CONSENT FOR CANCER RESEARCH

Project Title: A Phase II Study of Single Agent Brentuximab Vedotin in Relapsed/Refractory CD30 Low (<10%) Mature T Cell Lymphoma (TCL)

[redacted]

Investigational Product Supplier: Seattle Genetics

Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at Cleveland Clinic (CC) and Karmanos Cancer Institute.

1. Introduction

We are asking you to participate in a research study. The purpose of this document is to summarize your discussion with the research team and provide you with written information to help you decide whether you want to participate in research. Your decision is completely voluntary.

Your treating doctor may also be an investigator on this research study. If so, your doctor will have an interest in both your welfare and in the research study. You are not required to take part in this research study offered by your doctor. You may ask for a second opinion from another doctor who is not linked to this study. If you choose not to be in this study, the quality of your regular medical care will not be affected.

Please ask any questions you may have about the study or this consent form before signing it. Please take your time to make your decision. You will be given a copy of this form to keep.

This form tells you about the risks and benefits of this clinical trial and what will happen if you choose to take part. Your study doctor will also explain the clinical trial to you. After you read this document and your questions have been answered, you will be asked to decide whether or not you agree to be part of this research study. This process is known as informed consent.

One or more of the Investigators conducting this study serve as consultants for the company that makes products used in this study. These financial interests are within permissible limits established by the local institutional Conflict of Interest Policy. If you have any questions regarding conflicts of interest, please ask your study doctor or call the Cleveland Clinic Institutional Review Board at [redacted]

2. Purpose

You have been asked to take part in a clinical trial because you are a patient with mature T-cell lymphoma (MTCL) that has been treated with at least one type of chemotherapy, but your lymphoma is not responding or coming back after the previous treatment.

This clinical trial uses a drug called Brentuximab Vedotin. The Food and Drug Administration (FDA) has approved Brentuximab Vedotin for sale in the United States for certain diseases. Brentuximab is still being studied in clinical trials like this one to learn more about what its side effects are and whether or not it is effective in the disease or condition being studied. Brentuximab Vedotin has not been approved by the US FDA to treat mature T-cell lymphoma. We will refer to this drug as the study drug throughout this consent form.

Brentuximab Vedotin is a type of drug called an antibody drug conjugate (ADC). ADCs usually have 2 parts; a part that targets cancer cells (the antibody) and a cell killing part (the chemotherapy). Antibodies are proteins that are part of your immune system. They can stick to and attack specific targets on cells. The antibody part of Brentuximab Vedotin sticks to a target called CD30. CD30 is an important molecule on some cancer cells (including non-Hodgkin lymphoma) and some normal cells of the immune system. The cell killing part of Brentuximab Vedotin is a chemotherapy called monomethyl auristatin E (MMAE). It can kill cells that the antibody part of Brentuximab Vedotin sticks to. Brentuximab Vedotin has also been shown to kill cancer cells with levels of CD30 that cannot be seen by traditional methods.

This study is being done to test if the study drug has an effect on Mature T-cell Lymphoma with low levels of a target called CD30 and how your disease responds to the study drug.

About 31 people will participate in this study. The study will be conducted at multiple sites in addition to the Cleveland Clinic.

How long will I be on this study?
The time you will be receiving the study drug may vary according to how your disease responds to the study drug. You will receive the study drug once every 3 weeks until the disease worsen, unacceptable drug toxicity or reaction manifested, or if your physician decide it is better for you to be off the study. If you completed 17 cycles (approximately 13 months), the treating physician can determine if to continue or discontinue treatment in event there is no disease progression or unacceptable toxicity.

After finishing all your treatment cycles, you will be followed up to three years. In the next section you will have more specific information on each visit during the treatment and during the follow up period.

3. Study Procedures
You must follow the instructions given to you by your study doctor and have the tests and procedures that are part of the study. It is also important that you tell your doctor

about any change in how you are feeling and about all medications you are taking while you are taking part in the study.

If you choose to take part, you will have tests done at several times during the study. The sections below describe the tests and procedures that will be done as part of this study.

3.1 Screening/ Baseline Visit (done within 28 days of study treatment)

- **Informed consent**: during this visit, you will first sign this form after all your questions have been answered and you voluntarily decide to be on the study.

- **Study eligibility per inclusion/exclusion criteria**: your doctor and nurses will review all the laboratory tests done in the past and order new tests to find out if you are eligible to be on this study.

