Medical Research Informed Consent

Title of Study: 2019-135: A Phase II Study Evaluating Safety and Efficacy of Polatuzumab Vedotin in Combination with Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone in Patients with Previously Untreated Double and Triple Hit Lymphoma, Double Expressor Lymphoma, and High-Grade B Cell Lymphoma

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Key Information about this Study

This is a research clinical trial that is assessing whether medications Polatuzumab Vedotin with R-CHP is an effective treatment for patients with untreated double, or triple hit, double expressor, and high-grade B cell lymphoma. Participation in this trial is strictly voluntary.

This trial will require patients to attended approximately 25 clinic visits. These visits consist of a screening visit where your eligibility for the trial will be confirmed through various tests and health assessments. Should you be deemed eligible and you wish to participate in this trial, you will sign this consent form and be enrolled into the study. Once enrolled you will attend two clinic visits per cycle (a cycle lasts 21 days) for up to 6 cycles. During these cycle visits your health will be assessed through various tests, scans, and assessments and you will receive the study medication of Polatuzumab Vedotin with R-CHP. Once you have completed your treatment per-protocol or per the PI's discretion, you will attend an end of treatment visit where your overall health and response to the treatment will be assessed. The study team will follow your health status for up to 5 years after your last treatment dose. During this follow up period, you will have to come to clinic for a follow up visit once every 3 months for the first 2 years and then every 6 months for the remaining 3 years, unless you withdraw from the study, your disease progresses and/or you start a new anti-cancer treatment. A detailed list of the tests, procedures, and assessments that will occur at each visit can be found below in the procedures section of this document.

There are risks involved with this trial that range from common to extremely rare. A detailed list of risks associated with each study drug and procedure can be found below in the appropriate sections. There may be no direct benefit for you; however, information from this study may benefit other people with similar health issues now or in the future.

Finally, instead of enrolling on to this trial there may be alternative treatment options such as receiving other standard treatments or therapies to treat your condition. There could also be other

experimental drugs may be available through other clinical trials. Your doctor or members of the study staff will discuss alternative treatments with you.

Purpose

You are being asked to be in a research study of Polatuzumab Vedotin with R-CHP because you have untreated double or triple hit lymphoma, double expressor or high-grade B cell lymphoma. This study is being conducted at the Karmanos Cancer Institute (KCI) as well as other possible clinical institutions in the future. This study is being conducted by Dipenkumar Modi, MD at KCI, although certain services you may receive in connection with your care and treatment may be provided at facilities of the Detroit Medical Center. The University Physician Group may also provide services. The estimated number of study participants to be enrolled during the stage 1 portion of this trial is about 15 participants across all participating institutions. A total of about 34 participants will be enrolled at other sites and Karmanos Cancer Institute throughout the United States during the second stage of this trial. This trial will enroll approximately 49 total participants. Karmanos Cancer Institute is the sponsor of the study and Genentech will provide funding, as well as the study medication, polatuzumab vedotin. **Please read this form and ask any questions you may have before agreeing to be in the study.**

This study evaluates the safety and efficacy of combining the use of two therapies, R-CHP and polatuzumab vedotin, for the treatment of double ,triple hit lymphoma, and double expressor and high-grade B cell lymphoma. R-CHP is the abbreviated name for the combination of drugs that is commonly used as chemotherapy for your type of cancer. These drugs are rituximab, cyclophosphamide, doxorubicin, and prednisone. The study drug, polatuzumab vedotin, works by binding with cancer cells and releasing another chemotherapy drug, called monomethyl auristatin E (MMAE) via a protease-cleavable linker into the cell causing the cancer cells to die or stop growing.

Polatuzumab Vedotin is made by Genentech and is currently FDA approved to treat Diffuse Large B-Cell Lymphoma that has recurred after other treatments. Polatuzumab Vedotin is considered investigational for the initial treatment of double and triple hit lymphoma, and double expressor, and high-grade B cell lymphoma. This means it has not been approved by the U.S. Food and Drug Administration (FDA), Health Canada, the European Medicines Agency, (EMA) or any other national competent authority. This study will examine the effects of polatuzumab vedotin + R-CHP on your cancer and on your body including any side-effects that you may experience. This combination of drugs (R-CHP) has already been used together in Diffuse Large B-Cell Lymphoma.

This study has two components: Stage 1 and Stage 2. The primary objective for the Stage 1 part is to measure the response to the polatuzumab vedotin + R-CHP chemotherapy. If two or fewer patients respond to this treatment regimen study, accrual will be suspended. If three or more patients enrolled in stage 1 respond to this treatment regimen the study will move into stage 2. In stage 2, enrollment will be expanded to a total of 49 patients. The polatuzumab vedotin + R-CHP treatment regimen will remain the same throughout stage 1 and stage 2. The overall objective of this study is to measure the safety, efficacy, and overall rate of complete remission (CR) in study patients treated with polatuzumab vedotin + R-CHP therapy.

