CONSENT TO TAKE PART IN A CLINICAL RESEARCH STUDY
AND
AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Study Title:	**Phase II Trial of Ibrutinib and PD-1 Blockade in High Risk Chronic Lymphocytic Leukemia to Improve Immune Function**
Protocol Number:	**MCC# 19199**
Sponsor:	**Moffitt Cancer Center**
Principal Investigator: (Study Doctor)	**Julio C. Chavez, MD**
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WHAT IS THIS STUDY ABOUT?

You are being asked to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with family, friends and your general practitioner if you wish. Ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

You are being asked to take part in this research study because you have untreated Chronic Lymphocytic Leukemia (CLL). This study involves pembrolizumab, a drug that works by helping your immune system to fight your cancer and ibrutinib, an approved treatment for patients with CLL. The purpose of this study is to see how pembrolizumab and ibrutinib affects your CLL.

If you agree to participate and qualify for this study, you will be given the following study treatments:

- 200mg of pembrolizumab by intravenous infusion every 3 weeks for one year and up to 2 years
- 420mg of ibrutinib daily by mouth starting at week 6 for one year. If there is clinical benefit, an additional year may be prescribed.

After you are done taking the study treatments, you will be asked to return for the follow up visits listed below to see how you are doing after taking the study treatments:

- end of treatment visit within 3 days of taking your last dose of ibrutinib
- safety follow up visit within 35 days of your last dose of ibrutinib
- follow up visit about every 12 weeks for 12 months and up to 24 months

More information about what will be done at each study visit will be discussed in a later section of this informed consent form.

This study is only going to be done at Moffitt Cancer Center and there will be a total of 25 participants.

STUDY SCREENING PROCEDURES:

In order to determine if you are eligible to participate in the study you will complete the screening procedures (activities, tests, and evaluations) described in this form.

- Informed consent
- Demographic Questions – We will ask you to give personal information, such as your name, date of birth, race, and gender
- Health and Medication Questions – We will ask you to answer questions about your health, your medical history, and the medications you take.
- Childbearing potential – You will be asked about your sterility status and contraceptive methods, if applicable to you.
- Pregnancy Test (only for females who are able to become pregnant)
- Physical Exam – Vital Signs (blood pressure, heart rate, respiratory rate, and temperature), Weight, and Height
- Performance status – Your study doctor will assess and assign a score based on your ability to perform daily tasks by asking questions.
- Blood Testing – Whole blood samples will be taken from your arm for laboratory tests.
- Urine Testing – Take a urine sample to do laboratory tests.
- Blood and urine tests to monitor your health. It will check your blood counts (number of each type of blood cell), chemistries (elements and minerals in your blood), blood clotting and how well your organs are functioning.
- ECG – A test which records the electrical activity of your heart
- Disease Assessment – You study doctor will evaluate your disease status using bone marrow biopsy, imaging tests (like CT scans) and lab results.

STUDY PROCEDURES:

If you are eligible to participate in this study, you will undergo one or more of the study procedures described in this form at each study visit. The study doctor and study team will be able to answer any questions you have about these procedures.

- Physical Exam – See how tall you are and see how much you weigh. You should ask the study doctor or study staff about what else will happen during this exam.
- Health and Medication Questions – Ask you to answer questions about your health, your medical history, and the medications you take.
- Vital Signs – Check your blood pressure by putting a band around your arm (this will squeeze your arm for about a minute), count the number of heartbeats over time, count the number of times you breathe in and out over a period of time, and take your temperature.
- Blood tests to monitor your health. It will check your blood counts (number of each

type of blood cell), chemistries (elements and minerals in your blood), and how well your organs are functioning. You will be checked for hepatitis and HIV viruses.

- Prevnar 13 Vaccination – If you have not had this vaccination in the last 8 weeks, you will be given this vaccine. By giving you this vaccine, the investigators will be able to measure how well your immune system is working while you are in this study.
- Research blood samples- will be drawn to check your immune system on day 1, of week 1, week 6, week 21, and at the end of ibrutinib treatment.
- Bone marrow biopsy/aspirate – To collect a bone marrow biopsy/aspirate, an area around the hip or pelvis typically or other site is numbed, and a small amount of bone marrow and bone is sucked out through a needle.
- Pregnancy Testing – Test your blood or urine to see if you are pregnant. You will only have pregnancy testing if you are a woman and can have children.
  - The study doctor or study staff will tell you if the pregnancy test results are positive.
  - The results of the pregnancy testing must be negative in order for you to be in the study.
- Performance status – Your study doctor will assess and assign a score based on your ability to perform daily tasks by asking questions.
- Study Treatment – As described in an earlier section, you will be given pembrolizumab by IV. You will also be given a supply of ibrutinib oral medication and the study team will tell you how to take it. You will be asked to bring back all unused oral study drug, including empty bottles, to each visit.
- Disease Assessment - During the course of your study treatment, your study doctor will evaluate your response to study treatment using bone marrow, CT scans, and lab results.
- Study Diary - Give you a study diary and tell you how to use it. Ask you to bring the completed diary back to the study center at each visit.
- Post-study treatment visits – You may be asked to return to the study center for limited tests or you may receive a phone call to provide information, such as new therapies you may have started.

