Official Title:	A Window Study of Ixazomib in Untreated Indolent B-NHL
NCT Number:	NCT02339922
Document Type:	Informed Consent Form
Date of the Document:	December 27th, 2023

UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE
FRED HUTCHINSON CANCER RESEARCH CENTER
SEATTLE CANCER CARE ALLIANCE

Consent to take part in a research study:

A Window Study of Ixazomib in Untreated Indolent B-NHL

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Funding Support
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University of Washington Medical Center paging operator. Please ask the operator to page the hematology-oncology fellow on call.

We would like you to join this research study.
We are asking you to be in a research study. Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions. The purpose of this consent form is to give you the information you will need to help you decide if you want to be in the study. We do not know if the study drug in this study will help treat non-Hodgkin Lymphoma.

Following is a more complete description of this study. Please read this description carefully. Afterwards, you can ask questions that will help you decide whether to join the study. If you join this study, we would give you a signed copy of this form to keep for future reference.

This consent form may contain words that you do not understand. Please ask the researcher or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

We invite you to join this research study because you have indolent non-Hodgkin B-cell Lymphoproliferative disorder (B-NHL). Up to 36 people will join this study.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions.

You do not have to be in the study. You are free to say “yes” or “no”, or to drop out after joining. If you say “no,” you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

Why are we doing this study?
MLN9708, or Ixazomib, is an experimental drug that is being tested to see if it may be useful in treating patients with indolent non-Hodgkin B-cell lymphoproliferative disorders (B-NHL). Indolent refers to relatively slow development or progression of disease. Indolent B-NHL are cancers that begin in a type of white blood cell that normally fights infection, resulting in their multiplying in an uncontrolled way.

While there are many effective therapies for indolent B-NHL, these diseases are generally not considered curable. Treatments are therefore given to slow or temporarily reverse the progression of disease and improve any symptoms the disease is causing.

In this study, we want to learn what effects, good or bad, Ixazomib has on people with B-NHL both as a single therapy and in combination with rituximab, a proven and effective treatment for B-NHL. If you join this study, we would give you Ixazomib and watch carefully for any side effects.

What research tests, procedures, and treatments are part of this study?
If you decide to join this study, we will do these tests and procedures:

Screening/Baseline:

- **Medical history.** You will be asked questions about your medical history. This includes ongoing conditions you have and drugs you are taking.
- **Physical exam.** Physical exams will assess your overall health status and include measuring your vital signs. This includes blood pressure, heart rate, temperature, and breathing rate. Your weight will also be recorded. You will also be asked how easily you perform daily activities.
- **Routine laboratory tests.** Blood samples will be taken for routine tests. About 2 to 3 teaspoons of blood will be taken and your blood will be tested for levels for certain components to see if it is safe for you to receive treatment. A little over a teaspoon of blood may additionally be taken to perform tests which will give more information about your cancer, if clinically appropriate.
- **Pregnancy test.** If you are a female who could become pregnant, you will have a pregnancy test. Either a blood or urine sample will be taken for this test.
- **Bone marrow testing.** Bone marrow aspiration and biopsy may be done to see if your cancer has spread to the bone marrow. For the bone marrow aspirate, a sample of bone marrow cells is taken by a needle inserted into a bone in your body. For biopsy, a small piece of bone is removed. These tests are done under local anesthesia.
- **Computed tomography (CT) scans.** CT is a medical x-ray imaging method. It provides 3-dimensional pictures of the body and organs by sections. CT scans of the chest, abdomen, and pelvis will be done if there is known/suspected radiographically measurable disease.
- **Magnetic resonance imaging (MRI) scans.** MRI is a medical imaging method. It provides 3-dimensional pictures of the body and organs by sections. MRI may be performed if CT is not possible and there is known/suspected radiographically measurable disease.
- **Positron emission tomography (PET) scan.** PET is another imaging technique. It produces a 3-dimensional picture of processes going on at the cellular level in the body. A whole-body PET may be done if there is known/suspected radiographically measurable disease.
- **Lymph node (tumor) biopsy.** If clinically indicated, a lymph node (tumor) biopsy will be performed. Information from this “fresh” biopsy will be used in this study. In the event that you may have had a clinical lymph node biopsy performed or planned after your previous treatment we will request to use information from that previously-performed clinical biopsy (“archived tissue”). We will not request an additional biopsy for purposes of this study.