You will receive up to 6 cycles of polatuzumab vedotin + R-CHP chemotherapy. You will also receive a PET scan in-between cycles 3 and 4 of treatment to evaluate your response to therapy. Each cycle will last approximately 21 days. Your health status and disease will be followed for up to 5 years after your last dose of polatuzumab vedotin.

Study Procedures

If you agree to take part in this research study, and have signed this form, you will enter screening which can last up to 28 days before you receive your 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 these tests or procedures recently, they may or may not have to be repeated. If all tests and procedures need to be completed, it will take approximately 6-8 hours. The following procedures will be performed:

Screening Visit Tests and Procedures

- Written informed consent will be collected
- Medical history (this will include any medications you have used or are currently using for any other conditions)
- Tumor biopsy: These samples will be collected and tested to look at your disease at the beginning of the study to examine the abnormal tumor cells and also the surrounding normal cells in your tissue. If you have already had a prior tumor biopsy done as part of your lymphoma diagnosis workup, then there is no need to repeat the biopsy.
- Bone marrow aspirate/biopsy: This procedure may be performed if your physician requires it to look for lymphoma in your bone marrow before treatment. These samples will be collected and tested to look at your disease at the beginning of the study to examine the abnormal lymphoma cells and the normal blood-forming cells in your bone marrow. If you have already had a prior bone marrow aspirate/biopsy done as part of your lymphoma diagnosis workup, then there is no need to repeat the biopsy.
- Physical exam, including assessment of peripheral neuropathy (nerve pain) and including measurements of height, weight and vital signs (temperature, blood pressure, pulse, heart rate, and breathing rate)
- ECOG performance status- to evaluate your ability to perform everyday activities.
- PET/CT scan of head to mid-thigh. Performed to evaluate measurable disease at the beginning of treatment
- CT/MRI scan with contrast of neck, thorax and abdomen/pelvis. Performed to evaluate measurable disease at the beginning of treatment
- Blood samples will be obtained to evaluate your disease, to check for HIV and Hepatitis, and also to evaluate how your bone marrow, heart, kidneys, and liver are working, as well as whether your blood clots normally. This will include approximately 50 mL (10 teaspoons) of blood.
- Serum pregnancy test if you are a woman who is able to have children (the test must be negative in order for you to continue your participation in this research study)
- Echocardiogram (ECHO) or multi-gated acquisition (MUGA) scan is a test to see how well your heart is working

- Electrocardiogram (ECG) is a test that measures the rhythm of your heart
- Confirmation of eligibility for trial

At the discretion of the study doctor, you may be required to take 100mg tablet of the prednisone orally every day for up to 13 days leading up to your cycle 1 day 1 visit. The purpose of this is to control any tumor related symptoms prior to beginning your treatment.

Treatment Visit Tests and Procedures

You will have the following tests and procedures on Day 1 of each cycle. These visits may take approximately 4-6 hours.

- Physical exam, including assessment of peripheral neuropathy (nerve pain) and including measurements of weight and vital signs (temperature, blood pressure, pulse, heart rate, and breathing rate)
- Medical history (this will include any medications you have used or are currently using for any other conditions)
- Check for any adverse effects you may be experiencing
- Review of any symptoms you may be experiencing
- Having your ability to perform everyday activity evaluated
- Blood tests will be taken to determine your organ function and how well you are responding to the study treatment. This will include approximately 50 mL (10 teaspoons) of blood. Weekly blood draws may be required if determined by the study doctor for those patients with a history of diabetes.
- Serum or urine pregnancy test if you are a woman who is able to have children (the test must be negative in order for you to continue your participation in this research study)
- IV administration of Polatuzumab Vedotin + R-CHP chemotherapy. The dose will be determined based on your weight during the screening portion of this study.
- **Intrathecal methotrexate 15 mg as CNS prophylaxis on either day 1, 2 or 3 of each cycle of therapy**
- CT/MRI scan with contrast of neck, thorax and abdomen/pelvis
- An additional PET/CT scan will be done between Day 15 of Cycle 3 and Day 15 of Cycle 4 only to assess your body's response to treatment

You will have the following tests and procedures on Day 3 of each cycle. These visits may take approximately 4-6 hours.

- Will be given a bone marrow stimulant (Neupogen or Neulasta) as a precaution to help regrow white blood cells

End of Treatment Visit Tests and Procedures

Your end of treatment visit will occur within 30 days of your last dose of study treatment. You will have the following tests and procedures completed and it will take approximately 4-6 hours to complete:

- Physical exam, including assessment of peripheral neuropathy (nerve pain) and including measurements of weight and vital signs (temperature, blood pressure, pulse, heart rate, and breathing rate)

- Medical history
- Check for any adverse effects you may be experiencing
- Review of any medications you are taking
- Review of any disease related symptoms you may be experiencing
- Having your ability to perform everyday activity evaluated
- CT/MRI scan with contrast of neck, thorax and abdomen/pelvis. CT will be performed 6-8 weeks after last dose of study treatment.
- PET/CT scan will be taken to assess your body's response to treatment. This will occur 6-8 weeks after the last dose of study treatment.
- For patients with bone marrow involvement at screening, a repeat bone marrow biopsy at the end of treatment is warranted to assess response.