- **Medical history and medication you are taking**: you will be asked questions about your medical history, including information about other medical problems, medications you are taking including prescription medications, vitamins, herbal products and nutritional supplements, allergies to medications, and previous treatment for your cancer.

- Your doctor will conduct a **physical exam** including measuring your **height** and **weight.**

- **CD30/histological confirmation submission of tumor specimen for CD30 evaluation:** The most recent biopsy of your cancer will be sent to a doctor at a laboratory that is part of this hospital to check that you have the correct type of cancer for the study.

- **Correlative Studies:** Your most recent biopsy will also be sent to Cleveland Clinic Pathology and Laboratory Medicine at 2119 East 93rd street L25, Cleveland, OH 44106; to look at the amount of CD30 on your cancer cells by methods not used at routine labs. In case your cancer has come back or didn't respond to treatment since your last biopsy and biopsy not been done to confirm that your tumor comes back, a new biopsy will be taken. This procedure may be done under local anesthesia. All unused biopsy tissue will be stored at Cleveland Clinic for future research. The aim of such research is to better understand T cell lymphoma, develop new treatment, to better understand why some chemotherapies/drugs becomes not effective in treating T cell lymphoma, and other exploratory studies related to T cell lymphoma.
  This research includes genetic testing that studies the characteristics of and genes that are found I the body's cells. Genes are made of DNA. DNA (deoxyribonucleic acid) contains the instructions for your body's development and function. This information determines traits that are passed on from parent to child, such as eye and hair color and the risk/chance you will get certain diseases. Genes also tell your cells to make substances (including proteins) that appear in your blood. RNA (ribonucleic acid) is made from DNA. RNA is a genetic material that has a major role

in making proteins. Researchers are examining DNA, proteins (biomarkers) and RNA to look for genetic changes that cause cells to not work properly and cause disease. Some of the genetic changes that can cause disease are known.

Researchers are working on finding other genetic changes causing disease. Your samples collected for this research will be analyzed for the study. As part of the analysis, the research might include somatic and/or exome sequencing. This means researchers may look at your sample to learn about your genes (DNA). There are different ways to look at your DNA. Researchers often use a technology called sequencing to look at your DNA. Sequencing "reads" each letter of the DNA and finds changes (also called "variations" or "mutations") in your genes that may cause disease or affect how your body reacts to a certain disease. Somatic sequencing looks at genetic changes and the exome is your entire genetic code.

The research done with your tissue/blood may lead to the development of new therapies in the future. You and your family will not receive, either now or in the future, any compensation, royalty, or other financial benefits resulting from any new discoveries, procedure, or other items developed from studying your samples.

The correlative studies described are for research purposes only. It is not the purpose of these studies to look for or provide you with any medical information or diagnoses relating to your present condition or any other disease or illness. Therefore, you will not receive results from these research studies.

- **Human T-cell leukemia virus-1 (HTLV-1) status**: This test is intended to find out if you have been infected by a virus called Human T-cell leukemia virus-1 (HTLV-1). This virus is known to be present in people who have certain types of T-cell lymphoma.

- **Eastern Cooperative Oncology Group (ECOG) performance status:** This is an assessment done by your physician/nurses to look at your ability to carry out your daily activity.

- **Electrocardiogram (ECG):** This is a test that measures the electrical activity and health of the heart.

- **Echocardiogram (ECHO):** This is a test that uses sound waves to check the strength and function of your heart.

- **Diagnostic CT of neck, chest, abdomen, and pelvis**: with oral and intravenous (IV) contrast. This is a type of X-ray test (radiographic assessment) to measure the size of any tumors in your body. This test will be done with injecting contrast material this will improve visualization certain tissues in your body. You will also drink contrast material prior to the scan. Neck CT scan at this visit could be excluded (not done); if your physician thinks it is not necessary.

- **Positron Emission Tomography (PET) scan**: this is a radiographic assessment to see any rapidly growing tumors in your body. Sometimes a CT and PET scan are combined into one scan called a CT/PET. Your doctor will tell you if you will have the combined scan or two separate scans.

- **A bone marrow biopsy** will be taken to see if the cancer is in your bone marrow. For this biopsy, a small piece of bone is removed and we will also draw blood from your bone marrow for analysis. These tests are done under local anesthesia. If you have had a bone marrow biopsy within 60 days of starting treatment in this trial, you will not need to have another one at baseline.