Study Drug: Ixazomib

Ixazomib is a new drug that disrupts proteasomes. Proteasomes are found in cells and are responsible for breaking down old or faulty proteins. B-NHL rely on the function of proteasomes to ensure an environment in which they can continue to grow and multiply. Disrupting proteasomes with drugs similar to Ixazomib has proved successful in a number of cancers, including B-NHL. Ixazomib is currently being investigated in clinical

trials and is approved for the treatment of multiple myeloma but not for non-Hodgkin lymphoma.

You are not allowed to take certain medications while in this study as they may cause you to become ill or stop Ixazomib from working. These include the following medications:

strong inhibitors of the CYP1A2 enzyme	strong inhibitors of the CYP3A enzyme	strong inducers of the CYP3A enzyme
• fluvoxamine • Enoxacin • ciprofloxacin	• clarithromycin • telithromycin • itraconazole • voriconazole • ketoconazole • nefazodone • posaconazole	• rifampin • carbamazepine • phenytoin • phenobarbital • rifabutin • rifapentine

While in this study, you are not allowed to take dietary supplements including St John's word and Ginkgo biloba.

Your study doctor will review all of your medications with you. You must tell the study doctor about all medicines that you are taking including vitamins, herbs, and other kinds of therapies. If possible please bring these medications with you to your next visit so your study doctor can check them.

The study drug should be stored in the refrigerator. When it is time for you to take a dose, only *that* dose should be removed from the refrigerator.

Study Treatment:
All patients in this study will receive treatment with Ixazomib. You will be asked to take 4 mg of Ixazomib by mouth once a week. Upon completing the first 24 weeks of treatment, you will receive an additional drug called rituximab as an intravenous infusion. Rituximab is an antibody of CD20, a protein expressed on B cells. It is FDA approved for use in patients with indolent B-NHL. Rituximab will be given once a week for 4 weeks total. You will receive Ixazomib during and after receiving rituximab treatment.

Your study doctor will see you regularly for the duration of the study.

Clinical and Laboratory Evaluations
The evaluations will be conducted at the following time points:

- Within 3 days of each cycle (a cycle is 4 weeks) during the first 8 months of study treatment
- Within 6 days of each cycle thereafter

- **Physical exam.** Physical exams will assess your overall health status and include measuring your vital signs. This includes blood pressure, heart rate,

temperature, and breathing rate. Your weight will also be recorded. You will also be asked how easily you perform daily activities.

- **Routine laboratory tests.** Blood samples will be taken for routine tests. About 2 to 3 teaspoons of blood will be taken and your blood will be tested for levels for certain components to see if it is safe for you to receive treatment. A little over a teaspoon of blood may additionally be taken after the first cycle of therapy to perform tests which will give more information about your cancer.

If there was cancer in your bone marrow prior to treatment, during treatment, at its completion, or a complete remission of the cancer is suspected:

- **Bone marrow testing.** For the bone marrow aspirate, a sample of bone marrow cells is taken by a needle inserted into a bone in your body. For biopsy, a small piece of bone is removed. These tests are done under local anesthesia.

Imaging tests for patients with known/suspected measurable disease:
Every (approximately) 8 weeks for the first 8 months on therapy then every (approximately) 16 weeks thereafter:

- **Computed tomography (CT) scans.** CT is a medical x-ray imaging method. It provides 3-dimensional pictures of the body and organs by sections. CT scans of the chest, abdomen, and pelvis will be done. These will be done to see how your cancer is responding, so your doctor can determine if you should continue on treatment.
- **Magnetic resonance imaging (MR) scans.** MRI is a medical imaging method. It provides 3-dimensional pictures of the body and organs by sections. MRI may be performed if CT is not possible.
- **Positron emission tomography (PET) scan.** PET is another imaging technique. It produces a 3-dimensional picture of processes going on at the cellular level in the body. A PET scan may be performed to see how your cancer is responding, so your doctor can determine if you should continue on treatment.

