CONSENT FOR CANCER RESEARCH

Project Title: A Phase I/II Study of Carfilzomib in Combination with R-CHOP (CR-CHOP) for Patients with Diffuse Large B-Cell Lymphoma

Principal Investigator:
Brian Hill, MD, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, (216) 445-9451

Kirsten Boughan, DO, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Cleveland, OH 44106, (216) 844-3951

Investigational Product Supplier: Amgen, Inc.

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 Main Campus, Cleveland Clinic Regional Sites (Florida, Fairview, Hillcrest, and Sandusky), University Hospitals, and Roswell Park.

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.

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.

In addition to this clinical trial, there are other options that you should consider for your non-Hodgkin lymphoma. You and your doctor should discuss these options so that you know the risks and benefits of all your options before you decide.

Clinical trials include only people who choose to take part. Please take as much time as you need to make this decision. It is a good idea to discuss your decision with your friends and family. You can also discuss it with the doctors and nurses who provide your healthcare. If you have any questions, you should ask your study doctor before deciding whether you will take part. When you understand the study, including the risks and benefits, you must sign the form if you wish to take part. You will get a copy of the signed form to keep.

Conflict of Interest Disclosure

One or more of the Investigators conducting this study serve as paid speakers, consultants to advisory committee members for the company that is paying for this research or a company that makes products used in this study. These financial interests are within permissible limits established by the Cleveland Clinic Conflict of Interest Policy. If you have any questions, please ask your study doctor or call the Institutional Review Board at (216) 444-2924.

2. Purpose

You are being asked to take part in a clinical trial because you have been diagnosed with Diffuse Large B-cell Lymphoma that has never been treated.

This clinical trial uses a drug called Carfilzomib (C) in combination with Rituximab, Doxorubicin, Vincristine, Cyclophosphamide and Prednisone, a regimen known as R-CHOP. Carfilzomib is approved by the FDA as a single drug to treat patients with relapsed and refractory Multiple Myeloma. It is currently being studied in clinical trials like this one to learn more about how it functions as a component of combination therapy with other chemotherapy treatments in patients with Multiple Myeloma. This study is being conducted in order to evaluate how Carfilzomib functions in combination with R-CHOP in patients with newly diagnosed diffuse large B-cell Lymphoma.

Although Carfilzomib is approved by the FDA for Multiple Myeloma, it is not approved for use in Diffuse Large B-cell Lymphoma (DLBCL). In this study, Carfilzomib is considered an investigational drug, since it is being testing for indications other than their approved usage by the Food and Drug Administration (FDA). The purpose of this study is to find out what the side effects are and whether or not Carfilzomib is effective in combination with R-CHOP in patients that have been newly diagnosed with Diffuse Large B-cell Lymphoma.

As of July 2019, approximately 4,508 people have received Carfilzomib in Amgen-sponsored clinical trials and business-partner-sponsored clinical trials.. As of July 2019, approximately 6,582 people have received Carfilzomib in investigator-sponsored trials (ISTs). Since it was approved for sale, approximately 128,637 people have been prescribed Carfilzomib (Kyprolis®) for treatment.

This study is being done to test if the combination of Carfilzomib and R-CHOP has an effect on cancer in patients with newly diagnosed Diffuse Large B-cell Lymphoma. The side effects (unwanted effects) of this treatment in patients with Diffuse Large B-cell Lymphoma will also be studied. It is not known if Carfilzomib in combination with R-CHOP is better or worse than R-CHOP alone or other treatments.

About 50 people will take part in this research study at the Cleveland Clinic and other affiliated institutions.

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 be given study treatment and have tests done in 21-day cycles for 6 cycles. The sections below describe the tests, procedures, and study treatment administration that will be done as part of this study.

Screening

Screening studies and evaluations will be used to determine the eligibility of each subject for study inclusion. After you sign this informed consent form, screening and baseline tests will be done to see if you can take part in the study and to learn about your health before starting study treatment. All evaluations must be completed ≤ 28 days prior to administration of protocol therapy unless otherwise stated in the study protocol and approved by your physician.