- **Laboratory Tests**: around a tablespoon of blood will be taken from you to do the following tests:
    - **Chemistry panel**: sodium, potassium, chloride, bicarbonate, BUN, creatinine, calcium, glucose, total protein, albumin, alkaline phosphatase, total bilirubin, SGOT [AST], SGPT [ALT], lactate dehydrogenase (LDH) level, uric acid, phosphorous.
    - **CBC with differential:** this a general count of your blood cells.

- 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.

3.2 Treatment Cycles
You will receive the study drug every 21 days. We call this period of time a cycle of treatment. You will go through 17 cycles of treatment unless your disease progresses or your doctor thinks that you are better off to come off the study. During these cycles, you will have the following visits:

3.2.1 Day 1 of Cycle 1 through 17:
- You will be asked questions about your medications you are taking including prescription medications, vitamins, herbal products and nutritional supplements.
- ECOG performance status: this is an assessment done by your physician/nurses to look at your ability to carry out your daily activity.
- Your doctor will conduct a physical exam
- Laboratory Tests: around a tablespoon will be taken from your blood to do the following tests:
    - Chemistry panel: sodium, potassium, chloride, bicarbonate, BUN, creatinine, calcium, glucose, total protein, albumin, alkaline phosphatase, total bilirubin, SGOT [AST], SGPT [ALT]. Lactate dehydrogenase (LDH) level, uric acid and phosphorous will be drawn only on day 1 of cycle 1
    - CBC with differential
- You will receive the study drug on these visits

3.2.2 Cycle 4 and 10: Day 15 + 5 days

- During the third week of Cycle 4 and Cycle 10, you will have a CT neck, chest, abdomen and pelvis with oral and contrast. This is a type of X-ray test (radiographic assessment) to measure the size of any tumors in your body. This test will be done with injecting contrast material this will improve visualization certain tissues in your body. You will also drink contrast material prior to the scan. Neck CT scan at this visit could be excluded (not done); if your physician thinks it is not necessary and the CT scan done at your baseline visit showed that your disease was not affecting the lymph nodes in your neck.

3.3 End of Treatment Visit This visit will occur 30-45 days after your last treatment with the study drug.

The following procedures will take place:

- You will have a physical exam, including being weighed, measuring your height, and taking your vital signs such as temperature, pulse, and blood pressure.

- You will be asked questions about your medications you are taking including prescription medications, vitamins, herbal products and nutritional supplements.

- Laboratory Tests: around a tablespoon of blood will be taken to do the following tests:
    - Chemistry panel: sodium, potassium, chloride, bicarbonate, BUN, creatinine, calcium, glucose, total protein, albumin, alkaline phosphatase, total bilirubin, SGOT [AST], SGPT [ALT], lactate dehydrogenase (LDH) level.
    - CBC with differential

- If you are a female who could become pregnant, you will have a pregnancy test.

- ECOG performance status: this is an assessment done by your physician/nurses to look at your ability to carry out your daily activity.

- Diagnostic CT of neck, chest, abdomen, pelvis with oral and IV contrast. Neck CT scan at this visit could be excluded (not done); if your physician thinks it is not necessary and the CT scan done at your baseline visit showed that your disease was not affecting the lymph nodes in your neck.

- A positron emission tomography (PET) scan will be done. This is a radiographic assessment to see any rapidly growing tumors in your body. Sometimes a CT and PET scan are combined into one scan called a CT/PET. Your doctor will tell you if you will have the combined scan or two separate scans.

- If your bone marrow biopsy at the baseline visit showed that your bone marrow was affected by your lymphoma, then bone marrow biopsy will be repeated at this visit (between 30-45 days after the last cycle of therapy). This test will be done as described under section 3.1.

3.4 Follow-up visits

After you have completed study treatment, you will continue to come into the clinic until your cancer gets worse or until the study is closed, whichever comes first. These visits will be at 6, 12, 24 and 36-months after your last cycle of study drug. If you are unable to follow up in person, virtual visits may be used during long-term follow up only. Please discuss this option with your study doctor if you think it will be necessary. At these follow-up visits, the following will take place:

- You will have a physical exam, including being weighed, measuring your height, and taking your vital signs such as temperature, pulse, and blood pressure.
- You will be asked questions about your medications you are taking including prescription medications, vitamins, herbal products and nutritional supplements.