Optional Research Tests:

- **Optional Bone marrow testing.** Bone marrow aspiration and biopsy may be done during the first two cycles of treatment for correlative research purposes. For the bone marrow aspirate, a sample of liquid bone marrow is taken by a needle inserted into a bone in your body. For biopsy, a small piece of bone is removed. These tests are done under local anesthesia.
- **Optional Lymph node (tumor) biopsy.** If clinically feasible, a lymph node (tumor) biopsy may be performed during your first two cycles of treatment. Information from this “fresh” biopsy will be used for correlative research purposes.

End of Treatment:

- **Physical exam.** Physical exams will assess your overall health status and include measuring your vital signs. This includes blood pressure, heart rate, temperature, and breathing rate. Your weight will also be recorded. You will also be asked how easily you perform daily activities.

- **Routine laboratory tests.** Blood samples will be taken for routine tests. About 2 - 3 teaspoons of blood will be taken. A little over a teaspoon of blood may additionally be taken to perform tests which will give more information about your cancer.
- **Computed tomography (CT) scans.** CT is a medical x-ray imaging method. It provides 3-dimensional pictures of the body and organs by sections. CT scans of the chest, abdomen, and pelvis will be done for patients with known/suspected radiographically measurable disease.
- **Magnetic resonance (MR) scans.** MRI is a medical imaging method. It provides 3-dimensional pictures of the body and organs by sections. MRI may be performed if CT is not possible and there is known/suspected radiographically measurable disease.

Long Term Follow-Up (LTFU): Long-term follow-up means keeping track of your medical condition. In order to do this, we will obtain information from the following.

- **Physical exam.** Physical exams will assess your overall health status. This will be done per clinical standard of care, but a typical follow up schedule will be approximately once every 3 months. These LTFU physical exams can be performed with a local oncologist, not necessarily at the SCCA in Seattle.

We will ask your doctor to send the study team a copy of your medical records. This information will help us learn about the long-term effects of Ixazomib.

You do not have to be in long-term follow-up part of the study. You could say "yes" or "no". Either way, you could still participate in the treatment part of the study.
If you choose not to be in the long-term follow-up part of the study, you would not be contacted regularly, and we would not ask your doctor to send medical records, but we might still need to contact you for some other reason.

How do I take the study drug?
If you decide to take part, you also agree to take the study drug as directed by the study staff.

Your study doctor will give you enough study drug (Ixazomib) to take at home between visits at the SCCA. You will take 4 mg by mouth once a week. You should take your capsules on an empty stomach, at least 1 hour before eating or at least 2 hours after a meal. You should swallow the capsules whole with a sip of water. Do not open, chew, or dissolve the capsules. Be sure to keep the study drug out of reach from children or anyone who may have trouble reading the label.

If you have missed a dose or think you may have taken too many capsules, please tell your study doctor.

If you miss a dose, you can take the capsules as soon as you remember provided the next scheduled dose is more than 72 hours away. A double dose should not be taken to make up for a missed dose.

Unused capsules must be returned to your study doctor.

How long will I be in this study?
You will continue taking Ixazomib weekly for as long as you are tolerating it and your disease is not progressing.

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

- They think it is in your best interest not to continue in the study.
- You are unable or unwilling to follow study procedures.
- The whole study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information cannot be removed from the study records.

You may also withdraw from the study at any time, for any reason. This is your right and there will be no penalty for withdrawing from the study. If you are thinking about dropping out of this study, please tell the study doctor. You and the doctor can talk about what follow-up care and testing would help you the most. If you leave the study, your test results and information which have already been collected cannot be removed from the study records.

If you withdraw yourself from the treatment part of the study, the doctor may ask you if you will continue in the long term data follow-up part of the study.

What are the side effects (risks)?
In this part of the consent form, we tell you the side effects we expect from the tests and treatments in this study. There may be side effects we do not know about yet. If we learn about other side effects, we will tell you.

We carefully watch everyone in the study for side effects. If you want more information about side effects and risks, please ask your doctor or research staff.

