



## CONSENT FORM

IRB PROTOCOL # 345-16-FB

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### ADULT CONSENT - CLINICAL BIOMEDICAL

#### Title of this Research Study

A Single-center Phase IIa Study Evaluating the Safety and Tolerability of Umbralisib and Ibrutinib in Patients with Relapsed or Refractory Diffuse Large B-cell Lymphoma

#### Invitation

You are invited to take part in this research study. You have a copy of the following, which is meant to help you decide whether or not to take part:

- Informed consent form
- "What Do I need to Know Before Being in a Research Study?"
- The Rights of Research Subjects

#### Why are you being asked to be in this research study?

You are being asked to be in this study because you are an adult and have a diagnosis of relapsed or refractory diffuse large B-cell lymphoma (DLBCL).

If you are pregnant, nursing an infant, or plan to become pregnant during this study, you may not be in this study.

#### What is the reason for doing this research study?

This research study will test a combination of two oral drugs, umbralisib (formerly known as TGR-1202) and ibrutinib. This study will try to determine what the safest and most effective dose is for these chemotherapy pills.

Umbralisib is an investigational drug not approved for marketing by the FDA. It is available from TG Therapeutics for use in this research study.

Ibrutinib used in this research study is an FDA approved medication for patients with Mantle Cell Lymphoma who have received at least one prior therapy, for patients with Chronic Lymphocytic Leukemia (CLL) for CLL patients with 17p deletion, for patients with Waldenstrom's Macroglobulinemia, Marginal zone lymphoma (MZL) who require a medicine by mouth or injection (systemic therapy) and have received a certain type of prior treatment and Chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy. Ibrutinib is not approved for the treatment of patients with DLBCL.

It is planned that 24 patients total will be enrolled to this study at the University of Nebraska Medical Center.



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### What will be done during this research study?

There will be 3 treatment groups given one year (12 months) of therapy, you will be assigned to one of the 3 groups, to see what effects (good and bad) it has on you and your cancer and to find the doses that can be given safely.

All subjects will be assigned to only one group and receive a maximum of 52 weeks (1 year) of self-administered oral therapy. The first 3 subject to consent will be directly enrolled into Group C regardless of their decision to be included in the optional biopsy. Then the next subjects will be assigned in order to group A, B or C based on date of consent and those willing to consent to the optional biopsies. You will be informed as to which group of this research you are enrolled into. You will also be made aware of what dose of umbralisib and ibrutinib you are to receive.

- **Group A** will receive umbralisib 800 mg (four-200mg tablets) orally every day on days 1-8; then umbralisib 800 mg (four-200mg tablets) and ibrutinib 560 mg (four-140mg tablets) orally every day for one year (12 months). Group A (6 patients) will have the option to consent to 3 additional lymph node biopsies.
- **Group B** will receive ibrutinib 560 mg (four-140mg tablets) orally every day on days 1-8; then ibrutinib 560 mg (four-140mg tablets) and umbralisib 800 mg (four-200mg tablets) orally every day or one year (12 months). Group B (6 patients) will have the option to consent to 3 additional lymph node biopsies.
- **Group C** will receive umbralisib 800 mg (four-200mg tablets) and ibrutinib 560 mg (four-140mg tablets) orally every day or one year (12 months). Group C (12 patients) will have the option to consent to 3 additional lymph node biopsies.

The investigator will review your medical history and current medications to determine if you might qualify to participate in the study. If you choose to sign this informed consent form, you will continue with the screening process. Many of the tests may be the same as those you have already completed for the diagnosis of your lymphoma.

The screening process may take place over a period of up to 21 days before you start your study medication. These may take more than one visit and will include the following:

- A physical examination will be performed.
- Your actual health status and your well-being will be assessed. This is called a performance status assessment.



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- A little less than 3 teaspoons (15 mL) of blood will be taken for specific standard laboratory (lab) tests.
- If you are female and are able to have children, a pregnancy test will be done on your blood or urine. This test must be done within 14 days before receiving study medication. The test must be negative for you to be in the study.
- You will have tests completed to check the function of your heart. These tests include an Electrocardiogram.
- A PET/CT is mandatory pre-treatment (as part of your screening process).
- In addition, we will draw a blood sample for research testing, a little less than 4 teaspoons (20 mL), being completed for this project. (See mandatory sample collection below).
- Diagnosis of DLBC or transformed DLBC lymphoma will be confirmed by the pathologists at UNMC.
- Up to 4 teaspoons (20 ml) of blood will be taken for research samples (See mandatory sample collection below).
- An optional core biopsy will be obtained via US or CT guided biopsy of accessible lymph node before you begin treatment. ((See decision for optional biopsies at the end of this consent form)).

### Study Medication: (umbralisib is a tablet. Ibrutinib is a capsule.)

- The doses of umbralisib and ibrutinib will be determined by the group you are enrolled into the study.
- You will receive up to 12 cycles of oral study medication, umbralisib and ibrutinib.
- Each cycle will last for 28 days.
- Follow your medication calendar that is provided to you by the research nurse.
- During the first cycle you will be asked to take your assigned study medication by mouth once a day for 8 days and starting on day 9 and every day thereafter until the investigator tells you to stop, you will be asked to take your assigned study medication combination.
- **Umbralisib should be taken in the morning and ibrutinib should be taken in the evening.** (NOTE: After cycle 2 if no side effects have been seen you have the option to take umbralisib and ibrutinib dosing together at the same time of day.)
- You will be given a monthly Medication Diary. The diary will have a place for you to record the time you took your prescribed doses of umbralisib and ibrutinib.

### Things to know about taking your study medication:



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1. You should take your study medication each day with a full 8 ounce glass of water and food.
2. You should avoid grapefruit and Seville oranges (Known as Chinese Bitter Orange, bitter orange, sour orange, bigarade orange, or marmalade orange. The Seville orange variety is used in the production of marmalade/cooking) during treatment, as these can alter the absorption of the study medication.
3. You should swallow the tablets and capsules as a whole, do not chew or crush them.
4. If you miss a dose of your study medication, it should be taken as soon as possible on the same day. If it is missed for the entire day, it should not be made up. If a dose is missed make sure to mark it on your Medication Calendar.
5. If vomiting occurs, no attempt should be made to replace the vomited doses.

If the investigator thinks you are at risk for tumor lysis syndrome (complications caused by the breakdown products of dying cancer cells) you will receive pre-medication with allopurinol or a suitable alternative 12-24 hours prior to the first dose of chemotherapy. No routine pre-medications for nausea and vomiting should be needed, however, medications may be administered for symptoms or side effects when they occur, and the investigator may order other pre-medications if needed.