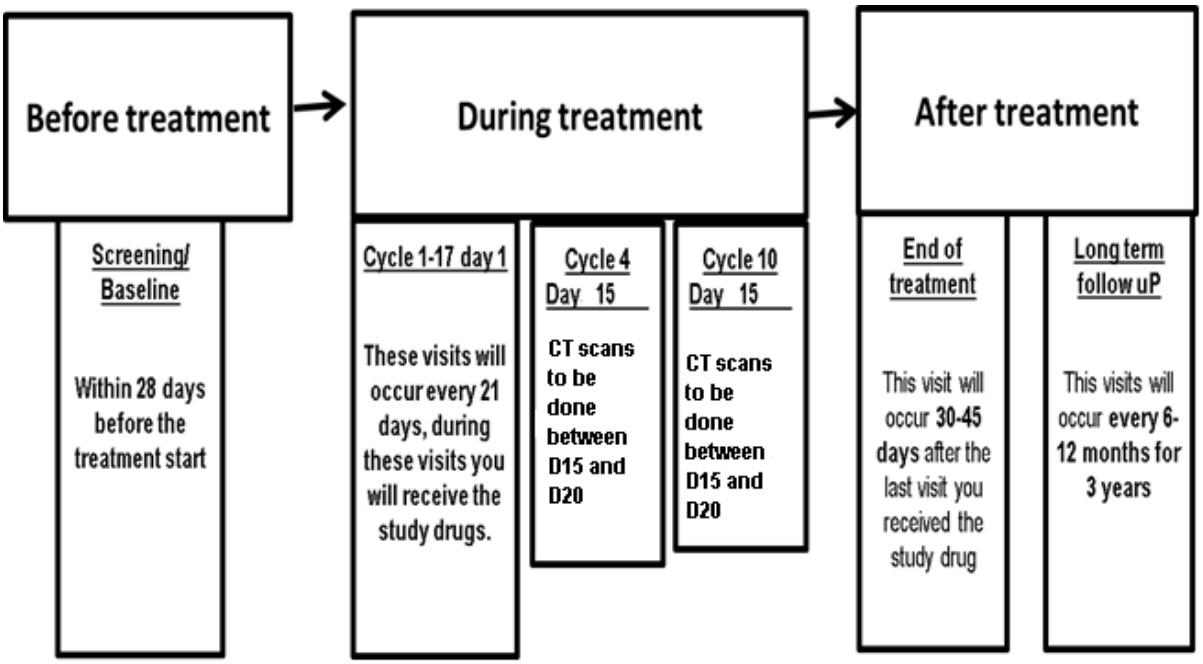
- Laboratory Tests: around a tablespoon of blood will be taken to do the following tests:

    - Chemistry panel: sodium, potassium, chloride, bicarbonate, BUN, creatinine, calcium, glucose, total protein, albumin, alkaline phosphatase, total bilirubin, SGOT [AST], SGPT [ALT], lactate dehydrogenase (LDH) level.
    - CBC with differential

- ECOG performance status: this is an assessment done by your physician/nurses to look at your ability to carry out your daily activity.

Diagnostic CT of neck, chest, abdomen, pelvis with oral and IV contrast. Neck CT scan at this visit could be excluded (not done); if your physician thinks it is not necessary and the CT scan done at your baseline visit showed that your disease was not affecting the lymph nodes in your neck.
If your disease has worsened and you come off the study you don't need to come for follow up visits.

The diagram below will help you to visualize your visits during the study.


Before treatment
During treatment
After treatment
Screening/ Baseline
Within 28 days before the treatment start
Cycle 1-17 day 1
These visits will occur every 21 days, during these visits you will receive the study drugs.
Cycle 4 Day 15
CT scans to be done between D15 and D20
Cycle 10 Day 15
CT scans to be done between D15 and D20
End of treatment
This visit will occur 30-45 days after the last visit you received the study drug
Long term follow uP
This visits will occur every 6-12 months for 3 years

The table below summarizes your visit schedule and the procedures that will take place during these visits.

