PRINCIPAL INVESTIGATOR: Steven Pavletic, MD

STUDY TITLE: A Study of Front Line Ibrutinib without corticosteroids for Newly Diagnosed Chronic Graft-Versus Host Disease

STUDY SITE: NIH Clinical Center

Cohort: *Affected Patient*

Consent Version: *4/26/2023*

WHO DO YOU CONTACT ABOUT THIS STUDY?

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KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

You are being asked to take part in this study because you have moderate to severe chronic Graft-Versus-Host disease (cGVHD). Chronic GVHD is a complication that can occur after a stem cell or bone marrow transplant where the new (also called "donor" or "graft") cells attack the recipient's (also called "host's") body.

The purpose of this study is to see if ibrutinib will help patients newly diagnosed with cGVHD.

The use of ibrutinib in this study is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration (FDA) as a first-line treatment of cGVHD. However, the FDA has given us permission to use ibrutinib in this study. Ibrutinib is a type of drug called a kinase inhibitor. Kinases are proteins inside cells that help cells live and grow. Ibrutinib blocks one of kinases important in immune cells. By blocking this kinase with ibrutinib, the transplanted donor cells are prevented from attacking the body and help to treat cGVHD in some patients.

Ibrutinib has been approved by the U.S. Food and Drug Administration (FDA) for treatment of cGVHD after failure of one line of therapy, but not as a first-line treatment of cGVHD. We hope that giving ibrutinib earlier in the treatment of cGVHD will help to treat it better.

This study will be conducted in several institutions. The information and samples collected at all institutions will be studied at the National Cancer Institute (NCI) of National Institutes of Health (NIH).

There are other drugs that may be used to treat cGVHD and these can be given by your regular doctor if you are not in this study. For example: steroids, sirolimus, and tacrolimus. The way in which treatment is given in this study (a medication taken by mouth) and the side effects are not very different than if you were to receive standard of care. The most common side effects of ibrutinib that are similar to other treatments include diarrhea, muscle and bone pain, nausea, low blood cell counts, rash and bruises.

If you decide to join this study, here are some of the most important things that you should know:

- First, we will perform tests to find out if you fit the study requirements. We will do standard blood tests and evaluations to test your health and the status of your disease.
- If you fit the study requirements and decide to take part, you will start your treatment with ibrutinib. During treatment we will need to see you at the Clinical Center every 2 weeks for first 2 months and approximately once a month after that while you are receiving treatment. You will get your treatment on an outpatient basis. Each visit should last no more than 8 hours.
- At each visit you will have clinical and laboratory tests to see how you are doing and see how your disease is responding. We will also collect required samples from you (such as: blood and tissue) for clinical and research purposes.
- As described above and later in more detail in this consent form, you may have side effects if you take part in this study. Some can be mild or very serious and may include death.
- The effects of ibrutinib on the developing fetus are unknown. For this reason you must agree to use highly effective methods of birth control during the period of therapy (hormonal or barrier method of birth control; abstinence) and for 30 days after the last dose of study drug.
- After the study treatment has ended, the study team will continue to contact you or your physician once a year for 2 years from the start of your treatment.

This study may benefit you by lessening your symptoms, such as pain, that are caused by the cGVHD. Even if you do not benefit from this study, the results from our research may help others in the future.

You are free to stop participating in the trial at any time. If you decide to stop, the study doctor may ask you to agree to certain tests to make sure it is safe for you to stop.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to

participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

This is a research study. The purpose of this research study is to see if ibrutinib as a first-line treatment will help patients with cGVHD.

We are asking you to join this research study because you have moderate to severe cGVHD. cGVHD is a serious condition where donor (or "graft") cells attached the patient's (or "host's") cells after a transplant.

Ibrutinib is often given after a patient fails other treatment(s) for cGVHD. This study will look at giving it prior to other treatments or first, known also as "first-line." Ibrutinib is considered investigational in this study as it has not been approved by the U.S. Food and Drug Administration as a first-line treatment of cGVHD.

Ibrutinib is a type of drug called a kinase inhibitor. Kinases are proteins inside cells that help cells live and grow. Ibrutinib blocks one of kinases important in immune cells. By blocking this, it is possible that the transplanted donor cells will be prevented from attacking your cells.

WHAT WILL HAPPEN DURING THE STUDY?

You will take ibrutinib by mouth once every day of every cycle. One cycle is 28 days. Try to take your dose at the same time every day. You should take it with a glass of water. If you forget to take it on your regular time, you can take it anytime during this day. If you vomit after taking ibrutinib, please, do not immediately take another capsule. You should simply proceed with next dose next day. If you forget to take your drug on any day, do not make-up the dose next day.