At time of Suspected or Known Progression: You will have the following tests and procedures completed and it will take approximately 4-6 hours to complete:

The following tests and procedures may be performed at any time if you have suspected or known progression:

- Physical exam, including assessment of peripheral neuropathy (nerve pain) and including measurements of weight and vital signs (temperature, blood pressure, pulse, heart rate, and breathing rate)
- Having your ability to perform everyday activity evaluated
- Medical history
- Tumor biopsy: This sample will be collected only if your doctor determines it is needed. This sample will be collected to look at your disease, but will not be kept for study purposes.
- Review of any disease related symptoms you may be experiencing
- CT/MRI scan with contrast of neck, thorax and abdomen/pelvis
- PET/CT scan will be taken to assess your body's response to treatment

Follow Up Visit Tests and Procedures

You will be required to come in for follow up clinic visits after your end of treatment visits for 5 years. These visits will happen once every 3 months for the first 2 years after discontinuation of study treatment and then every 6 months for the remaining 3 years unless you with draw your consent, your disease progresses and/or you start a new cancer therapy. These visits will last for about 4-6 hours. The following tests and procedures will be conducted at each follow up visit:

- Review of medical history
- Physical exam, including measurements of weight and vital signs (temperature, blood pressure, pulse, heart rate, and breathing rate)
- Check for any adverse effects you may be experiencing
- Review of any medications you are taking
- Review of any disease related symptoms you may be experiencing
- Having your ability to perform everyday activity evaluated
- Blood tests will be taken to determine your organ function.
- CT/MRI scan will be taken to assess your body's response to treatment

Benefits
As a participant in this research study, there may be no direct benefit for you; however, information from this study may benefit other people with similar health issues now or in the future.

Risks
You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study. Some risks described in this consent document, if severe, may cause death.

Study Drug Related Risks

Risks Associated with Polatuzumab Vedotin
Polatuzumab vedotin has had limited testing in humans. The known side effects of this study drug, as well as potential side effects based on human and laboratory studies or knowledge of similar drugs, are listed below. There may be side effects that are not known at this time.

Known Side Effects	
(Very common side effects (occurring in ≥ 1/10 patients)	
• Neutropenia (low numbers of neutrophils, or white blood cells) Neutrophils are a type of white blood cell that helps fight infections in your body. Low neutrophil counts may increase your risk of serious infections. Anemia (low number of red blood cells). Red blood cells contain hemoglobin and carry oxygen to different parts of the body. Some of the side effects of low red blood cells include dizziness, fatigue, lightheadedness, pale skin, fast heart rate, and shortness of breath. Thrombocytopenia (low number of platelets). Platelets are a type of blood cell that helps the body to control bleeding. Some of the side effects of low platelet count include easy or excessive bruising, superficial bleeding into the skin that appears as a rash of pinpoint sized reddish-purple spots, prolonged bleeding from cuts, or	• Peripheral sensory and/or motor neuropathy (tingling, pain, numbness, sensation of pins and needles in arms and/or legs, weakness, and imbalance) • Infections like pneumonia (including fungal pneumonias) and other infections, including viral infections such as shingles. Some of these infections can be serious or lead to death. • Gastrointestinal disturbance (such as vomiting, diarrhea, nausea, constipation, and abdominal pain) • Infusion-related reactions, which could include symptoms such as fever, chills, skin rash, nausea, vomiting, headache, cold-like symptoms, difficulty breathing, or shortness of breath.

bleeding from gums or nose	
Uncommon Side Effects (occurring in < 1/100 patients)	
• Serious infection of the blood (sepsis), which may be fatal. Including serious infection of the blood in addition to a reduction in white blood cells (neutropenic sepsis) and serious infection of the blood and low blood pressure (septic shock), which may be fatal.	
Unknown Frequency	
• Allergic reactions which may be mild (such as a skin rash or hives) to severe (such as breathing difficulties or shock).	
Potential Side Effects	
• Side effects on reproduction and fertility (the ability to become pregnant) • High levels of blood sugar; if severe may require hospitalization and urgent treatment • Fatigue • Hair loss • Alteration of taste • Eye disorders including blurring of vision • Progressive multifocal leukoencephalopathy or PML (a rare viral infection of the brain) • Immunogenicity (anti-drug antibodies, proteins made in the body that respond to a substance that is foreign to the body by your immune system, may be developed by your immune system)	• Changes in your liver, including abnormalities in liver function tests and/or changes in the appearance of the liver on imaging scans • Joint pain/arthralgia/skeletal pain • Changes to heart rhythm • Tumor lysis syndrome (metabolic abnormalities caused by the rapid destruction of a large number of tumor cells). Tumor lysis syndrome may be mild (resulting in some minor changes in blood tests) to severe (resulting in kidney damage), or life threatening. • Secondary malignancies (with other anti-cancer agents) • Lung damage (interstitial lung disease) • Weight loss • Weakness • Loss of appetite • Shortness of breath

Risks Associated with Rituximab or biosimilar

The side effects associated with rituximab are listed below. There may be side effects that are not known at this time.