Tasks	Baseline/screening Day -28 to 1	Cycle 1 day 1	Cycle 2 -17 Day 1±3days	Cycle 4 and 10 Day 15	Cycle 18 and beyond; Day 1 ±3days	EOT Day 30-45 post last cycle	Long term follow up			
							6 months	12 months	24 months	36 months
Informed consent	x									
Medical history	x									
Physical exam	x	x	x		x	x	x	x	x	x
CD30 status[e]	x									
HTLV-1 status	x									
ECHO	x									
EKG	x									
Vital signs, Height & weight	x[l]	x	x		x	x	x	x	x	x
Blood tests	x	x[k]	x		x	x	x	x	x	x
Pregnancy test	x[c]					x				
ECOG performance status	x	x	x		x	x	x	x	x	x
ConMeds	x	x	x		x					
Tumor tissue[f]	x									
CT neck/chest/abdomen/ Pelvis[a, h]	X[l]			x		x	x[d]	x[d]	x[d]	
BM aspiration and biopsy	X[g]					x[b]				
PET scan	x					x				
Brentuximab Vedotin		x	x		x					

a. Blood tests may include any of the following: serum chemistry, LDH, Uric Acid, Phosphorus, CBC with differential
b. Bone marrow biopsy only if positive prior to start of the study drug
c. Pregnancy test to be done within 72 hours of starting the study drug
d. Restaging CT scans not required if disease has progressed
e. CD30 status to be assessed by the site enrolling the patient
f. Tumor biopsy slides should be sent to CCF for correlative studies within 4 weeks of the start of the treatment
g. Bone marrow biopsy only if evidence of involvement previously, and/or suspicion of involvement at the time of current relapse.
h. For Cycles 18 and beyond, scans are to be done every six months +/- two weeks.

i. CT neck can be omitted at baseline if the investigator feels there is no or low suspicion for involvement. Subsequent CT neck can be omitted if there is no involvement at baseline.
j. These labs do not need repeated on C1D1 if they were performed at baseline within 72 hours of start of study treatment
k. Height is only required at screening.

What happens to the information collected for research?
If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent. Your collected samples and information will only be used to better understand T-cell lymphoma, develop new treatment, to better understand why some chemotherapies/drugs become not effective in treating T-cell lymphoma, and other exploratory studies related to T-cell lymphoma.

4. Risks

Certain side effects and discomforts of Brentuximab Vedotin may happen. You may have all, some, or none of the known side effects. There is also a risk that other rare or unknown side effects may occur. Your doctors and nurses will check you closely for side effects and may give you medicines or other treatments to stop or reduce some of these effects. Some side effects may go away soon after the study medication is stopped, but in some cases, side effects may be serious, long lasting, and/or permanent. There is even a chance that a side effect may cause death.

Brentuximab Vedotin Side Effects and Risks

Common Side Effects

The following side effects have been commonly seen in patients with cancer who received Brentuximab Vedotin in clinical studies:

Vomiting (15%)	Low red blood cells (11%)
Alopecia (hair loss) (10%)	Low white blood cells, neutrophils, which can give you a higher chance of getting an infection Neutropenia (18%) Neutrophil count decreased (2%)
Itching (12%)	Joint pain (13%)
Constipation (13%)	Nausea (28%)
Upper respiratory tract infection (14%)	Numbness/tingling in hands and feet, which can spread to arms and legs. You might have problems with muscle weakness, balance, or coordination. Peripheral sensory neuropathy (32%)
Cough (13%)	Rash (10%)
Diarrhea (24%)	Shortness of breath (12%)
Fatigue (feeling tired) (30%)	Headache (11%)
Fever (21%)	

Infusion-Related Reactions
Some patients had an allergic reaction while they were getting brentuximab vedotin or soon after. The allergic reactions included headache, rash, back pain, throwing up, chills, nausea, cough, itching, feeling out of breath, and low blood pressure. You may have a life-threatening allergic reaction (trouble breathing, hives, itching, swelling) that needs medical attention right away. If this happens, you might have to stop treatment with brentuximab vedotin.

Some patients became allergic to brentuximab vedotin during their treatments and developed antibodies against brentuximab vedotin. If you have an allergic reaction, you could have itching, chills, an upset stomach, rash, or low blood pressure. You could also have a very serious allergic reaction (anaphylaxis). This causes wheezing, swelling in the face or throat, feeling faint, or trouble breathing. If this happens, get emergency medical help **right away**. If you have an allergic reaction, you might have to stop treatment with brentuximab vedotin.

Peripheral Neuropathy
Some patients who were given Brentuximab Vedotin had problems with nerve function in their arms or legs (peripheral neuropathy). This can occur when damage is done to nerves that carry muscle movement information and feeling information such as touch, vibration, pain, and temperature. You may have a burning sensation, pain, weakness, or numbness and tingling (feeling of pins and needles) of your hands and/or feet. Some people had severe nerve function problems that caused difficulty walking.