- Informed Consent
- Demographics
- Medical History
- Complete physical examination
- Height and Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature.
- We will ask you about the medications you are taking including prescription medications, over-the-counter (OTC) medications and natural/herbal supplements.
- ECOG Performance Status (this describes how well you are functioning in your daily activities)
- Baseline Symptoms Assessment

- Blood and urine samples will be collected for safety and diagnostic tests, including Hepatitis and tests that make sure your organs are functioning normally.
- HIV testing
- 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.
- EKG
- MUGA or echocardiogram
- CT scan of neck, chest, abdomen and pelvis with oral and IV contrast (neck may be omitted at discretion of treating physician).
- PET/CT scan
- Bone Marrow Aspirate and Biopsy

Treatment Period

- Treatment cycles are 21 days long.

Cycle 1, Day 1

- Physical Examination
- Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature.
- We will ask you about the medications you are taking including prescription medications, over-the-counter (OTC) medications and natural/herbal supplements.
- ECOG Performance Status
- We will ask you about any side effects you may be having.
- Baseline Symptoms Assessment
- Blood samples will be collected in order to see how well your organs are functioning.
- Carfilzomib administration intravenously (into the vein)
- You will start to take a medication called Acyclovir. This is used to treat and prevent viral infections from the virus that causes chicken pox and shingles. Some patients develop shingles while receiving chemotherapy as a result of reactivation of dormant (temporarily inactive) virus during treatment.

Cycle 1, Day 2

- Vital signs including: blood pressure, pulse, respiratory rate and temperature.
- We will ask you about any side effects you may be having.
- Carfilzomib administration
- Rituximab administration intravenously (into the vein)

Cycle 1, Day 3

- Vital signs including: blood pressure, pulse, respiratory rate, and temperature.
- CHOP administration. Cyclophosphamide, Doxorubicin, and Vincristine are administered intravenously (into the vein) and Prednisone is administered orally (by mouth)

Cycle 1, Day 4

- Pegfilgrastim administration subcutaneously (under the skin) or ONPRO™ wearable device

Cycle 1, Day 8 optional at physician's choice

- Blood samples may be collected in order to see how well your organs are functioning:
    - Complete Blood Count (CBC) with differential and platelets
    - Serum Chemistries: albumin, alkaline phosphatase, total bilirubin, bicarbonate, BUN, calcium, chloride, creatinine, glucose, potassium, total protein, SGOT [AST], SGPT [ALT], sodium, lactate dehydrogenase (LDH) level, uric acid, phosphorous.
    - Calculated creatinine clearance will be determined using Cockcroft-Gault formula if creatinine and/or BUN are abnormal.

Cycles 2-6, Day 1

- Physical Examination
- Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature.
- We will ask you about the medications you are taking including prescription medications, over-the-counter (OTC) medications and natural/herbal supplements.
- ECOG Performance Status
- We will ask you about any side effects you may be having.
- Blood samples will be collected in order to see how well your organs are functioning.
- Carfilzomib Administration

Cycles 2-6, Day 2

- Vital signs including: blood pressure, pulse, respiratory rate and temperature.
- Carfilzomib administration
- Rituximab administration

Cycles 2-6, Day 3

- Vital signs including: blood pressure, pulse, respiratory rate, and temperature.
- CHOP administration.

Cycles 2-6, Day 4

- Pegfilgrastim administration

Cycles 2-6, Day 8 – optional at physician's choice

- Blood samples may be collected in order to see how well your organs are functioning. A test called Complete Blood Count will be done.

Cycle 3, Day 15-21

- CT scan of neck, chest, abdomen and pelvis with oral and IV contrast (neck may be omitted at discretion of treating physician).
- PET/CT scan (optional)
- Your physician will assess how are your responding to the study drug

Cycle 6, Day 21

Off Treatment Visit (To be conducted within 50 days of Day 1 of last treatment)

- Physical Examination
- Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature.
- We will ask about the medications you are taking including prescription medications, over-the-counter (OTC) medications and natural/herbal supplements.
- ECOG Performance Status
- We will ask you about any side effects you may be having.
- Blood samples will be collected in order to see how well your organs are functioning.
- EKG
- Echocardiogram
- Bone Marrow Aspirate and Biopsy (may be omitted if screening bone marrow biopsy was negative for involvement for lymphoma)
- CT scan of neck, chest, abdomen and pelvis with oral and IV contrast (neck may be omitted at discretion of treating physician).
- PET/CT to be obtained between 4-8 weeks after cycle 6, day 1. Unless your physician decides to defer these procedures until you complete other types of therapy such as radiation.
- Your physician will assess how are your responding to the study drug