Possible Side Effects of Rituximab (Table Version Date: July 13, 2023)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Rituximab, more than 20 and up to 100 may have:
• Infection, possibly in the blood, especially when white blood cell count is low • Anemia which may require blood transfusion • Nausea • Reaction during or following infusion of the drug • Numbness and tingling of the arms, legs, fingers, and/or toes

COMMON, SOME MAY BE SERIOUS In 100 people receiving Rituximab, more than 20 and up to 100 may have:
• Chills, fever • Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Rituximab, from 4 to 20 may have:
• Abnormal heartbeat which may cause fainting • High blood pressure which may cause headaches, dizziness, blurred vision • Low blood pressure which may cause feeling faint • Swelling of arms, legs • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Swelling and redness of the throat and sinuses (might not be caused by infection) which may cause difficulty breathing and swallowing • Bruising, bleeding • Prior liver infection that returns which may cause yellow eyes and skin, tiredness • Tumor lysis syndrome which may cause kidney damage which may require dialysis • A tear or a hole in the bowels that may require surgery • Sores in mouth which may cause difficulty swallowing • Belly pain, diarrhea, vomiting • Depression • Headache, dizziness • Pain in back, muscles, joints • Cold symptoms such as stuffy nose, sneezing, sore throat • Itching, rash, blisters on the skin

RARE, AND SERIOUS In 100 people receiving Rituximab, 3 or fewer may have:
• Heart attack which may cause chest pain, shortness of breath • Heart stops beating • Brain damage, progressive multifocal leukoencephalopathy (PML), which may cause tiredness, changes in thinking • Damage to the lungs which may result in shortness of breath, cough, wheezing • Stevens-Johnson syndrome which may cause severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Risks Associated with Cyclophosphamide, Doxorubicin, and Prednisone

Important side effects associated with cyclophosphamide, doxorubicin, and prednisone are listed below. The study doctor will provide information about these and other side effects. There may be side effects that are not known at this time.

Possible Side Effects of Cyclophosphamide (Table Version Date: May 4, 2021)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cyclophosphamide, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • Anemia which may cause tiredness, or may require transfusion • Bruising, bleeding • Blood in urine • Nausea, vomiting, diarrhea, loss of appetite, pain in belly • Sores in mouth which may cause difficulty swallowing • Absence of menstrual period which may decrease the ability to have children • Hair loss, skin changes, rash, change in nails

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cyclophosphamide, from 4 to 20 may have:
• Fluid around the heart • Damage to the bone marrow (irreversible) which may cause infection, bleeding, may require transfusions • Loss or absence of sperm which may lead to an inability to father children

RARE, AND SERIOUS In 100 people receiving Cyclophosphamide, 3 or fewer may have:
• Damage to the heart or heart failure which may cause shortness of breath, swelling of ankles, cough or tiredness • Swelling of the body including the brain which may cause dizziness, confusion • Damage to the lungs or scarring of the lungs which may cause shortness of breath • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Sinusodial obstructive syndrome (SOS) which may cause damage to the liver, yellowing of eyes and skin, swelling • Kidney damage which may cause swelling, may require dialysis • A new cancer (including leukemia) resulting from treatment of a prior cancer • Stevens-Johnson syndrome which may cause severe skin rash with blisters and peeling which can involve mouth and other parts of the body

Possible Side Effects of Doxorubicin (Table Version Date: October 15, 2020)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Doxorubicin, more than 20 and up to 100 may have:
• Nausea, vomiting • Red colored urine, saliva, or sweat • Hair loss

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Doxorubicin, from 4 to 20 may have:
• Heart failure or heart attack which may cause shortness of breath, swelling of ankles, cough or tiredness which may occur years after the dose • Abnormal heartbeat • Damage to the lungs which may cause shortness of breath when combined with radiation • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may cause tiredness, or may require transfusion • Kidney damage which may require dialysis • Sores in the mouth or throat • Belly pain • Diarrhea, dehydration • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Absence of menstrual period or early menopause • Damage to sperm • Muscle weakness • Damage to the skin which may cause pain • Swelling and redness at the site of the medication injection or area of previous radiation • Changes to the nails • Darkening of the nail beds or skin or hands and feet • Darkening of the gums

RARE, AND SERIOUS In 100 people receiving Doxorubicin, 3 or fewer may have:
• Severe blood infection • Damage to the bone marrow, caused by chemotherapy, which may result in leukemia (cancer of the bone marrow)

Possible Side Effects of Prednisone (Table Version Date: February 4, 2022)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Prednisone, more than 20 and up to 100 may have:
• High blood pressure which may cause headaches, dizziness, blurred vision • Swelling of the body, tiredness, bruising