### Follow-Up Process and Procedures

During the study, you will be followed closely to find out the effects of umbralisib and ibrutinib. If there are any safety concerns, additional blood tests may be required. If you experience any bad side effects, the investigator may delay treatment or re-start the study medications at a lower dose.

On day 8 of the first cycle before you begin treatment you will have the following:

- A physical examination will be performed.
- A little less than 3 teaspoons (15 mL) of blood will be taken for specific standard laboratory (lab) tests.
- In addition, we will draw a blood sample for research testing a little less than 4 teaspoons (20 mL) being completed for this project. (See mandatory sample collection below).
- An optional core biopsy will be obtained via US or CT guided biopsy of accessible lymph node before you begin treatment (See decision for optional biopsies at the end of this consent form).

Before each 28 day cycle of your treatment you will have the following:

- A physical examination will be performed. Any side effects and other



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medication use will be reviewed.

- Your actual health status and your well-being will be assessed. This is called a performance status assessment.
- Umbralisib and ibrutinib medication diaries will be reviewed and drug returns will be counted and additional umbralisib and ibrutinib will be ordered.
- A little less than 3 teaspoons (15 mL) of blood will be taken for specific standard laboratory (lab) tests (complete blood count, chemistry panel, as indicated).
- In addition, before the 2nd cycle, we will draw a blood sample for research testing a little less than 4 teaspoons (20mL) being completed for this project. (See mandatory sample collection below).

At the completion of the 2nd, 4th, 6th, and 9th, and 12th cycles (+/- 7 days) (before you begin the following cycles) you will have the following:

- The investigator will do a restaging assessment of your lymphoma, a PET/CT or a CT chest, abdomen and pelvis with contrast may be used at the investigators discretion. If your disease is improving or staying the same, you will continue to receive more cycles (a total of 12 cycles) of this combination therapy.
- In addition, we will draw a blood sample for research testing a little less than 2 teaspoon (10 mL) being completed for this project. (See mandatory sample collection below).

At the end of treatment (disease progression) or end of cycle 12 (+/- 7 days) of your treatment you will have the following:

- A little less than 3 teaspoons (15mL) of blood will be taken for specific standard laboratory (lab) tests (complete blood count, chemistry panel, as indicated).
- In addition, we will draw a blood sample for research testing a little less than 2 teaspoons (10 mL) being completed for this project. (See mandatory sample collection below).

After Month 12, restaging assessments of your lymphoma should occur at the investigators discretion with collection of a blood sample for research testing a little less than 2 teaspoons (10 mL) being completed for this project only if feasible.

### MANDATORY SAMPLE COLLECTION

The researchers doing this study need to do tests on blood (described below) to see how the cancer cells respond to the study drug combination. These tests will look for ways to help predict which patients are most likely to be helped by the combination



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treatment, including looking for DNA/tumor markers, peripheral mononuclear cells and cytokine profiles (proteins released by cells that have a specific effect on the interactions between cells, on communications between cells or on the behavior of cells).

The collection of these samples (research blood only) before you begin treatment (+/- 3 days) and at day 8 (+/- 3 days), 1 month (+/- 3 days) and the end of your cycle 2, 4, 6, 9, and 12 cycles (+/- 7 days) is a necessary part of this study and will be used only for these purposes. After Month 12, research blood samples obtained ONLY IF FEASIBLE during scheduled restaging assessments of your lymphoma that occur at the investigators discretion. The samples will not be sold.

At the end of this consent form, we will ask for your permission to store any left-over samples for future research.

### **What are the possible risks of being in this research study?**

You may need to be admitted to the hospital for treatment for the side effects. Every effort will be taken to lessen side effects, but there is no way to tell which side effects may happen or how bad they may be. Unless otherwise stated, the side effects are reversible.

You will be closely monitored for any side effects you experience on the study. The investigator can give you other medications to treat the side effects or can decrease the doses of medications to stop or reduce the severity of the side effect and allow you to continue in the study.

As with any medication, allergic reactions are a possibility.

### **Umbralisib**

**The following side effects are common (greater than 20% of people):**

- **Stomach and digestive disorders:** nausea, diarrhea
- **General disorders and administration site conditions:** tiredness

**Less Common (greater than or equal to 10% to less than or equal to 20% of people)**

- **Blood and lymphatic system disorders:** decrease in number of white blood cells
- **Stomach disorders:** vomiting
- **Metabolism and nutrition disorders:** decreased appetite



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- **Skin Disorders:** rash

### Uncommon (greater than or equal to 1% to less than 10% of people)

- **Blood and Lymphatic System Disorders:** decrease in number of red blood cells, fever with decrease in white blood cells, white blood cells above normal range, decreased number of platelets
- **Eye Disorders:** vision blurred
- **Gastrointestinal Disorders:** abdominal bloating, abdominal pain, constipation, dry mouth, indigestion, inflammation of the bowel that can cause severe diarrhea which may require hospitalization
- **General Disorders and Administration Site Conditions:** fever, weakness, chills, swelling of hands, arms, legs, ankles, and/or feet
- **Infections and Infestations:** yeast infection in the mouth, pneumonia, infection of the mouth or throat
- **Investigations:** increase in liver enzymes, increase in levels of creatinine in blood which can indicate decreased kidney function, increase in lymphocyte count (type of white blood cell), weight loss
- **Metabolism and Nutrition Disorders:** dehydration, increase in blood sugar levels, decrease in levels of potassium in blood, decrease in levels of phosphate in blood which can lead to bone weakness
- **Musculoskeletal and Connective Tissue Disorders:** pain in joints, muscle spasms, pain in arms and/or legs
- **Nervous System Disorders:** dizziness, change in taste, headache, numbness and/or tingling of the hands and/or feet, involuntary shaking or trembling
- **Psychiatric Disorders:** difficulty sleeping
- **Respiratory, Thoracic and Mediastinal Disorders:** cough
- **Skin and Subcutaneous Tissue Disorders:** hair loss, night sweats, itching