Follow-Up (Held at a minimum of 6, 12 and 24 months after Cycle 6, Day 1)

- Physical Examination
- Weight
- Vital signs including: blood pressure, pulse, respiratory rate and temperature.
- We will ask you about the medications you are taking including prescription medications, over-the-counter (OTC) medications and natural/herbal supplements.
- You will be instructed to stop taking acyclovir at your 6 month follow up visit.
- ECOG Performance Status
- We will ask you about any side effects you may be having
- Blood samples will be collected in order to see how well your organs are functioning.
- CT neck/chest/abdomen/pelvis (may omit neck if not deemed clinically indicated by investigator)
- ECHO will be performed at 6 month follow up visit
- Your physician will assess how are your responding to the study drug

Can I stop participation in the study?

The study doctor may stop you from taking part in this study at any time if he/she thinks it is in your best interest, or if you do not follow the study rules. Your study doctor or Amgen may decide to stop this study for either medical or other reasons at any time without your consent. Your study doctor will tell you if this happens and will talk to you about other treatment options.

You can decide to stop at any time and you may still be treated at your hospital or clinic. Tell your study doctor if you are thinking about stopping or decide to stop. You should talk to the doctor about leaving the study before you decide so that he/she can find out if you are having any side effects from study treatment. Another reason to tell your doctor that you are thinking about stopping is so that he/she can talk to you about any other treatments that could be helpful to you.

If you decide to stop being in this study, you will still be asked to come back to the hospital or clinic for the end of treatment tests as described. You may also be asked to take part in follow-up phone calls and/or visits. This information is important to make sure that there are no lasting side effects from the study treatment and to see if your cancer got better, stayed the same, or got worse after treatment.

4. Risks

You may have all, some, or none of the known side effects described in the following sections. 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.

Carfilzomib Risks & Side Effects

Very common side effects (may affect more than 1 in 10 people) include:

• Low red blood cell count (anemia) which may cause tiredness and fatigue • Low platelets, which may cause easy bruising or bleeding • Low white blood cell count, which may decrease your ability to fight infection • Shortness of breath • Cough; Cough with phlegm • Diarrhea • Nausea • Constipation • Vomiting • Stomach pain • Tiredness (fatigue) • Fever • Swelling of the hands, feet, or ankles • General weakness	• Infusion reactions • Respiratory tract infection • Lung infection (pneumonia) • Runny nose or nasal congestion • Decreased appetite • Back pain • Joint pain • Pain in limbs, hands, or feet • Muscle spasms • Headache • Dizziness • Numbness, tingling, or decreased sensation in hands and/or feet • Insomnia (difficulty sleeping) • Changes to blood tests (decreased blood levels of potassium, increased blood levels of sugar and/or creatinine • High blood pressure (hypertension)

Common side effects (may affect up to 1 in 10 people) include:

• Low white blood cell count, which may be associated with fever • Heart failure, and heart problems including rapid, strong, or irregular heartbeat • Blood clot in the lungs • Fluid in the lungs • Nose bleed • Change in voice or hoarseness • Pain in throat • Wheezing • Pulmonary hypertension • Blurred vision • Cataract • Indigestion • Toothache • Pain • Chills • Feeling too hot • Pain, swelling, irritation or discomfort where you received the injection into your vein • Liver problems including an increase in your liver enzyme in the blood • Sore throat • Bronchitis • Urinary tract infection	• Inflammation of the nose and throat • Flu-like symptoms (influenza) • Serious infection in the blood (sepsis) • Viral infection • Dehydration • Bone and muscle pain • Chest pain • Muscle weakness • Aching muscles • Anxiety • Kidney problems including decreased ability to make urine, increased creatinine in the blood, and kidney failure needing dialysis • Rash • Itchy skin • Redness of the skin • Increased sweating • Changes to blood tests (decreased blood levels of sodium, magnesium, protein, calcium, or phosphate, increased blood levels of calcium, uric acid, potassium, bilirubin, or c-reactive protein • Low blood pressure (hypotension) • Blood clots in the veins

Uncommon side effects (may affect up to 1 in 100 people) include:

• Heart attack • Reduced blood flow to the heart • Abnormal amount of fluid between the heart and the lining of the heart • Swelling and irritation of the lining around the heart • Heart muscle disease with may cause shortness of breath and tiredness • Lung problems	• Stroke • Extremely high blood pressure • Bleeding in the brain • Allergy to Carfilzomib • Tumor lysis syndrome (TLS) ○ Tumor lysis syndrome is caused by rapid killing of tumor cells during treatment. When the tumor cells die, they release their contents

• Bleeding in the lungs • Perforation in the stomach, small intestine, or large bowel • Bleeding in the stomach and bowels • Multi-organ failure • Liver failure • Itchy skin, yellow skin, very dark urine, and very pale stools which may be caused by a blockage in the flow of bile from the liver (cholestasis)	into the bloodstream. If cell killing is very rapid, this can affect blood chemistries and the kidneys. In severe cases, this can lead to shutdown of kidney function requiring dialysis.

Rare side effects (may affect up to 1 in 1000 people) include:

• Thrombotic Thrombocytopenic Purpura/Hemolytic Uremic Syndrome (TTP/HUS) – signs of this blood condition may include bleeding, bruising, weakness, confusion, fever, nausea, vomiting, diarrhea, and acute kidney failure. • Thrombotic microangiopathy • Venous thromboembolism • Swelling of the throat • Infection of the back of the eye (Cytomegalovirus) • Progressive Multifocal Leukoencephalopathy - a rare infection of the brain caused by the JC (John Cunningham) virus. Symptoms include general weakness, issues with balance, difficulty speaking and sensory loss. • Reinfection of the liver with the hepatitis B virus • Pancreatitis	• Posterior reversible encephalopathy syndrome (PRES) ○ Formerly termed reversible posterior leukoencephalopathy syndrome (RPLS). PRES is a rare, neurological disorder which can present with seizure, headache, lethargy, confusion, blindness, altered consciousness, and other visual and neurological disturbances, along with hypertension. The diagnosis is confirmed by neuroradiological imaging. If diagnosed early and treated, the symptoms of PRES may be reversed. Cases of PRES have been reported in patients receiving Carfilzomib. Discontinue Carfilzomib if PRES is suspected. The safety of reinitiating Carfilzomib therapy in patients previously experiencing PRES is not known

Myelodysplastic syndromes (MDS)/Acute Myeloid Leukemia (AML) - Myelodysplastic syndromes refer to a disorder that develops when the cells in the bone marrow (the soft inner part of the bones where new blood cells are made) do not work properly and have problem making new blood cells. A person with MDS may experience no symptoms or may experience fatigue, infection, easy bruising or bleeding. MDS can turn into a cancer of bone marrow cells called acute myeloid leukemia (AML).

Recent studies have shown that patients from the Asia-Pacific region (China, Japan, Taiwan, Singapore, Republic of Korea, and Thailand)are at an increased risk of cardiovascular events from Carfilzomib. Patients who are of Asian-Pacific ethnicity or ancestry should not be enrolled in this study to ensure patient safety. Please let your study doctor know if you have any concerns.

Vincristine Risks & Side Effects

Side effects that have been seen in patients who have received treatment with vincristine include the following:

• Alopecia (hair loss) • Anemia (decrease in the number of red blood cells) • Blindness and deafness due to nerve damage • Blockage of the intestines • Blockage of the vein leading from your liver to your heart (can lead to liver or kidney damage) • Bone pain • Changes in the way you walk (e.g., with a flat foot) • Constipation • Decreased blood platelets which can affect blood clotting • Damage to the intestines that could make it hard to digest food • Diarrhea • Difficulty breathing • Difficulty walking • Feeling of “pins and needles” in skin	• Loss of fertility (males) • Loss of reflexes • Pain due to nerve damage • Muscle wasting • Loss of ability to control bladder leading to increased or decreased frequency of urination • Leukopenia (decrease in the number of white blood cells)frequency of urination • Nausea • Rash • Seizures • Second cancer in addition to your lymphoma (e.g., leukemia) • Sensory loss • Shortness of breath • Sores in the mouth • Stomach cramps • Uncontrollable shaking • Women may stop having periods

• High or low blood pressure • Inability to move certain parts of the body • Jaw pain	• Water retention and decreased blood sodium • Loss of reflexes • Kidney damage that can lead to kidney failure

Rare cases of severe allergic reaction to vincristine have been reported.