PARTICIPANT RESPONSIBILITIES:

- In order for this study to provide good information about how the study drugs work in participants with your condition, you will be expected to do the following: starting with the pre-screening or screening visit through 90 days after the last dose of study treatment.
- Attend all study visits.
- Tell the study doctor if you are feeling bad or worse than before.
- Tell the study doctor if you have any changes in medications during the study.
- Follow the directions of the study doctor and research team, including requirements to use an appropriate birth control method.
- Refrain from participation in other research studies while you are a participant in this study.
- Do not change any of your medications or start any new medications without checking with your study doctor.
- Take and store your study drug as instructed and return the unused study drug and/or empty containers to the study doctor's office at each visit.
- Do not share your study drug with anyone. You are the only person allowed to take the study drug.
- Keep the study drug and study supplies out of the reach of children and persons of

limited ability to read or understand.
- Tell the study staff about any health problems you are having even if you don't think they are important.
- Tell the study staff if you wish to stop being in the study.
- Do not eat grapefruit, grapefruit products, Seville oranges (including marmalade containing Seville oranges) while taking Ibrutinib

STUDY DRUG RISKS:

Potential Risks Associated with Pembrolizumab

Pembrolizumab, which is approved in the USA and some other countries, is available by prescription to treat several different cancers, but is not approved to treat your type of cancer.

Pembrolizumab works by helping your immune system to fight your cancer.

However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects that may become serious or life-threatening, and in some cases, may lead to death.

VERY COMMON, SOME MAY BE SERIOUS (for example, causing hospitalization, life-threatening or where noted, may cause death). Out of 100 people who receive pembrolizumab, 20 or more people may have the following:

- Itching of the skin
- Loose or watery stools
- Cough

COMMON, SOME MAY BE SERIOUS (for example, causing hospitalization, life-threatening, or where noted, may cause death). Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

- Joint pain
- Rash
- Fever
- Back pain
- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools
- Low levels of salt in the blood that may cause you to feel tired, confused, have a headache, muscle cramps and/or feel sick to your stomach

UNCOMMON, SOME MAY BE SERIOUS (for example, causing hospitalization, life-threatening, or where noted, may cause death). Out of 100 people who receive pembrolizumab, at least 1 but less than 5 people may have the following:

- Inflammation of the lungs so you may feel short of breath and cough. Sometimes this might lead to death
- Too much thyroid hormone so you may feel anxious, angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools

- Infusion reaction, where you may feel dizzy or faint, flushed, get a rash, have a fever, feel short of breath at the time of receiving your infusion (IV) or just after, or pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (for example, peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection. These severe conditions can sometimes lead to death.

RARE, SOME MAY BE SERIOUS (for example, causing hospitalization, life- threatening, or where noted, may cause death). Out of 100 people who receive pembrolizumab, less than 1 person may have the following:

- Inflammation of the nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis
- Inflammation of the muscles so you may feel weak or have pain in your muscles
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and vomiting that gets worse when you eat
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and dark urine
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and belly aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan
- Type 1 Diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots.
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain
- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting. Sometimes this condition can lead to death
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy.
- A condition that may make you feel weak and tired and might have drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing

- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs
- Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness

Patients treated with pembrolizumab who then go on to allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), should inform their transplant physicians that they have received pembrolizumab in the past.

In patients with any hematologic malignancy (cancers of the blood like Hodgkin lymphoma, multiple myeloma): there is a potential for an increased risk of severe complications following allogeneic stem cell transplant in patients who previously received pembrolizumab.

Reports of clotting of blood within the liver and severe graft versus host disease (which can include skin, liver and gastrointestinal symptoms), including death, have been received for patients who received allogeneic stem cell transplant after pembrolizumab therapy.

Potential Risks Associated with 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 ibrutinib in clinical trials.