Side effects may be mild or very serious. The study team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking Ixazomib. In some cases, side effects can last a long time or never go away and may even result in hospitalization or death

You should talk to your doctor about any side effects that you have while you are in this study. Your doctor will advise you on the appropriate management of side effects, which may include reducing the dose of Ixazomib or taking medicine to control side effects.

Ixazomib

Taking part in this study has risks. Some of these risks we know about. There is also a possibility of risks that we do not know about and have not been seen in humans to date. Please call the study doctor if you have any side effects even if you do not think it has anything to do with this study. Many discomforts and risks go away shortly after the study drug is stopped or with treatment for the discomforts and risks, but in some cases, discomforts and risks may be serious, long lasting, or permanent and may even result in hospitalization or death.

Based on studies of Ixazomib, 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 more common side effects have been observed in more than 10% of patients taking Ixazomib:

- Low platelet count that may increase the chance of bleeding
- Gastrointestinal symptoms including diarrhea, constipation, nausea, and vomiting
- Skin rash that 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
- Nausea
- Vomiting
- Diarrhea
- Swelling or fluid build-up in the arms or legs
- Numbness or tingling or pain feelings in hands and feet
- Back pain
- Lung infections including pneumonia
- Eye symptoms including blurry vision, dry eyes, and conjunctivitis
- Swelling or fluid buildup in the arms or legs
- Flu-like symptoms and other upper respiratory tract infections
- Arthralgia or joint pain
- Lung infections including pneumonia or pneumonitis
- Herpes Zoster that can sometimes cause local pain that may last after recovery from the skin rash and does not go away for some time

Other discomforts and side effects 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
- Impairment of liver function
- 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 creatinine 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)
- Feeling tired or weak
- Chills
- Cough
- Fever
- Headache
- Feeling short of breath or difficulty breathing
- Pain in the abdomen or back
- Muscle weakness
- Feeling dizzy or dizziness
- 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
- Lowered red cells or anemia which may make you feel tired
- Lowered white blood cells called neutrophils that may increase your risk of infection and may be associated with fever
- Constipation
- Pain (muscular) in extremities
- Distortion of the sense of taste, i.e. an abnormal or impaired sense of taste
- Trouble falling asleep, staying asleep, or both
- Lowered red cells or anemia that may make you feel tired

Some discomforts and risks occur with lesser frequency (<1%) than those mentioned above. The following rare, but serious side effects should be noted because they are severe, life-threatening or fatal. With limited experience and because these events occurred while patients were receiving other drugs as well, we do not know if ixazomib causes such problems. Severe, life-threatening or deadly conditions that may involve rash, blistering, skin peeling and mouth sores including Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), Acute febrile neutrophilic dermatosis (Sweet's syndrome) and pemphigus vulgaris, have been reported in ixazomib studies when given in combination with other drugs. These rashes are disorders of the immune system, which differ from regular skin rashes and are generally more severe.

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.

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.

Transverse myelitis, also a rare condition (<1%), is an inflammatory disease causing injury to the spinal cord which has been reported in a patient receiving Ixazomib. This condition may cause varying degrees of muscle weakness, reduced movement in legs, changes in the feelings of the toes and feet, unusual muscle tightness, feelings of pain, changes in bowel (constipation) or urinary (loss of control) function or loss of leg movement. In general, recovery may be partial, complete, or not at all but most patients experiencing transverse myelitis have good to fair recovery of symptoms. We do not know whether Ixazomib causes transverse myelitis, however, as it happened to a patient receiving Ixazomib, we are not able to exclude the possibility that Ixazomib may have contributed to transverse myelitis.

Thrombotic microangiopathy (TMA), including thrombotic thrombocytopenia purpura (TTP) and hemolytic uremic syndrome (HUS), are rare, serious blood disorders that cause low levels of platelets and red blood cells, and result in blood clots in small vessels. Symptoms may include fatigue, fever, bruising, nose bleeds, and decreased urination. These disorders can occasionally be fatal. TMA, TTP, and HUS have been seen rarely (<0.1 in patients treated with ixazomib).

Overdose has been reported in patients taking ixazomib. Reports of accidental overdose have been associated with risks such as nausea, lung infections including aspiration pneumonia, multiple organ failure, and death. It is important to take only one dose of ixazomib at a time, and only at the prescribed intervals.