### Events Reported In Less Than 1% of Subjects

- **Blood and Lymphatic System Disorders:** Leukopenia, Hyperbilirubinemia, Bacteremia
- **Ear and Labyrinth Disorders:** Tinnitus
- **Eye Disorders:** Visual Impairment, Visual acuity reduced
- **Gastrointestinal Disorders:** Eructation, Flatulence, Gastroesophageal Reflux Disease, Abdominal Pain Upper, Mouth Ulceration, Anal Hemorrhage, Hypoaesthesia Oral, Paraesthesia Oral, Pancreatitis, Ileus
- **General Disorders and Administration Site Conditions:** Malaise, Mucosal Inflammation,
- **Hepatobiliary Disorders:** Hypocalcemia



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- **Immune System Disorders:** Allergic reaction
- **Infections and Infestations:** Candida infection, Fungal skin infection, Lung infection, Sinusitis
- **Investigations:** International Normalized Ratio Increase, Blood lactate dehydrogenase increase, Blood phosphorus increased, Blood sodium increased, Blood uric acid increased, White blood cell count decreased
- **Injury, Poisoning and Procedural Complications:** Contusion
- **Metabolism and Nutrition Disorders:** Hyperlipidemia, Hypertriglyceridemia, Hyponatremia
- **Musculoskeletal and Connective Tissue Disorders:** Muscular Weakness, Myalgia, Pain in Jaw
- **Nervous System Disorders:** Somnolence, Peripheral Sensory Neuropathy, Memory Impairment
- **Psychiatric Disorders:** Anxiety, Libido Decrease, Delirium, Parasomnia
- **Reproductive System and Breast Disorders:** Erectile Dysfunction
- **Respiratory, Thoracic and Mediastinal Disorders:** Dyspnea, Epistaxis, Hypoxia, Influenza, Respiratory Failure, Pulmonary edema
- **Skin and Subcutaneous Tissue Disorders:** Dermatitis, Dermatitis Acneiform
- **Vascular Disorders:** Hot Flush

In addition to the preceding adverse events, the following adverse events occurred in patients administered umbralisib but were deemed by investigators to be unlikely related or not related to umbralisib therapy. Due to the low number of patients evaluable for safety at this time, however we cannot rule out these events occurring in future:

- Liver Disorders: Elevated levels of certain liver enzymes
- Brain and nerve related disorders: Paresthesia
- Kidney disorders: Elevated blood urea nitrogen levels, elevated phosphorus, hyperuricemia
- Breathing and chest related disorders: Nasal congestion, upper respiratory tract infection
- General disorders: Arthralgia, myalgia

### **Ibrutinib**

You may develop side effects while participating in this study. You should tell the study doctor about any side effects that you develop.

The side effects listed below have been reported by patients who have received





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ibrutinib in clinical trials.

The **most common** side effects, occurring in at least 1 of every 5 patients ( $\geq 20\%$ ), have been:

- Increase in frequency of loose or watery stools, diarrhea
- Muscle and bone pain (Musculoskeletal pain)
- Low white blood cell count (cells that help fight infection) (Neutropenia)
- Bruises
- Rash
- Nausea

Side effects that have been seen in at least 1 of every 10 ( $\geq 10\%$ ) patients include:

- Sores in the mouth (Stomatitis)
- Sinus infection (Sinusitis)
- Fever (Pyrexia)
- Low platelet count, (cells that help blood to clot) (Thrombocytopenia)
- Constipation
- Swelling of the hands or feet (Oedema peripheral)
- Joint aches (Arthralgia)
- Common cold (Upper Respiratory Tract Infection)
- Vomiting
- Skin infection
- Pneumonia
- Headache
- Muscle spasms
- High blood pressure (Hypertension)

Side effects that have been seen in at least 1 of every 100 ( $\geq 1\%$ ) patients include:

- Dizziness
- Urinary tract infection
- Nose bleeds (Epistaxis)
- Increased level of uric acid in the blood (Hyperuricemia)
- Small red or purple spots caused by bleeding under the skin (Petechiae)
- Abnormal heart rhythm (Atrial fibrillation)
- Non-melanoma skin cancer
  - Type of non-melanoma skin cancer (Basal cell carcinoma)
  - Type of non-melanoma skin cancer (Squamous cell carcinoma)
- Blurry vision (Vision blurred)
- Low white blood cell counts with fever (Febrile neutropenia)
- Severe infection throughout the body (Sepsis)



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- Redness of the skin (Erythema)
- Increase in white blood cell counts (Leukocytosis)
- Breaking of the nails (Onychoclasia)
- Inflammation within the lungs that may lead to permanent damage (Interstitial lung disease)
- Increase in lymphocyte count (Lymphocytosis)

Side effects that have been seen in less than 1 of every 100 (< 1%) patients include:

- Unusual levels of chemicals in the blood caused by the fast breakdown of cancer cells, which may lead to changes in kidney function, abnormal heartbeat, or seizures. (Tumor lysis syndrome)
- Itchy rash (Urticaria)
- Bleeding around the brain (Subdural hematoma)
- Inflammation of the fatty tissue underneath the skin (Panniculitis)
- Swollen face, lip, mouth, tongue or throat (Angioedema)
- High WBC count with abnormal clumping that can lead to bleeding (Leukostasis syndrome)
- Severe rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome)
- Liver failure (Hepatic failure)

### **The combination of the study drugs ibrutinib and umbralisib:**

The following side effects were observed in patients treated with the combination of ibrutinib and umbralisib in another study and were considered at least possibly related to one or both study medications.

#### **Common (greater than 20% of people)**

- **Blood and lymphatic system disorders:** decreased number of white blood cells
- **General Disorders:** infusion related reaction, tiredness
- **Stomach disorders:** nausea, diarrhea

#### **Less Common (greater than or equal to 10% to less than or equal to 20% of people)**

- **Stomach Disorders:** vomiting
- **Nutrition Disorders:** decreased appetite

#### **Uncommon (greater than or equal to 1% to less than 10% of people)**

- **Blood and Lymphatic System Disorders:** decreased number of red blood cells, decreased number of platelets, paleness of membrane that lines the



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inside of the eyelids (which may indicate low levels of red blood cells), increase in bilirubin in blood