Cyclophosphamide, Doxorubicin, Prednisone Risks & Side Effects

Cyclophosphamide, doxorubicin, and prednisone are drugs that have been approved by the FDA. The following side effects have been commonly seen in patients with cancer who have received treatment with these drugs:

• Allergic reaction* • Alopecia (hair loss) • Bleeding gums • Changes in nail • Changes in the way your heart works possibly causing irreversible heart failure • Changes in skin color • Changes to the lungs • Chills • Constipation • Cough • Diarrhea • Difficulty sleeping • Excessive thirst • Fever • Frequent urination • Headaches • Itchiness • Jaw pain • Muscle aching • Mood swings • Low white blood cells	• Nosebleeds • Loss of fertility (males) • Low platelets that can lead to bruising or bleeding • Low red blood cells • Pain at the injection site or along the vein • Nausea • Pain when urinating • Puffy face • Rash • Sore mouth and ulcers • Sore throat • Stomach pain • Swelling due to fluid retention • Taste changes • Tiredness • Urine discoloration • Vomiting • Weight gain (increased appetite) • Weight loss (decreased appetite) • Women may stop having periods • Breathlessness

*Some people can have a severe allergic reaction to one or more components of CHP chemotherapy. Signs of this can include skin rashes and itching, a high temperature, shivering, dizziness, headache, and/or breathlessness.

Rituximab Risks & Side Effects:

Side effects that have been seen in patients who have received treatment with Rituximab include the following:

• Fever • Headache • Vomiting • Asthenia (feeling weak and having no energy) • Angioedema (swelling that affects deeper layers in your skin) • Pulmonary infiltrates (substances that linger in the lungs) • Myocardial infarction (heart attack) • Pancytopenia (abnormal decrease in the levels of all type of blood cells) • Neutropenia (condition in which the number of white blood cells, called neutrophils, is abnormally low) • Chills • Nausea • Rhinitis (nasal inflammation) • Hypotension (low blood pressure) • Hypoxia (a decrease of oxygen reaching body tissues)	• Acute respiratory distress syndrome (a severe, life-threatening medical condition characterized by widespread inflammation in the lungs) • Tumor lysis syndrome (Tumor lysis syndrome is caused by rapid killing of tumor cells during treatment. When the tumor cells die, they release their contents into the bloodstream. If cell killing is very rapid, this can affect blood chemistries and the kidneys. In severe cases, this can lead to shutdown of kidney function requiring dialysis) • Marrow hypoplasia (a condition where your bone marrow contains very few blood cells) • Increased risk of infection

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.

ECHO or MUGA Scan

Echocardiograms (ECHOs) and MUGA (multigated acquisition) scans are two tests that evaluate heart function. You and your doctor may choose either one of these to be done during this study. You do not need to have both.

There are no known risks from an echocardiogram 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. A microphone is rubbed across the chest on top of a lubricating gel to produce the pictures. Some coldness of the gel and pressure from the microphone might be felt.

In a MUGA scan an injection of a small amount of a radioactive material is made into a vein and then pictures are made of the heart's pumping action. You may feel some discomfort from the needle inserted into your vein during the MUGA scan. This test involves exposure to radiation. The total amount of radiation that you will receive from one MUGA scan is about 5.18 mSv (millisievert) or 518 mrem (millirem). This is approximately equivalent to a whole body exposure of 630 days (1.726 years) of exposure to natural background radiation. This use involves minimal risk. Persons participating in this research will have 2 MUGA scans, although some could have 3. You are allowed to choose to have an echocardiogram instead of a MUGA scan if you prefer and you may discuss this with your doctor.

HIV testing
As part of this protocol, you will be tested for HIV (human immunodeficiency virus, which is the virus that causes the acquired immunodeficiency syndrome (AIDS). You will be notified of the results of the testing, and counseled as to the meaning of the results, whether they are positive or negative. If the test indicates that you are infected with HIV, you will receive additional counseling about the significance for your medical care and possible risks to other people. We are required to report all positive results to the Ohio State Board of Health. The test results will be kept confidential to the extent permissible under the law. If you do not want to be tested for HIV, then you should not agree to participate in this study.