The most common side effects, occurring in at least 1 of every 5 (20%), patients have been:
Occurrence or increase in frequency of loose or watery stools (Diarrhea)

- Muscle and bone pain (Musculoskeletal pain)
- Nausea
- Low white blood cell count (cells that help fight infection) (Neutropenia)
- Bleeding (Hemorrhage)
- Rash
- Fever (Pyrexia)
- Side effects that have been seen in at least 1 of every 10 (10%) patients include:
- Low platelet count (cells that help blood to clot) (Thrombocytopenia)
- Common cold (Upper Respiratory Tract Infection)
- Pneumonia
- Constipation
- Swelling of the hands or feet (Oedema peripheral)
- Muscle spasms
- Vomiting
- Joint aches (Arthralgia)
- Sores in mouth (Stomatitis)
- Headache
- High Blood pressure (Hypertension)
- Skin infection
- Weakness, tingling, numbness, and pain from nerve damage, usually in the hands and feet
- (Peripheral neuropathy)

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

- Dizziness
- Urinary tract infection
- Sinus infection (Sinusitis)
- Increased level of uric acid in the blood (Hyperuricemia)
- Abnormal heart rhythm (Atrial fibrillation)
- Non-melanoma skin cancer
- Blurry vision (Vision blurred)
- Low white blood cell counts with fever (Febrile neutropenia)
- Severe infection throughout the body (Sepsis)
- Redness of the skin (Erythema)
- Increase in white blood cell counts (Leukocytosis)
- Breaking of the nails (Onychoclasis)
- Inflammation within the lungs that may lead to permanent damage (Interstitial lung disease)

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

- Increase in white blood cell count (Lymphocytosis)
- 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)
- 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)
- Abnormal rapid and/or irregular heart rhythm that starts from the lower chambers (ventricles) of the heart (Ventricular tachyarrhythmias).

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 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. 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
Abnormal rapid and/or irregular heart rhythm (atrial fibrillation, atrial flutter, and/or ventricular tachyarrhythmia) have been reported in patients treated with ibrutinib, especially when they also have heart conditions, increased blood pressure, infections, or had abnormal heartbeat in the past.
The heartbeat may be fast or irregular causing symptoms such as a pounding or racing heart, dizziness, weakness, feeling light-headed, shortness of breath, chest discomfort or fainting. 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. 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.

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.

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 may be 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 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, and 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 (for example, 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 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. 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.

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.

Reproductive effects
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, or sexual abstinence (which is defined as refraining from all aspects of sexual activity), while taking study treatment, as well as for 1 month after you stop taking study treatment, to prevent pregnancy, unless your partner is sterilized. A "highly effective method of birth control" is defined as a method that has a low failure rate (for example, less than 1% per year) when used consistently and correctly and includes implants, injectables, birth control pills with 2 hormones, some intrauterine devices (IUDs). If you are using hormonal contraceptives such as birth control pills or devices, a second barrier method of contraception (for example, 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. You should not donate sperm while you are taking the study drug and for 3 months after you stop taking the study drug.

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.

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 Sponsor will continue to collect information about your pregnancy and the birth of your baby even after study treatment is stopped.

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.

Breast-feeding
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.

PREGNANCY AND BREASTFEEDING RISKS:

The study drugs, pembrolizumab and ibrutinib, can cause harm to a pregnant woman, embryo, developing fetus, or nursing infants.

If you are female, you cannot participate in this study if you are pregnant, plan to become pregnant or are nursing a child. If you are able to have children you will need to use an appropriate form of birth control as directed by your doctor starting with the pre-screening or screening visit through 90 days after the last dose of study treatment.

If you are male and you have a sexual partner(s) who is able to get pregnant, you must agree that you and your partner(s) will use an appropriate form of birth control as directed by your doctor starting with the pre-screening or screening visit through 90 days after the last dose of study treatment.

RISKS RELATED TO STUDY PROCEDURES:

- Blood Testing/Research Blood Samples - Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.
- Bone marrow biopsy/aspirate - pain for a few days that requires some pain medication or rarely infection at the site can be risks.
- CT scans - involve radiation exposure. Scientists disagree on whether radiation doses at the low levels used in these scans are harmful. A possible effect that could occur at doses associated with this study is a slight increase in the risk of developing cancer later in life. You may have an allergic reaction to the contrast material that may cause rash, hives, shortness of breath, wheezing, and itching and, rarely, may cause your heart to stop beating (in other words, “cardiac arrest”). The use of contrast material

during these tests would be a normal part of measuring your response to therapy even if you were not taking part in this research study.