- **Ear and Labyrinth Disorders:** ear congestion
- **Eye Disorders:** vision blurred, swelling of the eye
- **Gastrointestinal Disorders:** indigestion, constipation, abdominal pain, sores in mouth, abdominal discomfort, swollen abdomen, passing gas, gastric reflux, excessive saliva, infection and swelling of the small and large intestine, burping, difficulty swallowing, discolored feces
- **General Disorders and Administration Site Conditions:** swelling of hands and/or feet, weakness, fever, chills, cold sweat, swelling of the face
- **Hepatobiliary Disorders:** decreased number of globulins (type of protein that helps fight infections)
- **Immune System Disorders:** hives
- **Infections and Infestations:** pneumonia, infection in the bloodstream that may cause organ failure, infection of the upper respiratory tract, skin infection, inflammation of the lungs (bronchitis), pink eye, herpes in the mouth, infection of the urinary tract, sinus infection, severe diarrhea caused by a bacteria, ear infection, fungal infection in or around the mouth, inflammatory response throughout the body that can cause organs to fail, wound
- **Investigations:** elevated liver enzymes, weight loss, increase in blood creatinine level which may indicate kidney damage
- **Metabolism and Nutrition Disorders:** dehydration, high levels of sugar in blood, low levels of potassium in blood, low levels of phosphate in blood which can indicate bone weakness, failure to thrive
- **Musculoskeletal and Connective Tissue Disorders:** muscle spasms, muscle weakness, pain or tenderness in the muscles, pain in extremity
- **Nervous System Disorders:** dizziness, altered taste, headache, drowsiness
- **Psychiatric Disorders:** anxiety, nervousness, agitation, difficulty with sleep
- **Renal and Urinary Disorders:** feeling of urgency to urinate, decreased kidney function, kidney damage
- **Reproductive System and Breast Disorders:** cysts on the scrotum, discolored semen
- **Respiratory, Thoracic and Mediastinal Disorders:** shortness of breath, infiltrated lungs, inflammation of the lungs with or without infection, choking, cough, low levels of oxygen in blood, hoarseness or strained voice, cough that expels mucus, persistent sore throat
- **Skin and Subcutaneous Tissue Disorders:** hair loss, bruising, rash, dry skin, itching
- **Vascular Disorders:** flushing, high blood pressure, nose bleeds



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Although rare, the events listed below have been reported in subjects treated with ublituximab and/or umbralisib

- erythrodermic eczematous rash (itchy, red and peeling rash that can be fatal)
- malignant melanoma (skin cancer)
- tumor lysis syndrome (a serious metabolic disorder caused by the breakdown of cancer cells and their release in the bloodstream)
- progressive multifocal leukoencephalopathy (a serious brain infection that can lead to severe disability and death)
- drug-induced hepatitis (inflammation of the liver due to toxic exposure to medication)
- pulmonary edema (excess fluid in the lungs)
- ileus (blockage in the intestines)
- allergic reaction

Most of these side effects listed above have been mild to moderate in severity; however severe side effects have occurred. Some side effects have been severe enough to lead to study drug discontinuation, dose modification or reduction, hospitalization, disability, and sometimes death.

You should tell your study doctor or medical team about any side effects you are having. Your study doctor may be able to give you medications to help treat the side effects and prevent them from becoming worse. Your study doctor may also choose to stop ibrutinib for a short time or reduce its dose to allow you to recover from any side effects.

### Bleeding

You may experience bruising or nosebleeds during treatment with ibrutinib. Rarely, serious internal bleeding, such as bleeding in your stomach, intestine, or brain may occur, sometimes resulting in death. If you take other medicines or supplements that increase the risk of bleeding, such as aspirin, non-steroidal anti-inflammatory drugs (NSAIDs) or medicines used to prevent or treat blood clots or stroke, ibrutinib may increase this risk. Blood thinners such as warfarin or other vitamin K antagonists should not be taken together with ibrutinib. Supplements such as fish oil and vitamin E preparations should be avoided while taking ibrutinib. Call your study doctor if you have signs or symptoms of serious bleeding, such as blood in your stools or urine or bleeding that lasts for a long time or that you cannot control.

### Effects on the heart



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Abnormal heartbeats (atrial fibrillation and/or atrial flutter) have been reported in patients treated with ibrutinib, especially when they also have heart conditions, increased blood pressure, acute infections, or had abnormal heartbeat in the past. Atrial fibrillation/flutter is a common type of abnormal heartbeat. The heartbeat may be fast or irregular causing symptoms such as a pounding or racing heart, dizziness, weakness, feeling light-headed or shortness of breath. If you develop any of these symptoms while on the study drug, you should tell your study doctor immediately.

### Infections

You may experience viral, bacterial, or fungal infections during treatment with ibrutinib. Some of these infections have led to hospitalization and death. Contact your study doctor immediately if you have fever, chills, weakness, confusion, body aches, cold or flu symptoms, vomiting, jaundice, feel tired or feel short of breath - these could be signs of an infection.

A rare and usually fatal viral disease in the brain, Progressive Multifocal Leukoencephalopathy (PML), has been reported in patients treated with ibrutinib in combination with rituximab and in patients who were previously treated with rituximab. If you experience symptoms such as weakness, paralysis, vision loss and/or impaired speech, you should tell your study doctor immediately.

### Lymphocytosis and leukostasis

You may experience an increase in the number of lymphocytes, which is a type of white blood cell, in your blood (lymphocytosis). This may occur in the first few weeks of treatment and you should not assume that this increase in white blood cells means that your disease is worsening. This increase may last for several weeks to months. Increased number of white blood cells in your bloodstream may change the blood flow, resulting in bleeding or clotting (leukostasis). Isolated cases of these events have been reported in patients treated with ibrutinib. Your study doctor will monitor your blood counts and may administer additional therapy as needed. Talk to your study doctor about what your test results mean.

### Decreased blood counts

Severe decreases in white blood cells, red blood cells, and platelets (neutropenia, anemia, and thrombocytopenia) were reported in subjects treated with ibrutinib. If you experience symptoms such as fever, weakness, or easy bruising and/or bleeding, you should tell your study doctor immediately.



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### Allergic reactions

Sometimes people have allergic reactions to drugs. Serious allergic reactions can be life-threatening. If you have an allergic reaction to ibrutinib, you might develop a rash, difficulty breathing, wheezing when you breathe, sudden low blood pressure with light-headedness, swelling around the mouth, throat or eyes, a racing heartbeat, and/or sweating.

Before starting the study drug, you must tell your study doctor about any drug allergies. You should tell the study doctor right away if you have any allergy symptoms listed above.

### Rash

A maculopapular rash (flat, red areas on the skin with small bumps) has been commonly reported in patients treated with ibrutinib alone or in combination with other drugs. Most rashes are mild to moderate in severity and begin 2 to 3 weeks or longer after starting ibrutinib.