Low Blood Cell Counts

Some patients had lower amounts of their blood cells during treatment with brentuximab vedotin. You could have any of the following:

- Low levels of a type of white blood cell called neutrophils that help your immune system (neutropenia). You could have a higher chance of getting an infection.
- Very low white blood cells with a fever (febrile neutropenia). This makes it easier to get an infection and can be life-threatening.
- Not enough red blood cells (anemia), which could make you feel tired or need a blood transfusion.
- Low levels of a type of blood cell called platelets (thrombocytopenia). This could make you have problems with your blood clotting, bruise easily, feel tired, or bleed longer than usual when you get cut.

Risk of Infection
Treatment with brentuximab vedotin may cause you to be less resistant to infections, including life-threatening infections. If you get a serious infection, you might need to be hospitalized or get antibiotics through an IV. Very serious infections can cause death. Some infections can cause long-term damage including long lasting pain, immune problems, or permanent disabilities. If you have a fever, sore throat, fast breathing, fast heartbeat, trouble breathing, low blood pressure, or painful sores around the mouth or anus, get emergency medical help **right away**. If you go to the emergency room, tell them your study doctor's name and that you are in a cancer treatment research study.

High Blood Sugar (Hyperglycemia)

Some patients who were treated with brentuximab vedotin had high blood sugar levels. This can cause serious health problems including diabetes. If you already have high blood sugar levels or have a high body mass index (BMI) because you are overweight, you may be more at risk. If you have high blood sugar, you could feel very thirsty, need to pee often, have blurry vision, feel tired, or have a headache. If this happens, tell your doctor **right away**. Your doctor will test the amount of sugar in your blood

Other Important Side Effects
The following important or possibly life-threatening side effects have been reported less often in patients who were given Brentuximab Vedotin.

- Serious painful rash that spreads to most of your skin (Stevens-Johnson syndrome/toxic epidermal necrolysis). This can cause death. Get emergency medical help **right away** if you have these symptoms: widespread skin pain, blisters, hives, swollen tongue, red or purple rash that spreads, or skin peeling.
- Damage to your organs including your kidneys, heart, and liver that can lead to death (tumor lysis syndrome, TLS). It is caused by a large number of tumor cells breaking apart quickly and releasing toxins into your blood. It usually happens

within a few days of starting your cancer treatment. If this happens, get emergency medical help **right away**.

- Brain damage from progressive multifocal leukoencephalopathy (PML), which is a rare and serious brain infection caused by a virus. If you have a weakened immune system, you could get PML. You could become confused, clumsy, have weakness on one side of your body, or have problems with speech or vision. This is a serious condition that can cause death or serious disability. If you have any of these symptoms, get medical help **right away**.
- Severe belly pain caused by a sudden and serious problem with your pancreas (acute pancreatitis). If this happens get emergency medical help **right away**.
- High levels of liver enzymes (ALT/AST elevation). This may mean that there are problems with your liver. If this becomes serious, it can cause death. Other symptoms of liver damage include yellow eyes or skin, feeling tired, sick to your stomach, vomiting, belly pain, bleeding that doesn't stop, sudden weight gain, or swollen hands or feet. If this happens, get emergency medical help **right away.**
- Infection or painful swelling in your lungs.You could have a cough, hard time breathing, or chest pain. You could cough up thick liquid (mucus), feel tired, have a fever, or have chills. If this happens, get medical help **right away.**
- Problems with your digestion that could need immediate medical help:
    - Loss of the ability of your gut to move and digest food, which could block your intestines (ileus)
    - Damage in your gut (neutropenic colitis). You could have a higher chance of getting an infection in your gut. This could happen suddenly. You could feel sick to your stomach, throw up, have belly pain, chills, a high fever, and watery poop.
    - Block in your throat or gut (gastrointestinal obstruction). You may get throat or belly pain, feel like throwing up, be unable to poop, or feel very bloated.
    - A tear or a hole in your stomach or gut that can cause belly pain and make you throw up blood (gastrointestinal perforation). You may feel tired, weak, and out of breath. This may require surgery and can be serious or cause death.

Patients Over 60 Years Old
Patients over 60 years old who got brentuximab vedotin for Hodgkin's lymphoma had similar side effects as younger patients. Most patients older than 60 had pain, weakness, or unusual sensations in their hands and feet (peripheral neuropathy). More older patients had severe cases of peripheral neuropathy (Grade 3 neuropathy) than

younger patients. This could be because of age. Or it could be because more patients over 60 had diseases that are connected with neuropathy, like high blood sugar (diabetes) and low levels of thyroid hormones (hypothyroidism). Patients who already had some neuropathy symptoms before treatment didn't seem more likely to get Grade 3 neuropathy.