COMMON, SOME MAY BE SERIOUS In 100 people receiving Prednisone, more than 20 and up to 100 may have:
• In children and adolescents: decreased height • Increased appetite and weight gain in the belly, face, back and shoulders • Pain in belly • Loss of bone tissue • Difficulty sleeping • Mood swings • Skin changes, acne

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Prednisone, from 4 to 20 may have:
• Irregular heartbeat • Heart failure • Blood clot which may cause swelling, pain, shortness of breath • Infection • Diabetes • Cloudiness of the eye, visual disturbances, blurred vision • A tear or a hole in the bowels which may cause belly pain or that may require surgery • Heartburn • Glaucoma • Damage to the bone which may cause joint pain and loss of motion • Numbness and tingling of the arms, legs, and upper body • Muscle weakness • Non-healing wound

RARE, AND SERIOUS In 100 people receiving Prednisone, 3 or fewer may have:
• Tiredness and low blood pressure which may cause feeling faint • Bleeding from sores in the stomach • Broken bones

Possible Side Effects of Methotrexate when given by spinal tap (Table Version Date: August 5, 2022)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Methotrexate, more than 20 and up to 100 may have:
• Headache • Nausea

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Methotrexate, from 4 to 20 may have:
• Swelling of the brain which may cause blurred vision, and/or confusion • Damage to the brain which may cause changes in thinking • Anemia which may require blood transfusions

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Methotrexate, from 4 to 20 may have:
• Bruising, bleeding • Infection, especially when white blood cell count is low • Pain • Vomiting • Confusion, dizziness • Difficulty with speaking • Tiredness • Rash

RARE, AND SERIOUS In 100 people receiving Methotrexate, 3 or fewer may have:
• Seizure • Damage to the brain which could lead to coma • Paralysis, weakness • Bleeding into the space of the spine at the site of the injection

Supportive Care Medications:

The following medications listed below will be given prior to the study medications listed above to prevent an infusion reaction or potential side effects from those medications.

Acetaminophen: The side effects you might experience with acetaminophen may be liver failure, inflammation of the lungs (pneumonitis) or a risk of rare but serious skin reactions (such as reddening of the skin, rash, blisters, and detachment of the upper surface of the skin). These severe skin reactions usually caused by adverse drug reactions and that predominantly involve skin and mucous membranes are known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can be fatal.

Diphenhydramine: The side effects you might experience with diphenhydramine may be sleepiness or life- threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure).

Risks Associated with Neupogen/Udenyca or Neulasta

Possible risks in greater than 10% of participants:

- Muscle and joint pain

Possible Risks in 1-10% of participants:

- **Limb pain**

Possible risks in less than 1% of participants:

- Fluid build in your lungs (Acute respiratory distress syndrome)
- Allergic Reaction (anaphylaxis)
- antibody development,
- Fluid and proteins leaking out of blood vessels (capillary leak syndrome)
- Skin redness
- Inflamed Kidneys (glomerulonephritis)
- Reddish-Purple skin lesions on lower limbs (hypersensitivity angiitis)
- Redness/inflammation at injection site ,
- Raise white cell count (leukocytosis)
- Local inflammation of the aorta (aortitis),
- Bleeding from lungs (pulmonary alveolar hemorrhage)
- Immune response (severe hypersensitivity)
- Sickle cell crisis in patients with Sickle Cell Hemoglobinopathy
- Skin Rash
- Enlarged Spleen (splenomegaly) rarely leading to rupture of the spleen.
- Sweet's syndrome (skin disease causing fever, elevated white blood cells, skin lesions)
- Hives
- **Thrombocytopenia** (low blood platelet level)

Allergic Reaction Risks

As with taking any drug, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Rash
- Wheezing and difficulty breathing
- Dizziness and fainting
- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

Please seek treatment immediately and tell the study doctor and study staff if you have any of these symptoms.

Pregnancy Risks

Participation in this study involves unknown risks to women who are or may become pregnant, to unborn babies, and to nursing infants. Therefore, to minimize the risks and to take part in this study, medically acceptable forms of birth control are required by (a) women during the study for at least 12 months after the study drug has been stopped and (b) men during the study and for at least 6 months after the study drug has been stopped. This will be explained below.

Medically acceptable birth control may include the following methods: barrier protection—such as condoms used with contraceptive jelly, intrauterine devices (IUD), and abstinence (not having sex). Oral contraceptives may be used, but should not be the only means of protection. The use of medically acceptable birth control may not be necessary if the female partner has had permanent hysterectomy (sterilization) with some form of tubal occlusion, or if the male partner has had a vasectomy (so long as the female partner does not get a new partner). No birth control method completely eliminates the risk of pregnancy.

For women: If you can become pregnant, you must use a reliable birth control method during the study and for, 12 months after your final dose of polatuzumab vedotin, 12 months after your final dose of rituximab, 12 months after your final dose of cyclophosphamide, doxorubicin, and prednisone, as applicable. You must not donate eggs during this same period. Talk with your study doctor about what method may be best for you. Tell your study doctor right away if you get pregnant during the study, or within 3 months after your last dose of study drug, or within 12 months after the last dose of rituximab.. If you get pregnant, the study doctor will want to follow up with you until the outcome of the pregnancy is known.