Ixazomib should not be taken if you have ever had an allergic reaction to the active substance or any of the inactive ingredients used in its formulation.

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

Other Side Effects

- By participating in this study, it may be possible to develop a resistance to Ixazomib. Such a resistance could impact the effectiveness of future cancer treatments.
- Ixazomib should not be taken if you have ever had an allergic reaction to boron or boron containing products.

- Tumor Lysis Syndrome may occur as a result of taking Ixazomib. Tumor Lysis Syndrome is the rapid death of cancer cells that may let large amounts of the cells into the blood that injures organs, such as kidneys.
- Possible more severe but rare side effects, 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.

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.

Reproductive Risks

Female subjects:

We do not know if the study drug Ixazomib will affect mother's milk or an unborn child. Therefore, breast-feeding and pregnant women are not allowed to take part in the study. Due to unknown risks and potential harm to the unborn child/ infant, you should not become pregnant or nurse a baby while on this 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.	

You must use birth control methods as directed above, unless you completely avoid having heterosexual intercourse.

Male subjects:

We do not know if using Ixazomib will affect sperm. Therefore, due to potential risk, you should not get your partner pregnant during the study drug treatment period (including interruptions in treatment). 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. Or, you should completely avoid having heterosexual intercourse.

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.

Rituximab
All patients will receive rituximab and will receive medications before rituximab to reduce the likelihood of infusion-related reactions. In 100 people receiving Rituximab, more than 20 and up to 100 people may have reported one or some of the side effects listed below. The most common side effects related to the antibody rituximab include:

- Fever
- Chills
- Rigors (muscle stiffening)
- Nausea
- Fatigue
- Decrease in white blood cells or B-cells (a type of white blood cell) that can increase your risk of developing an infection
- Numbness and tingling of the arms and legs
- Tiredness

In 100 people receiving Rituximab, 4 to 20 people may report the following side effects:

- Bruising, bleeding
- Abnormal heartbeat
- Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness
- Sores in eye
- A tear or a hole in the stomach that may require surgery
- Diarrhea, vomiting
- Pain
- Swelling of the body
- Hepatitis, or liver damage which may cause yellow eyes and skin
- Dizziness, headache
- Kidney damage which may require dialysis
- Cough
- Scarring of the lungs

- Stuffy nose
- Blockage of internal organs which may cause shortness of breath, wheezing, vomiting
- Increased sweating
- Itching, rash, blisters on the skin
- Severe skin rash with blisters and peeling which can involve mouth and other parts of the body
- Low blood pressure which may cause feeling faint

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:

- Pulmonary (lung) failure
- Seizure
- Kidney failure requiring dialysis or resulting in death
- Heart problems including chest pain (angina) and life-threatening irregular heartbeats
- Damage to the brain caused by a virus which may result in tiredness, weakness, changes in thinking and disability. This is called Progressive Multifocal Leukoencephalopathy (PML).

Allergic Reactions: Severe reactions from the initial infusion of rituximab have been reported. In some cases, these reactions were fatal. Signs and symptoms of severe allergic reactions include changes in blood pressure, shortness of breath or asthmatic-like conditions, and development of hives or welts beneath the skin.

Rituximab may also have an effect on the nervous system called posterior reversible encephalopathy syndrome (PRES) or reversible posterior leukoencephalopathy syndrome (RPLS), which is a neurological condition with symptoms of headache, nausea and vomiting, seizures, visual disturbances, and is often associated with an abrupt increase in blood pressure.

Severe mucous membrane reactions: Rarely, severe allergic-type skin reactions have been reported in patients who have received rituximab treatment. Some of these events have been fatal. The timing of these reactions has varied from 1 to 13 weeks following rituximab treatment. Depending on the type and extent of the skin changes, whether there is involvement of the mucous membrane (tissue lining or cover parts of the body such as the mouth and eyes), whether the reaction is localized or involves all of the body skin or mucous while you are on or off rituximab treatment, you should report these immediately to your study doctor so that he/she can determine whether you might be having an allergic reaction. Your study doctor will then take the appropriate steps to help you manage the reaction.