BENEFITS

You may or may not benefit from being in this study but your participation in this research study may benefit future patients with your disease or condition. Your condition may get better, it may get worse, or it may stay the same.

ALTERNATIVES TO PARTICIPATION

You do not have to participate in this study to get help for your condition. An alternative to the study is observation which is usually indicated in patients with asymptomatic CLL. Alternatives to this study for the treatment of your condition may include drugs already approved or being used for treatment of your condition, or other experimental drugs. Your study doctor can discuss the risks and advantages of these alternative treatment methods with you. In addition, you may discuss your options with your regular health care provider.

WILL IT COST ANYTHING TO BE IN THIS STUDY?

You and/or your insurance company will be financially responsible for hospital inpatient, outpatient and follow-up visits that would normally or routinely occur in the management of your disease. Inpatient and outpatient visits could include charges for treatments, medications, physician visits, laboratory tests and procedures. You and /or your insurance company will be responsible for paying for the charges which are considered routine, since you would have received these services even if you were not participating in this study. You will be responsible for any costs not covered by your insurance company, including deductibles, co-payments and all out-of-pocket expenses. Before you agree to be in this study, you should contact your health insurer to see if your plan will cover the costs required as part of your participation.

You and/or your insurance company will not be responsible for paying for study related items and services that are specifically required for this research study and are not considered part of the routine management of your disease, if these procedures are performed at Moffitt Cancer Center.

During your participation in this study, pembrolizumab will be provided Merck & Co., Inc. at no additional charge to you for up to 24 months. Ibrutinib will be provided by Janssen Scientific Affairs, LLC., at no additional charge for up to 12 months. If, per your treating physician, there is benefit with continuing ibrutinib, your insurance will be contacted about coverage for this drug. You and/or your insurance company will be responsible for the charges related to the administration of the study drugs.

If you would like more information on the costs of being on this study or have other insurance related questions then please let your clinical trial coordinator know or contact our Business Office at 813-745-8422.

REIMBURSEMENT AND PAYMENTS

You will not be paid for being in this study.

WHAT IF I GET HURT OR SICK WHILE I AM IN THIS STUDY?

If you need emergency care:

- Call 911 or go to your nearest emergency room right away. Moffitt Cancer Center does not have an emergency room or the facilities to provide emergency care.

If you do NOT need emergency care:

- Call or go to your regular doctor. It is important that you tell your regular doctor that you are participating in a research study. If possible, take a copy of this consent form with you when you go.

If you experience a side effect or a change in the way that you feel, call the study doctor at the telephone number listed on the first page of this form.

By signing and dating this informed consent and research authorization form, you have not given up any legal rights to seek compensation for injuries from the sponsor**.**

MOFFITT CANCER CENTER INJURY STATEMENT

If you believe you have been injured as a result of your participation in this study or if you have questions about your rights as a person who is taking part in a research study, you may call the Moffitt Cancer Center Risk Manager at 813-745-4219. Moffitt Cancer Center and its investigators have made no provision for monetary compensation in the event of physical illness or injury resulting from this study. Likewise, Moffitt Cancer Center and its investigators have made no provision for payment of lost wages, disability, or discomfort in the event of physical illness or injury resulting from this study. Florida law (Statute 768.28) limits the liability of Moffitt Cancer Center. This statute provides that damages are available only to the extent that negligent conduct of a Moffitt Cancer Center employee caused your injuries, and are limited by law. A copy of this statute is available upon request at 813-745-1869.

HOW WILL MY INFORMATION BE KEPT CONFIDENTIAL?

We understand that information about you and your health is personal, and we are committed to protecting the privacy of that information. Because of this commitment and because of federal law, we must obtain your written authorization before we use or disclose your information for this study.

By signing this form, you are permitting researchers at Moffitt Cancer Center to use personal health information for research purposes within its organized health care arrangements. You are also allowing the Moffitt Cancer Center to disclose your personal health information to outside organizations or individuals that participate in this study. We may publish what we find out from this study. If we do, we will not let anyone know your name. We will not publish anything that would directly let people know who you are.

Your research samples collected during the trial, will be coded with a number and will not contain any of your personal information.

WHO WILL DISCLOSE, RECEIVE, AND/OR USE YOUR INFORMATION?

Your records and research blood sample results are confidential and they will be kept in a secure environment and protected to the full extent of the law.