Other Risks with Brentuximab Vedotin
The risks described above are not all inclusive. Talk to your doctor about other less common and less serious risks that could happen from taking the study medication. Ask your doctor about any risks that might be higher for you because of your medical history.

Risks of Additional Procedures
Blood Samples: Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or get an infection with redness and irritation at the place where the needle enters your vein.

Diagnostic Procedures*:* These include bone marrow aspirate and biopsies, tissue biopsies, CT and PET scans, and ECGs. These are all part of standard care for your cancer. Each of these procedures has risks associated with it, and you should talk to your study doctor or the person doing these procedures about the risks before they start.

Pregnancy and Breastfeeding

Brentuximab Vedotin is known to cause harm in animal reproductive studies.

If you or your partner is a woman who can become pregnant, you must use birth control during the study. You must also use birth control for 6 months after stopping treatment. Methods of birth control you can use include intrauterine device (IUD), hormonal (birth control pills, injections, implants), condoms, diaphragm, tubal ligation (“tubes tied”), vasectomy (for males), or complete abstinence. Your doctor can talk to you about these and other birth control options.

Males must also use birth control while on the study to avoid pregnancy of a female partner. Acceptable methods include spermicidal foam and condoms or prior vasectomy. You should notify your study immediately if your partner becomes pregnant.

If you are pregnant or breastfeeding, you will not be allowed to be in this study. If you or your partner become pregnant or think you are pregnant while taking part in this study or within 6 months after stopping treatment you should tell your study doctor right away. Neither men nor women should attempt conceiving children while being in this study. Females who become pregnant while on study will be removed from the study immediately. If you or your partner should become pregnant during this study, you should know that the effects of Brentuximab Vedotin to an unborn baby are not known.

You should not receive Brentuximab Vedotin if you are pregnant because it may harm your unborn child. Brentuximab Vedotin affects the testes (sperm-producing organs) in animals; therefore, men should not get their female partner pregnant while being treated with Brentuximab Vedotin. Seattle Genetics will follow the pregnancy to term. In addition, your infant will be followed for potential side effects up to 8 weeks after birth.

It is not known whether Brentuximab Vedotin or its breakdown products ends up in breast milk. If it does end up in breast milk, it could cause harm to a nursing baby.

Fertility Risks
It is possible that treatment with brentuximab vedotin could lower your chances of becoming pregnant for several months after stopping treatment. When a drug similar to brentuximab vedotin was tested in female animals, changes in the ovaries where eggs mature was observed. The changes in the ovaries showed signs of reversing when treatment was stopped. It is not known if these changes will happen in people who get brentuximab vedotin.

Unknown Risks
As this is a new drug, side effects that are not yet known may also occur. The side effects of Brentuximab Vedotin may be a minor inconvenience or could be severe enough to be life-threatening or cause death. You will be watched closely for side effects, and the drug will be stopped if unwanted or serious side effects develop.

There may also be other unknown effects that could harm you (or your embryo or fetus, if you become pregnant or father a child) during the time you take part in the study or after the study has been completed.

You will be notified of any significant new findings that become known that may effect your willingness to continue in the study.

Correlative Sample Risks
Your medical and genetic information are unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. While the chance that someone could access and misuse your information is believed to be very small, it is possible that the risk may increase in the future as people find new ways to access information.

5. Benefits
Taking part in this study may or may not make your health better. Even though Brentuximab Vedotin was approved by the FDA for certain diseases it is not know if Brentuximab Vedotin will be more useful than the usual treatment for your type of cancer. Information from this study will help doctors learn more about Brentuximab Vedotin as a treatment for cancer. This information could help future cancer patients.

6. Alternatives to Participation
Your other choices may include:

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

Talk to your doctor about your choices before you decide to take part in this study.