Stomach pain and bowel problems: Serious stomach and bowel problems such as bowel obstruction (blockage of the small or large intestine) and bowel perforation (development of a hole in the small or large intestine) have been seen in some patients. In some cases, these events were fatal. A relationship between rituximab and these

events has not been established. The average time for rituximab patients to develop a bowel perforation was 6 days from the start of therapy. If abdominal pain is experienced, especially early in treatment, you should contact your study doctor immediately.

Hepatitis B virus (HBV) reactivation and other viral infections: In people who have ever been infected with hepatitis B virus, there is a risk that the virus can flare up during treatment with drugs that affect your immune system, such as rituximab. This could lead to liver failure or even death. This risk of hepatitis B virus flaring up may continue for several months after you stop taking rituximab. If you become jaundiced (yellowing of the skin and eyes) or develop viral hepatitis while taking rituximab or after stopping treatment, you should tell your study doctor immediately. Your study doctor will discuss this risk with you and explain what testing is recommended to check for hepatitis.

The following additional serious viral infections, either new, reactivated or made more severe, have been reported in some patients receiving rituximab in combination with chemotherapy. These viral infections include JC virus (which can lead to PML, a rare and often fatal brain disease), cytomegalovirus (CMV), herpes simplex virus, parvovirus B19, varicella zoster virus, West Nile virus, and hepatitis C. In some cases, the viral infections occurred up to one year after stopping rituximab and resulted in death. Because there are no warning signs of PML, you should contact your study doctor immediately if you experience major changes in vision or unusual eye movements, loss of balance or coordination, and periods of disorientation or confusion. You should also contact your study doctor right away if you have a persistent cough, fever, chills, congestion, or any flu-like symptoms while receiving rituximab (or several months after discontinuation of rituximab therapy). These symptoms may be signs of a serious infection.

Blood Draws
Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or get an infection. Infection rarely happens. There may be redness and irritation at the place where the needle enters your vein.

Bone marrow aspiration and biopsy
Complications from a bone marrow aspiration and biopsy include pain, infection and bleeding.

Lymph node (tumor) biopsy
The risks of a lymph node biopsy are pain, bruising, bleeding and very rarely, infection.

Risks from other procedures
There is a very rare chance of developing allergic dermatitis. This is itching and redness of the skin due to the sticky pads used for EKG tests.

What are the benefits?
We do not know if this study will help you. We are testing Ixazomib to see its effects on people with indolent B-NHL. You might get better after receiving Ixazomib, but your condition could stay the same or worsen. We hope the information from this study will help other people with indolent B-NHL in the future.

The information developed in this study may help patients with cancer in the future. Your participation in this research study may contribute to the development of commercial products from which Millennium Pharmaceuticals, Inc. or others may derive an economic benefit. You will have no rights to any patents or discoveries arising from this research, and you will receive no economic benefit.

You have other choices besides this study.
You do not have to join this study. You are free to say "yes" or "no". Your regular medical care will not change if you decide to say "no" and not take part in this study

If you do participate in this study, you have other choices for treatment. Each of these has risks and benefits. You should talk to your doctor about these choices.

Your other choices may include:

- Another research treatment
- Standard treatment
- No treatment
- Comfort care

Enrollment in this study may exclude you from other research studies.

Protecting your Privacy as an Individual and the Confidentiality of Your Personal Information
Some people or organizations may need to look at your research and medical records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- Millennium Pharmaceuticals and their agents.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Research Center IRB. An IRB is a group that reviews the study to protect your rights as a research participant.
- Fred Hutchinson Cancer Research Center, University of Washington, and Seattle Cancer Care Alliance.
- US National Institutes of Health, National Cancer Institute, Office for Human Research Protections, Food and Drug Administration, and other agencies as required.

These people are interested in study data, not your personal information. *Personal information* is information that can identify you. It may include your name, date of birth, social security number, phone number, or other information.

We will do our best to keep your personal information confidential. But we cannot guarantee total confidentiality. Your personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use your personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

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.

If you join this study, information about participation would be made part of your permanent medical record. This information would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.

Financial disclosure statement.
The maker of Ixazomib, Millennium, is providing funding support and study drug.