There have been rare reports of severe skin reactions (known as severe cutaneous adverse reaction or SCAR, involving more than 50% of the body) or rash with blisters and peeling skin, which may include open ulcers or sores in the mouth and other areas of the body (Stevens - Johnson syndrome). These skin rashes could be life-threatening. You should notify your study doctor immediately if you develop a rash that spreads quickly, or if you notice peeling of your skin, with or without ulcers or sores in your mouth.

### Non Melanoma Skin Cancer and Other Cancers

Non melanoma skin cancer (basal cell carcinoma and squamous cell carcinoma of the skin) have been reported with more frequency and maybe related to the use of ibrutinib. Other cancers have been reported such as solid tumors and blood cancers the relationship to the use of ibrutinib is unknown. You should tell your study doctor if you develop a new cancer while in the study.

### Tumor Lysis Syndrome (TLS)

Unusual levels of chemicals in the blood caused by the fast breakdown of cancer cells have happened during treatment of cancer and sometimes even without



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treatment. This may lead to changes in kidney function, abnormal heartbeat, or seizures. Your study doctor may do blood tests to check for TLS.

### Hypertension

Hypertension is also called high blood pressure, and has been commonly reported in subjects treated with ibrutinib. Sometimes, people with high blood pressure may have headaches, dizziness, nervousness, sweating, difficulty in sleeping, facial flushing or nosebleeds, but in some cases, there may be no symptoms and it may go undetected. After starting ibrutinib, your doctor may measure your blood pressure regularly. You should let your study doctor know if you have any of the symptoms of high blood pressure which may mean that you have developed hypertension or that your hypertension is getting worse. Your study doctor may adjust existing anti-hypertensive medications and/or initiate anti-hypertensive treatment as appropriate.

### Liver Failure

Rare cases of liver failure have been reported in patients treated with ibrutinib. Symptoms of liver failure include yellowing of the eyes and skin (Jaundice), itching of the skin, dark colored urine, gray or clay-colored stools, confusion, nausea, loss of appetite, fatigue or diarrhea,. You should tell your study doctor immediately if you have any of these symptoms which may suggest liver disease. Your study doctor may be able to diagnose and provide you required medical care.

### Interstitial lung disease

Interstitial lung disease is a group of lung disorders in which the tissues become inflamed and may become damaged. Interstitial lung disease is not associated with infections (e.g., bacteria, viruses, fungi) and has been reported in patients treated with ibrutinib. You should report to your physician if you have cough, any signs of new or worsening respiratory symptoms such as shortness of breath or difficulty breathing.

### Interference with other drugs

Some foods like grapefruit juice and Seville oranges, as well as some medications, may interfere with the way your body processes ibrutinib. This interference could cause the amount of ibrutinib in your body to be higher or lower than expected. It is also possible that taking the study drug with your regular medications or



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supplements, including fish oil, Vitamin E, or other vitamins, may change how your regular medications, or your regular supplements, work. It is very important that you avoid grapefruit juice and Seville oranges and tell the study doctor about all medications, supplements, or herbal medicine like St. John's wort that you are taking during the study. You should notify your study doctor immediately about any side effects to avoid possible harm

### **Drug interruption for any surgical procedures**

Ibrutinib may increase the risk of bleeding with any surgical procedure. Ibrutinib should be held at least 3 to 7 days before and after surgery depending upon the type of surgery and the risk of bleeding. The ibrutinib will not be held for optional biopsies. Please contact your study doctor if you have any planned surgical procedures. For emergency surgical procedures, ibrutinib should be discontinued (stopped) after the procedure until the surgical site is reasonably healed (not oozing fluid).

Please contact your study doctor as soon as possible and your study doctor will tell you when to stop ibrutinib and when to restart it following a surgical procedure.

### **Breastfeeding**

It is not known whether ibrutinib or its metabolites are excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from ibrutinib, breast-feeding should be discontinued during ibrutinib treatment.

In addition to the risks listed above, there could be unknown or unexpected side effects associated with the use of ibrutinib. You will be told in a timely manner, verbally and in writing, of any new information, findings, or changes to the way the research will be done that might influence your willingness to continue your participation in this study.

You may have all, some, or none of the listed side effects of ibrutinib. Your study doctors and nurses will check you closely for side effects. You may receive medicines or other treatments to prevent or reduce some of these effects. Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think they are related to the study drug.

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.





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### Risks of Study Procedures/Tests

**Echocardiogram:** The echocardiogram uses sound waves to measure the pumping function of the heart and does not pose any additional risk.

**X-RAY/ PET CT, CAT Scans:** X-rays, PET CT, and CT Scans involve exposure to radiation. The risk of harmful effects from a single exam is very small. The dye that is injected into a vein for the CT scan is usually well tolerated. Some people feel dizzy or queasy or get a headache with it or notice a cold feeling near the injection site. There is a chance of having an allergic reaction to the dye that rarely can be serious and life threatening. The radiologist will obtain a separate informed consent explaining this procedure in specific detail.

**Drug Administration/Blood Drawing:** Some known risks, although rare, are associated with placing a needle into a vein or under the skin (when the study drug is given or when blood samples are taken). These include the possibility of infections, inflammation, a hole poked through the other side of the vein by the needle, bleeding, discomfort, pain, bruising, and a change in skin color at the site. Fainting may occur shortly after having blood collected.

- **Venous Access Device (Central Line):** In order to undergo this therapy you may need a central line. You may already have one from prior therapy. These are the risks associated with these central lines:
  - *Placement of Vascular Access Device:* The surgeon or radiologist who puts this catheter in will explain the risks in detail before he/she performs the procedure. These risks include the risks associated with anesthesia as for any operation, infection and bleeding. There may also be pain at the site where the device is inserted. Although it is rare, occasionally the lung is punctured during placement of a device and a tube must be placed in the chest to re-inflate the lung. It is also possible that there may be injury to a major blood vessel, which could lead to severe bleeding.
  - *Use of Venous Access Device:* These devices can become infected and these infections may require antibiotics, or occasionally removal of the device. It is possible for a blood clot to develop at the end of the catheter in the vein. This might prevent the catheter from working or rarely lead to swelling of the arm or neck and face, or to pain. Sometimes the device would need to be removed and replaced.

### Trial Risks:

A trial of a new combination of drugs may involve increasing risk, to a small number



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of participants. In studies of small numbers of subjects, toxicity may more readily become apparent through close monitoring of individual subjects. This new combination of drugs may be less effective than standard of care treatments.

### **Other and Unknown Risks:**

It is possible that other rare side effects could occur which are not described in this protocol. It is also possible that you could have a side effect that has not occurred before.