7. Costs and Compensation
You or your health insurance company will be billed for parts of the study that are standard care for your disease. Standard of care means the tests or procedures that your doctor would recommend as part of routine care for your disease even if you do not participate on this study. Your health insurance company may or may not pay for these charges. You will be responsible for all of the costs linked with this study that are related to standard care and are not covered by other payers (HMO, Health Insurance Company, etc.). The study drug will be provided by Seattle Genetics at no cost to you. Procedures that are done only for the study will be paid for by Seattle Genetics which include the additional biopsy described at the screening assessment in this consent form.
You will not be compensated for taking part in this study or for any discovery, invention, development or method of treatment that may result from you taking part in this research.
For more information on clinical trial and insurance coverage, you can visit the National Cancer Institute's (NCI) website at:

http://cancer.gov/clinicaltrials/understanding/insurance-coverage

You can print a copy of the 'Clinical Trials and Insurance Coverage' information from this website. Another way to get information is to call 1-800-4-CANCER (1-800-422-6237) and ask NCI for a free copy.

8. Research-Related Injury
If injury occurs as a result of your involvement in this research, medical treatment is available from Cleveland Clinic or another medical facility conducting this research. However, you/your medical insurance will be responsible for the cost of this treatment. A research injury is an injury that happens as a result of taking part in this research study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study, that is not considered a "research injury". There are no plans for payment of medical expenses or other payments, including lost

wages, for any research-related injury. To help avoid injury, it is very important to follow all study directions.

Further information about research-related injuries is available by contacting the Cleveland Clinic Institutional Review Board at [redacted]

9. Privacy and Confidentiality

Your information will be kept in a coded form and not attached to your name. We will store the code in a secure area and allow only the study team (the researchers, research nurse and other study staff) to have access to this code. We will keep this code in order to maintain a link between your name and the information about you created and collected during this study. The coded information, without your name attached, may be shared with others outside the research.

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to Dr. Deepa Jagadeesh (CC) and the research staff at Cleveland Clinic for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition.

Some of the tests and procedures done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record.

In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the Cleveland Clinic Institutional Review Board and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to:

- The studies investigational product supplier, Seattle Genetics, Inc., its licensees and collaborators, and all the clinical research organizations that help manage the study;
- Federal agencies, such as the Food and Drug Administration, the Department of Health and Human Services, and the National Cancer Institute (NCI);
- Other Institutional Review Boards;
- Data Safety and Monitoring Boards; An independent committee of physicians and experts that will review safety information from this study periodically
- Hospital accrediting agencies

- Individuals or businesses outside the hospital that provide services; for example, insurance companies, legal offices and data storage companies
- Regulatory agencies from other countries; quality assurance and/or quality control auditors

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely but you may stop [redacted] Authorization, your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as a part of this research and by the individuals and organizations as described in this Authorization. Also, information already disclosed outside the Cleveland Clinic and/or University Hospitals cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic will not use your information collected in this study for another research purpose without your written permission; unless the Cleveland Clinic Institutional Review Board (IRB) assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

10. Voluntary Participation

Your participation in this research study is voluntary. Choosing not to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

Termination of Participation

Your participation may be terminated by the investigator or the study supporters without regard to your consent if your doctor decides that it is best that you leave the study, you need a treatment that is not allowed to be taken during the study or if the study is ended by the study supporters or the FDA. If your participation is terminated, you will be asked to complete the termination procedures which include weight, blood tests for safety

purposes and a pregnancy test if applicable. If your participation is terminated, you will continue to see your physician at standard time points to manage your disease.
You may withdraw your consent to participate in this study at any time.

11. Questions about the Research
If you have any questions, you can ask the Principal Investigator and/or research staff by calling [redacted]

Emergency or After-hours Contact information
If you are a Cleveland Clinic patient, you should contact the page operator at [redacted] or toll free at [redacted] and ask for the oncologist (cancer doctor) that is on call.

If you have questions about your rights as a research subject, you may contact the Institutional Review Board (IRB) at Cleveland Clinic IRB [redacted]

Where Can I Get More Information?
You may call the National Cancer Institute's Cancer Information Services at:
1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may also visit the NCI website at http://cancer.gov
- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo

You will get a copy of this form. If you want more information about this study, ask your study doctor.

US National Institutes of Health (NIH) Clinical Trial Database
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 study results. You can search this Web site at any time**.**

12. Signature

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

_____	_____	_____
Signature of Participant	***Date***	***Printed Name of Participant***

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____	_____	_____
Signature of Person Obtaining Consent	***Date***	***Printed Name of Person Obtaining Consent***

You have had the above research study explained to you and as an individual likely to understand the subject's situation and acting in their best interest, you give your permission (or authorize) for participation in this research

_____
Printed Name of Subject

_____
Printed Name of LAR

_____ _____
LAR Signature Date