Will you pay me to be in this study?
You may be able to receive reimbursement for certain travel-related costs. Reimbursement is available at $0.575 per mile traveled, roundtrip, per each study visit for a maximum of $150 per visit. Please speak to a member of the study team for additional information.

How much will this study cost me?
There are some extra costs for being in this study. You or your insurer will have to pay these costs. Some insurers will not pay for research. Check with your insurer before you join this study.
The costs are:

- Cost of tests that may be performed more often than per typical standard practice to monitor your health while you are receiving treatment.
- Cost of standard doctor visits and lab tests.
- Cost of any other medical care you may need because of this study.

You or your insurer will have to pay for the costs of treating your cancer in this study.

You will **not** be billed for:

- The Ixazomib itself.
- Any research testing done on your tissue or blood solely for the purposes of this research study.
- Optional bone marrow and tumor biopsy testing performed during the first two cycles of this study.

What if I get sick or hurt in this study?

For a life threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

If you get sick or hurt in this study, tell your study doctor in person or call Dr. Gopal at 206-606-2035.

If you have a research related injury or illness, a limited amount of free medical treatment may be available at approved locations. Limited funds may be available to pay for treatment at other locations. You or your insurer will be billed for any additional costs. The study staff can provide more information.

There are no funds to pay you for loss of work or other costs, lost time, or pain to you or your family. You or your insurer will be billed for treatment of problems that results from your cancer or from standard clinical care.

For all other medical problems or illness related to this research, immediately contact the study team. They will treat you or refer you for treatment. You or your health insurance will have to pay for the treatment. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You will not lose your legal right to seek payment for treatment if you sign this form.

Your Rights

- You do not have to join this study. You are free to say yes or no. Your regular medical care will not change.
- If you join this study, you do not have to stay in it. You may stop at any time (even before you start). There is no penalty for stopping. Your regular medical care will not change.
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.

During the study, we may learn new information you need to know. For example, some information may affect your health or well-being. Other information may make you

change your mind about being in this study. If we learn these kinds of information, we will tell you.

For more information
If you have questions or concerns about this study, you may talk to your doctor anytime. Other people you can talk to are listed below.

If you have questions about:	**Call:**
This study (including complaints and requests for information)	206-606-2037 (Dr. Gopal, Principal Investigator)
If you get sick or hurt in this study	206-606-2037 (Dr. Gopal, Principal Investigator)
Your rights as a research participant	206-667-5900 (Institutional Review Office, Fred Hutchinson Cancer Research Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	206-606-1377 (Patient Financial Services, Seattle Cancer Care Alliance)

Emergency number (24 hours): 206-598-6190
University of Washington Medical Center paging operator. Please ask the operator to page the hematology-oncology fellow on call.

Optional Research Tests

Please indicate which kinds of samples you are willing to allow the study team to use in this study by checking yes or no in the appropriate box provided below:

☐ Yes ☐ No **Bone Marrow Testing**

If you agree to share samples of bone marrow, the test may be done during the first two cycles of treatment for correlative purposes.

☐ Yes ☐ No **Tissue Sample from a biopsy or surgery**

If you agree to share samples of a lymph node (tumor), a sample may be taken during a biopsy during the first type cycles of treatment if clinically feasible.

CONSENT

I have read this consent form (or it has been read to me). All my questions about the study and my part in it have been answered. I freely consent to be in this research study.

By signing this consent form, I have not given up any of my legal rights.

_____
Subject Name (printed)

_____ _____
Signature of Subject Date

_____
Name of Person Conducting Informed Consent Discussion (printed)

_____ _____
Signature of Person Conducting Informed Consent Discussion Date

---------- Use this section only if applicable ----------

If this consent form is read to the subject because the subject is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject. The subject freely consented to be in the research study.

_____
Printed Name of the Impartial Witness

_____ _____
Signature of the Impartial Witness Date

If you served as an interpreter or witness during the consent process, sign below to indicate you attest to the accuracy of the presentation to the participant and the apparent understanding of the research by the participant.

_____
Printed Name of Interpreter

_____ _____
Signature of Interpreter Date

Copies to: Participant,
Medical Records,
Research File