Hepatitis testing
The state of Ohio and applicable regulations require laboratories to report new cases of Hepatitis B, and Hepatitis C infection to governmental agencies. The reports may include the patient's name, social security number, and other identifying information. Information about these new infections is used to track these diseases statewide and nationwide. Other than this required reporting, your results will be treated confidentially by the research study staff.

Pregnancy

Females of childbearing potential should avoid becoming pregnant while being treated with carfilzomib. Carilzomib has been shown to have cytotoxic effects in vitro, therefore both men and women should not attempt pregnancy and women should not be pregnant or breast-feeding while participating in this study. It is suggested that females and males on carfilzomib should use effective contraception methods or abstain from sexual activity during and for 30 days after treatment with carfilzomib. Barrier contraceptives (condoms or diaphragms) with spermicide, intrauterine devices, hormonal contraceptives (Depo-Provera, Norplant), oral contraceptive pills, and complete abstinence are examples of effective methods. If pregnancy should occur, notify your doctor immediately. You may be required to stop the study drug at which time other treatment options will be discussed with you. Due to an increased risk of venous thrombosis associated with carfilzomib, subjects currently using oral contraceptives or a hormonal method of contraception associated with a risk of thrombosis should consider an alternative method of effective contraception.

Males of reproductive potential are advised against fathering a child while being treated with carfilzomib. The potential for carfilzomib to be transferred via semen and its effect on sperm are unknown. Male subjects treated with carfilzomib and/or their female partners (if of childbearing potential) should use effective contraceptive methods or abstain from sexual activity while treated with carfilzomib and for 90 days after treatment. Notify study staff immediately if you or your partner becomes pregnant.

Unknown Risks

Side effects that are not yet known may also occur. The side effects of study treatment 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.

5. Benefits

Taking part in this study may or may not make your health better. There is no proof that combining Carfilzomib with R-CHOP will be more useful than the usual treatment (R-CHOP) for the type of cancer that you have. Information from this study will help doctors learn more about Carfilzomib as a treatment for patients with Diffuse Large B-Cell Lymphoma. 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.

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. 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.). You will be responsible for all copays and deductibles. The study drug will be provided by Amgen at no cost to you. Procedures that are done only for the study will be paid for by Amgen. These research procedures may include pregnancy tests, blood tests, and echocardiograms.

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 you experience physical injury or illness as a result of participating in this research study, medical care is available at the Cleveland Clinic, University Hospitals or elsewhere. The drug suppliers (Amgen) will not pay for necessary medical treatment of the injury. There are no plans to provide compensation for lost wages, direct or indirect losses. You are not waiving any legal rights by signing this form.

Further information about research-related injuries is available by contacting the Cleveland Clinic Institutional Review Board at (216) 444-2924 or University Hospitals Cleveland Medical Center's Research Subject Rights phone line at (216) 983-4979.

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. Brian Hill, Dr. Kirsten Boughan, 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 study's investigational product supplier, Amgen, its licensees and collaborators, and all the clinical research organization 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 these uses and disclosures at any time by writing to Brian Hill, MD, PhD, 9500 Euclid Avenue, CA6, Cleveland, OH 44195, (216) 445-9451, or Kirsten Boughan, DO, Division of Hematology/Oncology, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Cleveland, OH 44106, (216) 844-3951. If you revoke this Authorization, your participation in the research will stop, but any information ly 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 cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic and University Hospitals 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) or University Hospitals 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.

11. Questions about the Research

If you have any questions, you can ask the Principal Investigator and/or research staff. Dr. Brian Hill at the Cleveland Clinic, 216-445-9541, or Dr. Kirsten Boughan at University Hospitals Cleveland Medical Center, 216-844-3951

Emergency and After-hours Contact Information

If you are a Cleveland Clinic Main Campus patient, you should contact the page operator at (216) 444-2200 or toll free at (800) 223-2273, and ask for the oncologist (cancer doctor) that is on call.

If you are a Cleveland Clinic Florida patient, please call 954-659-5000 and ask for the doctor that is on call.

If you are a University Hospitals patient, and you need to contact study staff outside normal business hours, you may contact (216) 844-3951 and you will be transferred to the answering service, which can put you in contact with the oncologist (cancer doctor) 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 216-444-2924 and/or University Hospitals Cleveland Medical Center's Research Subject Rights phone line at (216) 983-4979.

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 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***