You will be given a Medication Diary to record the date and time of each dose of ibrutinib. You will also be asked to record missed doses. Please bring the diary with you to every study visit.

At each visit, please also bring empty bottles and any unused medication you may have.

Treatment may continue for up to 2 years but can be stopped earlier if you have unacceptable side effects or you are no longer benefiting from the study therapy.

Treatment and all study related procedures will be done during outpatient visits without planned hospitalization.

You will need to supply a complete list of your current medications to the study doctor. This includes over-the-counter medications and herbal supplements. Some medications may interact with the study drug and it is important that your study doctor be aware that other medications can be prescribed if needed. If you do not already do so, please carry a list of your medications at all times.

Before you begin the study

During the screening period, your doctor will make sure you are able to take part in the study.

Blood samples may be drawn at your local medical doctor's office, your local laboratory, or at the NIH. Samples drawn at an outside location will be sent to the NIH.

The following tests are needed to determine whether you are eligible for this trial:

- Routine blood tests (about 5 tablespoons)
- Pregnancy test (blood or urine) if you are a woman of childbearing potential
- Other testing for microbes and viruses including Hepatitis B and C infection (if you have results of viral tests that are less than 3 months old, you may not need to have this test redone). If you are found to be positive for Hepatitis B or Hepatitis C then you will be informed of your status, counseled about potential infection of sexual contacts, and will inform about potentially curative treatment options for Hepatitis C.
- Complete physical exam and vital signs
- Electrocardiogram (ECG) – a test for your heart
- An assessment of your general well-being and ability to perform activities of daily life (also called an assessment of performance status)

If the tests or if your answers show that you are not able to take part in the study, you will not be able to continue. Your study doctor will discuss other care options with you.

During the study

You may not have to repeat some of the tests performed at baseline (before you begin taking ibrutinib) if you have already done them as a part of screening.

The following routine tests and procedures will be performed at every visit, and may be repeated after screening and before the first dose of study drug if not done recently unless otherwise noted:

- Physical exam, including vital signs and assessment of your performance status
- Review of all your current medications
- Routine blood tests (about 5 tablespoons)
- CT scan of the chest (without contrast) only at visits if the doctor feels this is necessary

The following research tests and procedures will be done at the visits as noted:

- Pulmonary function testing to look at lung function (Baseline/prior to treatment, and after Cycle 6 and Cycle 12)

- cGVHD Questionnaires to evaluate your quality of life and current symptoms of cGVHD. Questionnaires will take 15-30 minutes to complete. Questionnaires will be obtained from English speaking patients only. (Baseline/prior to treatment, and after or during Cycles 2, 4, 7, 10 and 12)
- Research blood and tissue testing as described in more detail in the next section

Additional research testing

Research testing will be performed on your blood and on tissue samples (biopsies) from your skin and your mouth. They will be used to study how your immune system responds to the study drug and to measure the levels of drug in your body. The amount of blood to be collected at any visit for research will be about 4 tablespoons.

Optional oral/skin biopsy at Baseline, Cycle 7 Day 1, Cycle 12 Day 28: The biopsy (ies) is (are) exclusively for research purposes. Although it will not benefit you, it might help other people in the future. All of the oral/skin biopsies are optional. Even if you say "yes" to have the biopsy, you can change your mind at any time.

If you agree to have the optional biopsy, you will be asked to sign a separate procedure consent before you have the procedure.

When you are finished taking the drugs (treatment)

When you complete your study therapy you will have the following tests performed at your last study visit:

- History and physical exam, vital signs
- Disease assessments including: CT scans (if your physician thinks necessary); cGVHD questionnaires
- Routine blood tests (about 5 tablespoons)
- Research blood tests - The amount of blood to be collected at any visit for research will be about 4 tablespoons.

If you discontinue the study therapy at any other time, you will be asked to return to the clinic within 30 days after your last dose to complete the above assessments.

Regardless of the reason for stopping study therapy, all patients will be contacted by phone ~ 30 days after your last dose of study therapy. We will ask you about any side effects that you might experience. We may follow you for side effects for longer if they are still present at the 30-day phone call.

Annual Telephone Follow up

After you finish taking the study medication, at one year and two years after you started taking ibrutinib, you will be contacted by telephone to ask how you are feeling and if you have taken any other medications to treat cGVHD.