For men: If your partner is able to become pregnant, you must use a condom during the study and for 5 months after your final dose of polatuzumab vedotin, 3 months after your final dose of rituximab, 6 months after your final dose of cyclophosphamide, doxorubicin, prednisone, as applicable. Talk with your study doctor about what method may be best for you. You must not donate sperm during this same period. If your partner is pregnant, you must still use a condom. Tell your study doctor right away if your partner gets pregnant during the time periods listed above (when contraception with a condom is required). The study doctor may ask you and your partner for permission to collect information about the pregnancy and the baby. No matter what you and your partner decide, you can continue to take part in this study.

In order to participate in this study, you must use at least two forms of medically acceptable birth control.

You should inform the study doctor (PI) immediately if you or your partner intends to get pregnant, or if you or your partner should become pregnant while participating in this research study, so that your choices and options can be explored and discussed.

The following information must be released/reported to the appropriate authorities if at any time during the study there is concern that:

- you have a reportable communicable disease (i.e., certain sexually transmitted diseases or HIV)

- you disclose illegal criminal activities, illegal substance abuse or violence

Study Procedure Risks

Blood Tests: Blood sampling and needle punctures carry some risk. Possible side effects include, but are not limited to, fainting, bleeding, bruising, discomfort, dizziness, infection, and/or pain at the puncture site.

Electrocardiogram (ECG): An ECG is a test that measures the electrical activity of your heart. It involves putting sticky pads on your skin while the electrical activity of the heart is recorded. Skin irritation from the ECG electrodes or pain when removing the ECG leads is a possible risk.

Bone Marrow Biopsy or Aspirate: A biopsy or aspirate is a procedure used to remove a piece of tissue or a sample of cells from your body so that it can be analyzed in a laboratory. For the majority of cancers, the only way to make a definitive diagnosis is to perform a biopsy to collect a sample of cells in order to characterize your specific cancer You may have side effects from this procedure, which may include fainting, bleeding, bruising, discomfort, dizziness, infection, and/or pain at the puncture or incision site, and at the site from which the tissue is removed. Your doctor will describe the procedure to be used for your cancer in detail and will answer any questions and address any concerns you may have. Bone marrow biopsies or aspirates are optional for this study.

CT Scans: This research study involves exposure to radiation from CT scans. This procedure is routinely used to monitor response after people are treated for lymphoma.. The estimated radiation dose that you will receive as a participant for this type of research has been compared to the limits allowed for a radiation worker. This limit is low and is not expected to be harmful. This research gives patients about the same amount of radiation as they would get from living in a high altitude city such as Denver for 229 weeks, or taking 528 airplane flights from New York to Los Angeles. The person obtaining your consent can answer any questions you have. The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. Although the risk from radiation is cumulative, it is not expected to adversely affect your condition or treatment. The risk from radiation exposure of this magnitude is considered to be comparable to other everyday risks.

PET Scans: If you have a PET scan, PET scan involves injecting a very small amount of a radioactive material (tracer) into your vein. Allergic reactions to the tracer are very rare. You could also experience pain, redness or swelling at the injection site. Most of the tracer will be eliminated from your body within 6 to 24 hours (through your urine or stool) so be sure to promptly flush the toilet and thoroughly wash your hands with soap and water following each trip to the bathroom. Please talk to your study doctor about the amount of radiation from these scans. This research gives participants about the same amount of radiation as they would get from living in a high altitude city such as Denver for 229 weeks, or taking 528 airplane flights from New York to Los Angeles. A possible health problem seen with radiation exposure is the development of a second cancer later in life. This extra cancer risk is higher at younger ages and for girls and women. The extra lifetime risk of dying of a fatal cancer due to the radiation exposure from this research is low. At such low radiation exposures, scientists disagree about the amount of risk. These estimates are very uncertain, and there may be no extra risk at all.

Echocardiogram (ECHO): An ECHO may be taken to measure the function of your heart. An ECHO measures heart function by ultrasound (a test that uses high-pitched sound waves to produce an image of the heart). An ECHO is typically very safe, because the test uses only sound waves to evaluate your heart. These high-frequency sound waves have not been shown to have any harmful effects.