### **Pregnancy Risks:**

It is possible that the medicines used in this study could injure a fetus if you, or your partner, becomes pregnant while taking them. You have already been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse, or counselor who is not part of this study to discuss the potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks, you, or your partner, must not become pregnant while you are participating in this study. Women must have a negative pregnancy test before entering the study.

If you are sexually active and can get pregnant, or can get your partner pregnant, you must use TWO appropriate methods of birth control every time you have sex, or you must not have sex.

Because of the nature of this research, methods of natural family planning are not, by themselves, sufficiently reliable to avoid pregnancy.

You can get additional information about methods to avoid pregnancy by calling the UNMC Research Subject Advocate's Office at (402) 559-6941.

The effects of ibrutinib on a developing baby are unknown; therefore, women who are pregnant or nursing are not allowed to be in this study. Nobody knows what these risks are right now. Some drugs cause women to have their babies prematurely (early) or to have babies with birth defects.

Women: If you are able to have children, you must use a highly effective method of birth control and a barrier method while taking study treatment, as well as for 1 month



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after you stop taking study treatment, to prevent pregnancy in either you or your partner. A highly effective method of birth control is defined as a method that has a low failure rate (i.e., less than 1% per year) when used consistently and correctly and includes implants, injectables, birth control pills with 2 hormones, some intrauterine devices (IUDs), sexual abstinence (which is defined as refraining from all aspects of sexual activity) or a sterilized partner. If you are using hormonal contraceptives such as birth control pills or devices, a second barrier method of contraception (e.g., condoms) must be used.

Men: You must use a barrier method while on treatment with ibrutinib and for 3 months after the last dose of treatment to prevent pregnancy of your partner.

Note: Some birth control pills may not work when you are taking certain drugs. If you have any questions about this, please discuss this with the study doctor.

Be aware that you can still become pregnant even if you use a highly effective method of birth control.

Men: If your partner becomes pregnant while you are on study treatment, or within 3 months of your last dose of ibrutinib, you must notify the study staff. The study staff will discuss this with you further. You should not donate sperm while you are taking the study drug and for 3 months after you stop taking the study drug.

Women: If you become pregnant while you are on study treatment or within 1 month of your last dose of ibrutinib you must notify the study staff. If you become pregnant on the study, you must immediately stop taking the study treatment. The Investigator will ask if information may be collected about the pregnancy and the birth of the baby even after study treatment is stopped. You may refuse to provide this information.

### **What are the possible benefits to you?**

It is hoped that the use of protocol therapy may result in tumor shrinkage or stabilization of your disease.

You may not get any benefit from being in this research study.

### **What are the possible benefits to other people?**

Information obtained from this study may help subjects in the future with the same disease by contributing to the knowledge of whether this therapy offers advantages over other therapies available.



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### **What are the alternatives to being in this research study?**

Instead of being in this research study, you can choose not to participate.

If you choose not to participate in this study you may elect to receive standard salvage therapy as per your primary oncologist, which may include other chemotherapy drugs given alone or in combination. You may also have the option of receiving palliative therapy or hospital care.

### **What will being in this research study cost you?**

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

The study will pay for the handling of the optional research biopsy, sample collection and storage. While you are participating in the study, the drug supply for ibrutinib orally daily for up to a year of treatment will be supplied to you free of charge by Janssen Scientific Affairs LLC. The drug supply for umbralisib orally daily for up to a year of treatment will be supplied to you free of charge by TG Therapeutics.

All other clinically indicated tests and procedures (laboratory tests, radiology tests, chest CT, physical examinations) will be your responsibility or your health insurance company's responsibility as these are considered standard cancer treatment. You or your health insurance company might also have to pay for other drugs or treatments that are given to help you control side effects.

You will be responsible for any applicable insurance deductibles and co-payments. If you wish to speak with a financial counselor about your insurance coverage and benefits, let the investigator or other study personnel know. A contact for personal assistance will be made available for you.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institutes Web site 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 the information is to call 1-800-4-CANCER (1-800-422-6237) and



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ask them to send you a free copy.

### **Will you be paid for being in this research study?**

You will not be paid to be in this research study.

### **Who is paying for this research?**

Janssen Scientific Affairs LLC and TG Therapeutics are providing monetary support and study drug. The Institution receives money from these companies to conduct this study.

Dr. Matthew Lunning, the Principal Investigator on this study, provides consulting services to Janssen Pharmaceuticals, the sponsor of this study, in which he receives money

Dr. Lunning also receives money for participating on the Advisory Board for TG Therapeutics.

This research is being paid for by the Fred & Pamela Buffett Cancer Center at the University of Nebraska Medical Center.

### **What should you do if you are injured or have a medical problem during this research study?**

Your welfare is the main concern of every member of the research team. If you are injured or have a medical problem as a direct result of being in this study, you should immediately contact one of the people listed at the end of this consent form. Emergency medical treatment for this injury or problem will be available at the Nebraska Medical Center. If there is not sufficient time, you should seek care from a local health care provider.

The Institution has no plans to pay for any required treatment or provide other compensation. If you have insurance, your insurance company may or may not pay the costs of medical treatment. If you do not have insurance, or if your insurance company refuses to pay, you will be expected to pay for the medical treatment.

Agreeing to this does not mean you have given up any of your legal rights.

### **How will information about you be protected?**

You have rights regarding the protection and privacy of your medical information collected before and during this research. This medical information is called "protected health information" (PHI). PHI used in this study may include your medical



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record number, address, birth date, medical history, the results of physical exams, blood tests, x-rays as well as the results of other diagnostic medical or research procedures. Only the minimum amount of PHI will be collected for this research. Your research and medical records will be maintained in a secure manner.

### **Who will have access to information about you?**

By signing this consent form, you are allowing the research team to have access to your PHI. The research team includes the investigators listed on this consent form and other personnel involved in this specific study at the Institution.

Your PHI will be used only for the purpose(s) described in the section What is the reason for doing this research study?

You are also allowing the research team to share your PHI, as necessary, with other people or groups listed below:

- The UNMC Institutional Review Board (IRB)
- Institutional officials designated by the UNMC IRB
- Federal law requires that your information may be shared with these groups:
  - The HHS Office of Human Research Protections (OHRP)
  - The Food and Drug Administration (FDA)
- The HIPAA Privacy Rule requires the following groups to protect your PHI:
  - Your health insurance company
  - The Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC)

Your PHI may also be shared with the following groups. However, these organization(s) do not have the same obligation to protect your PHI:

- Janssen Scientific Affairs and TG Therapeutics, these companies provide the study drugs and funds to the Institution to conduct this research
- Data and Safety Monitoring Committee (DSMC)
- The National Cancer Institute's (NCI) Clinical Trial Reporting Program

You are authorizing us to use and disclose your PHI for as long as the research study is being conducted.