Remote Assessments

In the first quarter of 2020, a pandemic was announced for COVID-19 (Coronavirus Disease 2019) which is caused by the virus SARS-CoV-2. In light of the pandemic, tele-medicine has been used as an alternative way to perform assessments without having participants in clinical trials come to the clinic. Your study doctor may determine that the risks associated with you visiting the clinic during the COVID-19 pandemic may outweigh the benefit from seeing you in person at the clinic. Remote assessments may be performed at the discretion of your study doctor via phone, email, or video chat to speak with you directly about the following: patient history, verbal exam, symptom reporting, education, and questionnaires.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for 2 years.

The expected length of your participation depends on how your cGVHD reacts to the study drug and how well you tolerate the study drug. You will have to come to the clinic every 2 weeks for the first 2 months, and then once every 28 days after that. Extra visits may be added if needed. You will be asked to come for a follow-up visit 30 days after your last dose of the study drug. The study staff will contact you approximately every year by phone, e-mail or postal mail until 2 years from the date you started the treatment to see how you are doing.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have about 20 people participate in this study at the NIH.

Up to 40 people might take part across all study sites.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

The drug used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last longer.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.

The study doctor may adjust the study drugs to try to reduce side effects.

What side effects or risks can I expect from the treatment?

The side effects listed below have been reported by patients in other clinical studies who have received ibrutinib.

COMMON, SOME MAY BE SERIOUS (reported in >10% of subjects)	OCCASIONAL, SOME MAY BE SERIOUS (reported in >5-10% of subjects)	RARE, SOME MAY BE SERIOUS (reported in >2-5% of subjects)
• Diarrhea • Fatigue/tiredness • Nausea • Anemia • Low white blood cell count (cells that help fight infection) (neutropenia/neutrophil count decreased) • Low platelet count (cells that help blood to clot) (thrombocytopenia)	• Cough • Upper Respiratory Tract Infection • Fever (pyrexia) • Joint Pain (arthralgia) • Muscle spasms • Constipation • Pneumonia • Vomiting • Decrease/Loss of appetite • Rash • Sores in the mouth which may cause difficulty swallowing (stomatitis) • Bruises	• Swelling of arms or legs (peripheral edema) • Headache • High Blood Pressure (hypertension) • Shortness of breath (dyspnea) • Urinary Tract Infection • Abdominal pain • Contusion • Dizziness • Low potassium (hypokalemia) • Abnormal heartbeat (atrial fibrillation)

Bleeding

You may experience bruising or nose bleeds during dosing with the study drug. Rarely, serious internal bleeding, such as bleeding in your stomach, intestine, or brain may occur sometimes resulting in death. If you take medicines or supplements that increase your 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. Call your Study Team immediately if you have signs or symptoms of severe bleeding in or around the brain such as sudden severe headaches, weakness in the arms or legs, difficulty speaking or understanding speech, or loss of balance. Also, 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

Abnormal rapid and/or irregular heart rhythm (atrial fibrillation, atrial flutter and/or ventricular tachyarrhythmia) and heart failure, including some fatal events, which could sometimes be sudden, have been reported in patients treated with ibrutinib, especially when they also have heart conditions, increased blood pressure or have diabetes, infections, or had abnormal heartbeat in the past. Tell your stud doctor immediately if you have any symptoms of heart problems such as

feeling as if your heartbeat is fast and irregular, lightheadedness, dizziness, shortness of breath, chest discomfort, swollen legs, or you faint.

Infections

You may experience viral, bacterial, or fungal infections during treatment with ibrutinib. Some of these infections have led to hospitalization and death. There is a small but well recognized risk of serious fungal, mold (Aspergillus), infections of the lung or the central nervous system and doctors will prescribe medications to prevent these to minimize chance of its occurrence. Contact your study doctor immediately if you have fever, chills, weakness, confusion, body aches, cold or flu symptoms, vomiting, jaundice, abnormal liver function tests, feel tired or feel short of breath – they could be signs of an infection or any other signs or symptoms of a possible infection. Your study doctor may start or continue medication to help prevent or treat 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. In rare instances, cases of hepatitis E, which may be chronic have occurred in patients treated with ibrutinib.

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 dosing and you should not assume that this increase in white blood cells means your disease became worse. This increase may last for several weeks to months. An 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 participants who received ibrutinib. Your Study Doctor will monitor your blood counts and may administer 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.

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 2-3 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.

Before starting the study drug, you must tell your Study Team about any drug allergies. You should tell the Study Team right away if you have any allergy symptoms listed above or any other side effects during the study.

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 observed in patients who have been treated with ibrutinib. These include solid tumors, skin cancer, and cancers of the blood. The causal relationship with ibrutinib is unknown. You should tell your Study Doctor if you develop a new cancer while taking study drugs.