To do this research, the following people and/or organization(s) will be allowed to disclose, use, and receive your information, but they may only use and disclose the information to the other parties on this list, to you or your personal representative, or as permitted by law:

- Every research site for this study, including the Moffitt Cancer Center, and each site's study team, research staff and medical staff.
- Any person who provides services or oversight responsibilities in connection with this study.
- Every member of the Moffitt Cancer Center workforce who provides services in connection with this study.
- Any laboratories, individuals, and organizations that use your health information in connection with this study.
- Any sponsor of the study, including the following sponsors: Merck & Co, Inc. and Janssen Pharmaceuticals, Inc.
- Any federal, state, or local governmental agency that regulates the study (such as the U.S. Food and Drug Administration (FDA) and Florida Department of Health (FDH). The U.S. Department of Health & Human Services (DHHS), Office for Human Research Protections (OHRP).
- Other government agencies in this or other countries.
- The designated Protocol Review and Monitoring Committees, Institutional Review Boards such as Advarra IRB, Privacy Boards, Data and Safety Monitoring Board and their related staff that have oversight responsibilities for this study.
- The National Cancer Institute in evaluating the ongoing research of the Moffitt Cancer Center as a Comprehensive Cancer Center.

The organizations and people listed above may employ or pay various consultants and companies to help them understand, analyze and conduct this study. All of these people may not be known now, but if you would like to have more specific information about this at any time during the study, you may ask the study doctor and your questions will be answered.

Moffitt Cancer Center cannot guarantee the privacy of your information, or block further use or distribution, after the information has left the Moffitt Cancer Center. Others listed above may further disclose your information, and it may no longer be covered by federal privacy regulations. If all information that does or can identify you is removed from your records, the remaining information will no longer be subject to this authorization and may be used or shared for other purposes. You might have the right to see and copy your health records related to this research. Any results from testing on your research blood samples will not be disclosed to you. You might not be able to see or copy some of your records until after all participants finish the study. If it is necessary for your care, your records will be provided to you or your regular doctor.

WHAT INFORMATION WILL BE USED OR DISCLOSED?

By signing and dating below, you authorize the use and disclosure of your entire study record and any medical or other records held by Moffitt Cancer Center, including, but not limited to, HIV/AIDS, mental health, substance abuse or genetic information. The purpose for the uses and disclosures you are authorizing is to conduct the study explained to you during the informed consent and research authorization process and to ensure that the information relating to that study is available to all parties who may need it for research purposes.

Your authorization to use your health information will never expire unless and until you expressly revoke it in writing to the study doctor listed on the first page of this form.

Any data collected before your letter will continue to be used as necessary to preserve the integrity of the study, however no additional information will be collected after you withdraw your authorization.

You will receive a signed and dated copy of this form.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Participant Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Participant Adviser: Pro00027749.

WHERE CAN I GET MORE INFORMATION?

You may call the National Cancer Institute's (NCI) Information Service at:

1-800-4-CANCER (1-800-422-6237).

Visit the NCI's Websites at:

- CancerTrials: comprehensive clinical trial information at: http://cancertrials.nci.nih.gov
- CancerNet: accurate cancer information including PDQ at: http://cancernet.nci.nih.gov

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.

Use of Your Research Samples

As part of this study, there will be tests performed in a Moffitt laboratory using your blood samples. The tests are to learn how the study treatment affects your immune system. If you agree below, you can change your mind at any time. If you want to withdraw your consent for the use of your samples during the study, tell your study doctor that you no longer want your samples stored or used for research. If you want to withdraw your consent after the close of the study, follow the instructions provided to you by the study doctor. Then, any samples that remain will be destroyed. If you change your mind and your samples have already been tested, those results will still remain as part of the overall research data. In the event of your death or loss of competence, your specimens and data will continue to be used as part of the study doctor's sample storage. If you withdraw or discontinue from the study, your samples will continue to be stored and used for research unless you specifically ask that they be destroyed.

My remaining blood samples from the study may be used by Moffitt researchers this study and for future research on CLL and CLL-related diseases.

Please indicate your preference below:

YES _____ (initials) I agree to participate in the sub-study described above.

NO _____ (initials) I do not agree to participate in the sub-study described above.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

The Investigator or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons.

If you leave the study for any reason, the Investigator may ask you to have some end-of-study tests for your safety.

STATEMENT OF CONSENT

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

STATEMENT OF PERSON OBTAINING INFORMED CONSENT/RESEARCH AUTHORIZATION

I attest that the participant named above had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

_____

Printed Name of Person Explaining Consent

_____ _____

Signature of Person Explaining Consent Date