MUGA Scan: A MUGA scan creates images of the chambers of your heart to check whether the heart is pumping blood properly. It involves putting sticky pads (electrodes) on your skin and using a small amount of radioactive material by injection or by IV. Skin irritation from the electrodes and pain from injection or IV insertion are possible risks. The technologist will then ask you to lie still on a table and place a special camera that uses gamma rays to track the tracer above your chest. The radioactive substance you receive is safe for most people. Allergic reactions to the radioactive tracer are rare, but could occur. The amount of exposure is small and is equal to the amount of radiation that the average person would be exposed to from the environment in a period of 10 days. The amount of radiation is so small that it is not a risk for the people you come in contact with after the test. This research gives patients about the same amount of radiation as they would get from living in a high altitude city such as Denver for 229 weeks, or taking 528 airplane flights from New York to Los Angeles. A possible health problem seen with radiation exposure is the development of a second cancer later in life. This extra cancer risk is higher at younger ages and for girls and women. The extra lifetime risk of dying of a fatal cancer due to the radiation exposure from this research is low. At such low radiation exposures, scientists disagree about the amount of risk. These estimates are very uncertain, and there may be no extra risk at all. Your body will get rid of it through your kidneys within about 24 hours. *You should inform the physician or technologist if you are pregnant, or suspect to be, as this exam may cause harm to unborn babies.* Your physician or technologist can explain the procedure and risks in greater detail and clarify any concerns or questions.

MRI Risks: When having an MRI (Magnetic Resonance Imaging) scan, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your doctor. Your doctor may give you a medication to make you feel more comfortable. As images are taken, a loud banging noise will be produced. Earplugs or

headphones will be available if needed. The MRI can be stopped at any time at your request, but the scan may not be complete.

Tumor Biopsy: Tumor biopsies are usually taken from an area that can be easily reached with an instrument similar to a needle. These areas include the skin, lymph nodes, the liver, the colon, or other organs. This biopsy may involve the use of an imaging machine, such as a CT scan or a Doppler ultrasound, if necessary, to help guide the doctor performing the procedure. The risks or side effects involved with a tumor biopsy may include bruising, discomfort, and bleeding after the procedure. Your doctor will also discuss the risks and processes associated with the procedure.

Lumbar Puncture (LP): Lumbar Punctures are performed by inserting a needle into the spinal canal through your lower back while you are laying on your side. The purpose of this procedure is to collect spinal fluid to evaluate lymphoma involvement and to inject low dose of chemotherapy (methotrexate) during each cycle of chemotherapy. This is done to prevent lymphoma spread to brain. Possible LP side effects include temporary headaches and back pain. Your doctor will also discuss the risks and processes associated with the procedure.

There may also be risks involved from taking part in this study that are not known to researchers at this time.

Alternatives

You may elect not to enter this study and instead receive other standard treatments or therapies available to treat your condition. In addition, other experimental drugs may be available through other clinical trials. Your doctor or members of the study staff will discuss alternative treatments with you. Before you decide to take part in this study, you should discuss with your doctor and family your treatment options, the benefits and risks of the study, the resources and time required to fulfill your commitment to this study and then decide if this study is appropriate to you.

Study Costs

You or your insurance company will be charged for the following items and procedures that are considered routine care for your disease. These include physical exams; routine blood tests including hepatitis and HIV; ECGs; ECHO/MUGA; CT scans; PET scans; bone marrow aspirate/biopsy; tumor biopsy; Neulasta/Neupogen and their administration; prednisone if needed; and the administration of the study drug.

The sponsor will provide the study drug, Polatuzumab Vedotin, and cover the cost of the collection of tissue at no cost to you and/or your insurance company during your participation in this research study.

Compensation

You will not be paid for taking part in this study.

Research Related Injuries

In the event that this research related activity results in an injury, treatment will be made available including first aid, emergency treatment, and follow-up care as needed. Cost for such care will be billed in the ordinary manner to you or your insurance company. No reimbursement, compensation, or free medical care is offered by Wayne State University, the Detroit Medical Center, Karmanos Cancer Institute, McLaren Health Care, Wayne Health, Genentech, and any other facility involved with this study. If you think that you have suffered a research related injury, contact the PI right away at 313-576-8739.

Confidentiality

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. You will be identified in the research records by a code name or number. Information that identifies you personally will not be released without your written permission. However, the study sponsor, Karmanos Cancer Institute, McLaren Health Care Corporation, the Detroit Medical Center, Wayne State University, the Institutional Review Board (IRB) at Wayne State University, the National Cancer Institute (NCI), National Institutes of Health (NIH), Genentech, who is providing study drug Polatuzumab vedotin, or federal agencies with appropriate regulatory oversight [e.g., Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), Office of Civil Rights (OCR), etc.] may review your records.

When the results of this research are published or discussed in conferences, no information will be included that would reveal your identity.

A description of this clinical trial will be available on http://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.

Voluntary Participation/Withdrawal

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you decide to take part in the study, you can later change your mind and withdraw from the study. You are free to only answer questions that you want to answer. You are free to withdraw from participation in this study at any time. Your decisions will not change any present or future relationship with Wayne State University or its affiliates, or other services you are entitled to receive.

The PI may stop your participation in this study without your consent. If you have any side effects that are very serious or if you become ill during the course of the research study you may have to drop out, even if you would like to continue. The PI will make the decision and let you know if it is

not possible for you to continue. The decision that is made is to protect your health and safety, or because it is part of the research plan that people who develop certain conditions or do not follow the instructions from the study doctor may not continue to participate.

While taking part in this study you will be told of any important new findings that may change your willingness to continue to take part in the research.