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 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, also called high blood pressure , 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.

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 a cough, or any signs of new or worsening respiratory symptoms such as shortness of breath or difficulty breathing.

Stroke

Cases of stroke, with and without changes in heartbeat rhythm and/or hypertension have been reported with the use of ibrutinib. Some of these cases have led to death. Seek immediate medical attention if you notice or someone notices in you, any of the following: sudden numbness or weakness in the limbs (especially on one side of the body), sudden confusion, trouble speaking or understanding speech, sight loss, difficulty walking, loss of balance or lack of coordination, and/or sudden severe headache with no known cause. These may be signs and symptoms of a stroke.

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.

Interference with other drugs/supplements/food

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 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 now and during the study. You should notify your study doctor immediately about any side effects to avoid possible harm. **Do not start any new medication or over the counter supplement without first consulting with your Study Team.**

Drug interruption for any surgical procedures

Ibrutinib may increase the risk of bleeding with any surgical procedure. Ibrutinib should be stopped at least 3 to 7 days before and after surgery depending upon the type of surgery and the risk of bleeding. Please contact your Study Doctor if you have any planned surgical procedures. For emergency surgical procedures, ibrutinib should be 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 after a surgical procedure.

Side effects of study procedures

Blood Sampling

The possible side effects of drawing blood include pain, bleeding, bruising, light-headedness, fainting and, on rare occasions, local blood clot formation or infection with redness and irritation of the vein. Up to approximately 9 tablespoons of blood will be collected during one visit and no more than 20 tablespoons will be collected over an 8-week period.

Biopsy Samples

The risks of the biopsy procedure include pain at the biopsy site, bleeding from the skin, bruising, and infection of the biopsy site. Please ask the study doctor if you have questions about the risks of the study procedures.

Study Questionnaire

Questionnaires may contain questions that are sensitive in nature. You are asked to only answer questions that you are comfortable with.

What are the risks related to pregnancy?

If you are able to become pregnant, we will ask you to have a pregnancy test before starting this study. You will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 3 months after you finish study treatment (the restricted period). If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus. You must tell the study doctor if your birth control method fails during the restricted period. If you think or know you have become pregnant during the restricted period, please contact the study team as soon as possible.

If you are a sexually active person with a partner able to become pregnant, it is important that your partner not become pregnant during the restricted period. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you think your partner has become pregnant during the restricted period, please contact the study team as soon as possible. If you and your partner plan for your partner to become pregnant after the restricted time period, please discuss this with the study team.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

However, the potential benefit to you might be the lessening of your symptoms that are caused by the cGVHD. Because there is not much information about the drug's effect on your cGVHD, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

Are there any potential benefits to others that might result from the study?

The information from this study may help other people with cGVHD. It may also help doctors learn more about the study drug as an early treatment for cGVHD.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could:

- choose to be treated with drugs or other treatments already approved by the FDA for your disease
- choose to take part in a different study, if one is available
- choose not to be treated for cGVHD but you may want to receive comfort care to relieve symptoms.

You should discuss with your doctor your other choices and their risks and benefits.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

We do not plan to return research results to you. A summary of the research results will be posted on Clinicaltrials.gov at completion of the study.

EARLY WITHDRAWAL FROM THE STUDY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your cGVHD worsens, or does not improve based on the doctor's assessment after 6 months of treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if you do not come to your clinic visits, do not follow the study instructions given to you or miss too many doses (>20%) of your study medication
- if you become pregnant
- if the ibrutinib may become unavailable
- if new information shows that another treatment would be better for you
- if the study is stopped for any reason

In this case, you will be informed of the reason therapy is being stopped.

After therapy is stopped we would like to see you for a safety visit 30 days after your last dose.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines,

information collected on you up to that point may still be provided to Pharmacyclics LLC, or designated representatives.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved for use in other research studies?

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding cGVHD, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

Will your specimens or data be shared for use in other research studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document.

We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. These researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

How long will your specimens and data be stored by the NIH?

Your specimens and data may be stored by the NIH indefinitely.

Risks of storage and sharing of specimens and data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

The NIH and the research team for this study are using ibrutinib developed by Pharmacyclics LLC through a joint study with your study team and the company. The Company also provides financial support for this study.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor, Center for Cancer Research, or their agent(s)
- Qualified representatives from Pharmacyclics LLC, the pharmaceutical company who produces ibrutinib

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Steven Pavletic, MD, pavletis@mail.nih.gov, 240-764-6174. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

Signature of Witness	Print Name of Witness	Date

NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.