You may cancel your authorization for further collection of PHI for use in this research at any time by contacting the principal investigator in writing. However, the PHI which is included in the research data obtained to date may still be used. If you cancel this authorization, you will no longer be able to participate in this research.



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### **How will results of the research be made available to you during and after the study is finished?**

In most cases, the results of the research can be made available to you when the study is completed, and all the results are analyzed by the investigator/sponsor of the research. The information from this study may be published in scientific journals or presented at scientific meetings, but your identity will be kept strictly confidential.

If you want the results of the study, contact the Principal Investigator at the phone number given at the end of this form or by writing to the Principal Investigator at the following address:

*Matthew A. Lunning, D.O*  
*Assistant Professor of Medicine*  
*986840 Nebraska Medical Center*  
*Omaha, NE 68198-6840*

A description of this clinical trial will be available on [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

### **What will happen if you decide not to be in this research study?**

You can decide not to be in this research study. Deciding not to be in this research will not affect your medical care or your relationship with the investigator or the Institution. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

### **What will happen if you decide to stop participating once you start?**

You can stop participating in this research (withdraw) at any time by contacting the Principal Investigator or any of the research staff.

Deciding to withdraw will otherwise not affect your care or your relationship with the investigator or this institution. You will not lose any benefits to which you are entitled.

For your safety, please talk to the research team before you stop taking any study drugs or stop other related procedures. They will advise you how to withdraw safely. If you withdraw you may be asked to undergo some additional tests. You do NOT have to agree to do these tests.

You may be taken off the study if you do not follow instructions of the investigator or the research team.



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Any research data obtained to date may still be used in the research.

Any tissue (e.g., blood sample) obtained to date may also be used in the research. Should you wish to have any leftover tissue samples withdrawn from use in future research, a request must be made in writing to the Principal Investigator at the address indicated above.

### **Will you be given any important information during the study?**

You will be informed promptly if the research team gets any new information during this research study that may affect whether you would want to continue being in the study.

### **What should you do if you have any questions about the study?**

You have been given a copy of "*What Do I Need to Know Before Being in a Research Study?*" If you have any questions at any time about this study, you should contact the Principal Investigator or any of the study personnel listed on this consent form or any other documents that you have been given.

### **What are your rights as a research participant?**

You have rights as a research subject. These rights have been explained in this consent form and in *The Rights of Research Subjects* that you have been given. If you have any questions concerning your rights, or want to discuss problems, concerns, obtain information or offer input, or make a complaint about the research, you can contact any of the following:

- The investigator or other study personnel
- Institutional Review Board (IRB)
  - Telephone: (402) 559-6463.
  - Email: IRBORA@unmc.edu
  - Mail: UNMC Institutional Review Board, 987830 Nebraska Medical Center, Omaha, NE 68198-7830
- Research Subject Advocate
  - Telephone: (402) 559-6941
  - Email: unmcrsa@unmc.edu

## OPTIONAL SAMPLE COLLECTIONS

### **Sample Collections for Biobanking for Possible Future Studies**

This research study also involves the collection and storage of blood and tissue for future studies that are not a part of the study in which you are participating. The





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process of collecting and storing blood or tissue for future research is referred to as tissue banking. A collection of blood or tissue available for use by researchers is referred to as a tissue bank or bio-repository.

A UNMC designated Laboratory manages the bio-repository for the samples collected in this study. The purpose of storing the samples is to make them available to researchers including those from TG Therapeutics, and Janssen Scientific LLC who have approved new ideas for research that require studying human tumors or blood. As part of this study, your samples and health information collected from your medical records (after removal of your name, date of birth and medical record number and identified only by a code) may be shared with other investigators who are conducting research regarding the causes, prevention, diagnosis, and treatment of cancer.

The samples will be kept until they are used up or destroyed.

Most future research studies will focus on cancer, some research projects may also include other diseases, such as heart disease, diabetes or Alzheimer's disease. This may also include research on inherited traits also known as hereditary genetic testing (to find out if cancer runs in your family). The research that may be done is unknown at this time.

Reports about any research tests done with your samples will not be given to you or your oncologist, or family doctor. These reports will not be put in your medical records.

This research may not benefit you, but may help people in the future who have the same kind of cancer as you have. You can indicate your wish to participate in this additional research, and have your samples stored by the UNMC designated central repository for future extended research purposes when signing this consent form. You may decide not to participate in the "optional" study and still participate in this main study

### **Optional US or CT Image Guided Lymph Node Biopsies for Research:**

The researchers doing this study are interested in doing additional research now in tumor cell signaling ( a complex system of a communication that activates basic cellular activities and coordinates cell actions) or in the future on the optional ultrasound (US) or computer tomography (CT) guided lymph node biopsy samples collected from you to better understand the nature of cancer and how patients respond to treatment. Errors in cellular information processing are responsible for



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diseases such as cancer and diabetes for example. By understanding cell signaling, diseases may be treated effectively. Rapid advances in technology make it impossible to predict what new tests or studies may be possible in the future.

The collection of these 3 optional lymph node biopsies will be obtained via US or CT guided biopsy of accessible lymph nodes at day 0 (pre-treatment; core biopsy), day 8 (fine needle aspirate) and end of treatment (progressive disease, toxicity, or end of 1 year of study drug; core biopsy) so as to assess the change in signaling resulting from treatment. The samples will not be sold. Once these tests have been completed, and with your permission any leftover samples will be saved and stored for future use. Again, your samples and health information collected from our medical records will have your name, date of birth and medical record number removed and samples will be identified only by a code.

During an image guided (US or CT scan) biopsy, a small amount of tissue is removed from the abnormal area (lymph node) with a needle. Radiologists or the investigator will use image guidance (ultrasound) in performing the biopsies to obtain tissue from the right spot and to avoid injuring important nearby body parts. This can be performed on an outpatient basis using local anesthetic. Conscious sedation can also be used when necessary.

Reasons for choosing an image guided biopsy rather than a surgical biopsy include:

- Smaller incision
- No stitches
- No scar
- Shorter procedure
- Minimal bruising
- No or minimal cosmetic disfigurement
- Less expensive

### ***Types of Image Guided Biopsies:***

Following is information on two types of image guided biopsies performed by radiologists or the investigator in this optional biopsy for research.