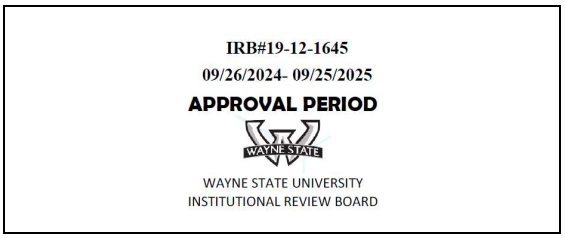
Questions

If you have any questions about this study now or in the future, you may contact Dipenkumar Modi, MD or one of his research team members at the following phone number 313-576-8739. If you have questions or concerns about your rights as a research participant, the Chair of the Institutional Review Board can be contacted at (313) 577-1628. If you are unable to contact the research staff, or if you want to talk to someone other than the research staff, you may also call the Wayne State Research Subject Advocate at (313) 577-1628 to discuss problems, obtain information, or offer input.

Consent to Participate in a Research Study

To voluntarily agree to take part in this study, you must sign on the line below. If you choose to take part in this study, you may withdraw at any time. You are not giving up any of your legal rights by signing this form. Your signature below indicates that you have read, or had read to you, this entire consent form, including the risks and benefits, and have had all of your questions answered. You will be given a copy of this consent form.

_____	_____
Signature of participant	Date
_____	_____
Printed name of participant	Time
_____	_____
Signature of witness**	Date
_____	_____
Printed of witness**	Time
_____	_____
Signature of person obtaining consent	Date
_____	_____
Printed name of person obtaining consent	Time



_____	_____
Signature of translator	Date
_____	_____
Printed name of translator	Time

Continue to HIPAA Authorization on next page

HIPAA Authorization

A federal regulation, known as the "Health Insurance Portability and Accountability Act (HIPAA)" gives you certain rights concerning the use and disclosure (sharing with others) of your Protected Health Information (PHI). This regulation provides safeguards for the privacy and security of your information. Your permission (authorization) is required for the use and sharing of any protected health information collected as part of this research study. If you are not willing to sign this authorization to use and/or disclose your PHI by the research team, you will not be eligible to take part in this research study.

The principal investigator (PI) and his research team will use your medical records and information created or collected as part of this research study. Your PHI is important for the PI and his research team in order to collect information about you during the study, to be able to contact you if needed, and to provide treatments to you during the study, if required. The PI may send out your study related health information to the sponsor or other entities involved in this study.

Your medical records, which may contain information that directly identifies you, may be reviewed by representatives from groups identified below. The purpose of these reviews is to assure the study is being conducted properly, that data is being obtained correctly or for other uses authorized by law. These reviews occur at the study site or in the PI's research office and can take place anytime during the study or after the study has ended.

The PHI that will be "USED" for this research includes the following: name, address (street address, city, state and zip code), e-mail address, elements of dates, telephone numbers, fax numbers, social security number, medical record number, and any unique identifying numbers or characteristics or code.

The PHI that will be "DISCLOSED" or shared with others for this research includes the following: name, address (street address, city, state and zip code), elements of dates, phone number, and any unique identifying numbers or characteristics or code.

Your study information may be **used** or **shared** with the following people or groups:

- The PI, co-investigators, and key personnel of WSU, KCI, and DMC associated with the research project
- WSU's Institutional Review Boards (IRB)
- Authorized members of WSU's, KCI's, McLaren Health Care Corporation's, and the DMC's workforce who may need to access your information in the performance of their duties.
- The study drug provider or representative, including companies it hires to provide study related services, which include: Genentech
- Federal agencies with appropriate regulatory oversight (e.g., FDA, NCI, NIH, OHRP, OCR, etc.) may review your records

Once your information has been released according to this Authorization, it could be released again and may no longer be protected by the HIPAA regulations.

This Authorization does not expire. The research team may need to correct it or provide missing information about you even after the study has ended, and your medical records may be needed to assist in this process.

- During your participation in this study you will have access to your medical record and any study information that is part of that record. The PI is not required to release research information that is not part of your medical record.

You may withdraw (take back) your permission for the **use** and **disclosure** of your PHI for this research at anytime, by **writing** to the PI at the address on the first page of this form. Even if you withdraw your permission, the PI for the research project may still use your PHI that was collected prior to your written request if that information is necessary to the study. If you withdraw your permission for use of your PHI, you will also be withdrawn from the research project. Withdrawing your authorization **will not** affect the health care that will be provided by the Detroit Medical Center and/or the WSU School of Medicine Practice Plans.

Authorization to use and disclose PHI

- By signing this document, you are authorizing the PI to **use** and **disclose** PHI collected about you for the research purposes as described above.

Signature of participant	Date
Printed name of participant	

- For participants unable to give Authorization, the following individual is acting on behalf of the research participant (e.g., children, mentally impaired, etc.).

Signature of authorized representative	Date
Printed name of authorized representative	Relationship to the participant
Signature of person obtaining Authorization	Date
Printed name of person obtaining Authorization	Time