of skin on hands or soles of feet
- Skin rash
- Darkening of the finger or toe nails, or nail loss

- Eye infections
- Itching
- Dehydration
- Fever, chills, hives
- Problems with fertility*

* You should not assume that you cannot get pregnant or that you cannot get someone else pregnant.

Rarely, the following side effects of Doxorubicin have been seen in humans:

- Treatment related acute leukemia or myelodysplasia
- Damage to large intestine
- Doxorubicin can damage the heart muscle and may cause heart problems, including possibly fatal heart failure. Heart problems may occur during doxorubicin therapy or months to years after receiving this medication. Your risk of developing heart problems depends on your dose, medical history (including previous heart disease, radiation therapy in the chest area), and previous use of this and other drugs.
- Allergic reactions, such as fever, urticaria (hives) and anaphylaxis (acute allergic reaction) occur rarely.
- Severe tissue damage may occur if doxorubicin leaks out of the vein into the surrounding tissue

Possible Discomforts And Risks Of Dexamethasone

Some of the more serious risks and side effects of receiving Dexamethasone include:

- Allergic reactions. Get emergency medical help if you have any of these signs of an allergic reaction: hives; difficulty breathing; swelling of your face, lips, tongue, or throat.
- Problems with your vision;
- Swelling, rapid weight gain, feeling short of breath;
- Severe depression, unusual thoughts or behavior, seizure (convulsions);
- Bloody or tarry stools, coughing up blood;
- Pancreatitis (severe pain in your upper stomach spreading to your back, nausea and vomiting, fast heart rate);
- Low potassium (confusion, uneven heart rate, extreme thirst, increased urination, leg discomfort, muscle weakness or limp feeling); or
- Dangerously high blood pressure (severe headache, blurred vision, buzzing in your ears, anxiety, confusion, chest pain, shortness of breath, uneven heartbeats, seizure).

You should call your doctor at once if you have any of these serious side effects above.

Less serious side effects may include:

- Sleep problems (insomnia), mood changes, irritability;
- Acne, dry skin, thinning skin, bruising or discoloration;
- Slow wound healing;

- Increased sweating;
- Headache, dizziness, spinning sensation;
- Nausea, stomach pain, bloating;
- Muscle weakness;
- Increased appetite, weight gain, changes in the shape or location of body fat (especially in your arms, legs, face, neck, breasts, and waist).

C3. OTHER RISKS OF THIS RESEARCH STUDY

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

Blood Draw: In addition to the risks of all study drugs, routine needle sticks for blood samples may cause pain, bruising and rarely, infection at the site where blood is drawn.

Bone Marrow Biopsy or Aspirate: Possible side effects of bone marrow aspirate and biopsy include bleeding, infection, bruising, discomfort and/or pain at the biopsy site and possible side effects from the local anesthetic (pain or bruising at the injection site).

Multi Gated Acquisition (MUGA) Scan: MUGA scan is a radioactive heart scan to see how well your heart pumps blood. A radioactive agent is injected into a vein, after which you lie on a table. A special camera that detects radioactivity takes pictures of your heart. The MUGA scan procedure has minimal if any risks. The test is painless except for a brief sting from the needle used to inject the tracer into your vein. Allergic reactions to the radioactive tracer are rare. Occasionally, some soreness or swelling may develop at the injection site. The radioactive agent is completely gone from the body within a few days of the test.

Echocardiogram (ECHO): ECHO is a noninvasive scan of the heart using sound waves. This test will be used to see how well your heart pumps blood. This test has no known risks or side effects.

C4. REPRODUCTIVE RISKS

Risks to women who could become pregnant

The drugs in this study might affect a baby, before or after the baby is born. We do not know if the drugs causes harm to a baby, so we do not want anyone who might be pregnant to enter the study. You should not become pregnant or nurse a baby while in this study. Unless you cannot have children because of surgery or other medical reasons (you had an effective tubal ligation, or had the ovaries or the uterus removed; or you are post-menopausal), you must use two effective methods of birth control from the time of signing the informed consent form, for the entire study drug treatment period (including interruptions in treatment), and for 90 days after completing study drug treatment. You must tell the study 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 study.

You must have a negative pregnancy test prior to enrolling in the study.

Unless you cannot have children because of surgery or other medical reasons (you had an effective tubal ligation, or had the ovaries or the uterus removed; or you are post-menopausal), you must use two effective methods of birth control from the time of signing the informed consent form, for the entire study drug treatment period (including interruptions in treatment), and for 90 days after completing study drug treatment. It is strongly recommended that at least one of these two methods be highly effective (see examples below).

Highly effective methods	**Other effective methods (barrier methods)**
Intra-uterine devices (IUD)	Latex or non-latex condom with or without a spermicidal agent
Hormonal (birth control pills/oral contraceptives, injectable contraceptives, contraceptive patches, or contraceptive implants)	Diaphragm with spermicide; Cervical cap with a spermicide; Sponge with a spermicide
If one of the highly effective methods cannot be used, using two effective methods at the same time are recommended.	

Risks of fathering a child
You should not father a baby while taking part in this study because it is unknown if the drugs in this study 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. Even if you are surgically sterilized (i.e. have had a vasectomy) you must agree to use an appropriate method of barrier contraception (latex or non-latex condom with a spermicidal agent) during the entire study drug treatment period, and for 90 days after completing study drug treatment. You must tell the study doctor right away if you think your partner is pregnant.