***Fine Needle Aspiration Biopsy (Radiologist or Investigator):*** Ultrasound or CT guided for accurate placement of the needle. Uses a tiny needle, smaller than the needle used to draw blood. Commonly used on the thyroid gland, salivary glands, breasts, and lymph nodes. CT guidance will only be used by the radiologist.

***Needle Core Biopsy (Radiologist only):*** Ultrasound guided for accurate placement of



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the needle. Uses a larger needle than a fine needle aspiration biopsy. Used to remove tissue from many organs and body structures.

The risks involved in an image guided biopsy include the following:

- Bleeding and infection at the puncture site
- A hematoma or collection of blood may form at the biopsy site
- Infection or abscess

### **MAKING YOUR CHOICE:**

\_\_\_\_\_ I agree to up to three US or CT guided biopsies of accessible lymph nodes samples taken from me for extended research (optional).

\_\_\_\_\_ I do not agree to the three possible US or CT guided biopsies of accessible lymph nodes samples taken from me for extended research (optional).

### **MAKING YOUR CHOICE:**

\_\_\_\_\_ I agree to allow storage and use of the optional lymph node tissue samples taken from me for extended research (optional).

\_\_\_\_\_ I do not agree to allow optional lymph node tissue samples taken from me to be stored for extended research (optional).

### **Optional extended research on your blood samples collected during the research**

The researchers doing this study are interested in doing additional research now or in the future on the samples collected from you to better understand the nature of cancer and how patients respond to treatment. Rapid advances in technology make it impossible to predict what new tests or studies may be possible in the future.

The collection of the research blood samples before you began treatment and before the 2nd cycle and at the end the 2nd, 4th, 6th, and 9th, and 12th cycles (+/- 7 days) cycle (research blood only), as well as after month 12, restaging assessments of your lymphoma when they occur and only if feasible (research blood only) is a necessary part of this study and will be used only for these purposes. The samples will not be sold. Once these tests have been completed, and with your permission any leftover samples will be saved and stored for future use.

### **MAKING YOUR CHOICE:**



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\_\_\_\_\_ I agree to allow storage and use of **blood** samples taken from me for extended research (optional).

\_\_\_\_\_ I do not agree to allow **blood** taken from me to be stored for extended research (optional).

### **Confidentiality of ALL Samples**

To protect your identity, the information that will be on your research samples will be limited to your pathology identification number (if applicable), and your participant code, which may include your initials.

### **Withdrawal of ANY Samples**

If you no longer want your samples to be used in this research, you should tell the study doctor. The study doctor will notify the sponsor-investigator who will ensure the samples are returned to the hospital from which they were obtained if needed, or destroyed. If tests have already been done on your sample(s) it will not be possible to withdraw those results. However, no further testing will be done.

### **Documentation of informed consent**

You are freely making a decision whether to be in this research study. Signing this form means that:

- You have read and understood this consent form.
- You have had the consent form explained to you.
- You have been given a copy of The Rights of Research Subjects
- You have had your questions answered.
- You have decided to be in the research study.
- If you have any questions during the study, you have been directed to talk to one of the investigators listed below on this consent form.
- You will be given a signed and dated copy of this consent form to keep.

Signature of Subject \_\_\_\_\_

Date \_\_\_\_\_

My signature certifies that all the elements of informed consent described on this consent form have been explained fully to the subject. In my judgment, the subject possesses the legal capacity to give informed consent to participate in this research and is voluntarily and knowingly giving informed consent to participate.

Signature of Person obtaining consent \_\_\_\_\_

Date \_\_\_\_\_



PT NAME:

MR#:

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**Authorized Study Personnel  
Secondary**

\* Armitage, James  
phone: 402-559-7290  
alt #: 402-888-7290  
degree: M.D.

\* Bierman, Philip  
phone: 402-559-5520  
alt #: 402-888-1004  
degree: MD

\* Bociek, Robert (Greg)  
phone: 402-559-5388  
alt #: 402-888-2630  
degree: MD

\* Vose, Julie  
phone: 402-559-3848  
alt #: 402-305-0790  
degree: M.D.

## What Do I Need To Know Before Being In A Research Study?

You have been invited to be in a **research study**. Research studies are also called "clinical trials" or "protocols." **Research** is an organized plan designed to get new knowledge about a disease or the normal function of the body. The people who are in the research are called **research subjects**. The **investigator** is the person who is running the research study. You will get information from the investigator and the research team, and then you will be asked to give your **consent** to be in the research.

**This sheet will help you think of questions to ask the investigator or his/her staff. You should know all these answers before you decide about being in the research.**

What is the **purpose** of the research? Why is the investigator doing the research?

What are the **risks** of the research? What bad things could happen?

What are the possible **benefits** of the research? How might this help me?

**How is this research different** than the care or treatment I would get if I wasn't in the research? Are there other treatments I could get?

Does **everyone** in this research study get the same treatment?

Will being in the research **cost** me anything extra?

Do I have to be in this research study? Will the doctor still take care of me if I say **no**?

Can I **stop** being in the research once I've started? How?

Who will look at my **records**?

How do I reach the investigator if I have more **questions**?

Who do I call if I have questions about being a **research subject**?

**Make sure all your questions are answered before you decide whether or not to be in this research.**

## **THE RIGHTS OF RESEARCH SUBJECTS AS A RESEARCH SUBJECT YOU HAVE THE RIGHT ^**

**^ to be told everything you need to know about the research before you are asked to decide whether or not to take part in the research study.** The research will be explained to you in a way that assures you understand enough to decide whether or not to take part.

**^ to freely decide whether or not to take part in the research.**

**^ to decide not to be in the research, or to stop participating in the research at any time.** This will not affect your medical care or your relationship with the investigator or the Nebraska Medical Center. Your doctor will still take care of you.

**^ to ask questions about the research at any time.** The investigator will answer your questions honestly and completely.

**^ to know that your safety and welfare will always come first.** The investigator will display the highest possible degree of skill and care throughout this research. Any risks or discomforts will be minimized as much as possible.

**^ to privacy and confidentiality.** The investigator will treat information about you carefully, and will respect your privacy.

**... to keep all the legal rights you have now.** You are not giving up any of your legal rights by taking part in this research study.

**^ to be treated with dignity and respect at all times**

**The Institutional Review Board is responsible for assuring that your rights and welfare are protected. If you have any questions about your rights, contact the Institutional Review Board at (402) 559-6463.**