Highly effective methods	**Other effective methods (barrier methods)**
Vasectomy	Latex or non-latex condom with or without a spermicidal agent
	Diaphragm with spermicide; Cervical cap with spermicide; Sponge with spermicide
If one of the highly effective methods cannot be used, using two effective methods at the same time are recommended.	

All subjects (male or female): If you or your partner becomes pregnant during this study, you must tell the study doctor immediately. The doctor will advise you of the possible risks to your unborn child and discuss options for managing the pregnancy with

you. For female subjects who become pregnant while on this study, the study drug will be stopped immediately and the pregnancy will be followed until conclusion.

If you do not understand what any of these discomforts and risks mean, please ask the study doctor or study staff to explain these terms to you.

C5. ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

This study may or may not help you, but we hope the information from this study will help us develop better treatments for adults with relapsed or refractory acute lymphoblastic leukemia/lymphoma, lymphoblastic lymphoma or mixed phenotype acute leukemia.

D1. ARE THERE ANY COSTS TO BEING IN THE STUDY?

Most of the medical care that you will receive in this study is considered routine care for your condition and would be recommended whether you join the study or not. Costs for routine care will be billed to you or your insurance carrier. Activities / costs that are part of the study that will not be billed to you or your insurance company are: Ixazomib, processing, of research samples. Some insurers will not pay for drugs, tests or hospitalization that are part of research studies, so check with your insurer before you join this study. If you have questions regarding study costs, please contact Dr. Atallah.

D2. WILL I BE PAID FOR PARTICIPATING IN THE STUDY?

There is no payment for being in this study. You will not receive payments of any kind for discoveries, patents or products that may be developed from this study.

D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this study. You are free to say yes or no. If you do not join this study, your doctor can discuss other healthcare choices with you.
Your other choices may include:

- Getting treatment or care for your cancer without being in a study.
- Joining a different research study
- Getting no treatment
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE STUDY?

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

D5. WHAT HAPPENS IF I AM HARMED BECAUSE I TOOK PART IN THE STUDY?

No funds have been set aside to pay any costs if you become ill or are harmed because of this study. If you think that you have become ill or were harmed because of this study, let the study doctors know right away by calling 414-805-6800. By signing this form, you do not give up your right to seek payment for harm you receive while participating in this study.

If you think that you have become ill or were harmed because of this study, let the study doctors know right away by calling 414-805-6800.

By signing this form, you do not give up your right to seek payment for harm you receive while participating in this study.

D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

- If you have more questions about this study at any time, you can call Dr. Atallah at 414-805-6800.
- If you have questions about your rights as a study participant, want to report any problems or complaints, obtain information about the study, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

E1. What health information will be collected and used for this study?

To do this research study, we need your permission to collect and use some of your health information, or 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 study.

The health information to be collected and used for this study is:
All or portions of your medical chart:

- ⇨ Hospital/Medical Records
- ⇨ Physician/Clinical Records
- ⇨ Lab and/or Pathology Reports
- ⇨ Radiology Reports
- ⇨ Biological Samples
- ⇨ Interview/Questionnaires

E2. Who will see the health information collected for this study?
The only MCW/Froedtert Hospital employees allowed to handle your health information are those on the study 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.

The study team may share your information with people who don't work at MCW/Froedtert Hospital because they planned, pay for, or work with us on this study. The federal Privacy Rule may no longer protect your health information once it leaves MCW/Froedtert Hospital. For this study, we plan to share information with those doctors, researchers or government representatives working with us on this study at the institutions or companies listed here:

U.S. Food and Drug Administration, Rockville, MD
Millennium and its collaborators or designees
Representatives of Central Laboratories
Any Independent ethics committee, which approved this study
Other Regulatory Agencies and/or Their Designated Representatives
Those required by law

We may record your research information, including results of tests and procedures done for research, in your Froedtert Hospital and/or Medical College 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.

We will not use your personal health information for a different study without your permission or the permission of a hospital research review board (IRB). Once all personal identification is removed, the information might be used or released for other purposes without asking you. Results of the study may be presented in public talks or written articles, but no information will be presented that identifies you.

E3. What are the risks of sharing this health information?
One risk of taking part in a research study is that more people will handle your personal health information collected for this study. The study 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 study doctor about whether this could apply to you.

E4. How long will you keep the health information for this study?
If you sign this form, we plan to keep your information without any end-date in case we need to check it again for this study.

E5. 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:

Ehab Atallah, MD
Froedtert & Medical College of Wisconsin
Division of Hematology and Oncology
9200 W. Wisconsin Avenue
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 study. We may still use the information we have already collected.

F1. FOR MORE INFORMATION ABOUT THE STUDY

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 study by referring to the ClinicalTrials.gov number (NCT01887587) or by asking the study team for a printed copy.

CONSENT TO PARTICIPATE IN THE STUDY

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 study's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the study team use and share the health information and other information gathered for this study.
- I voluntarily agree to participate in this research study. I agree to follow the study 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.

Subject's Name *please print*	**Subject's Signature**	**Date**
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 person discussing/ obtaining consent** *please print*	**Signature of person discussing/obtaining consent**	**Date**

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