The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title:	**A Phase I Study of Duvelisib in Combination with Nivolumab for Patients with Richter's Syndrome and Transformed Follicular Lymphoma**
Principal Investigator:	**David Bond, MD**
Drug Support:	**Secura Bio**

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study
The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

You were selected as a possible participant because you have a type of cancer considered an aggressive lymphoma which has come back (relapsed) or has not responded to standard treatment (refractory) or because you have chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) which has transformed into aggressive lymphoma (Richter's syndrome).

The study has two phases, a Dose Escalation Phase and an Expansion Phase. You will only be taking part in one of these phases, not both. You will be treated on this study until either

you experience side effects requiring the study medication to be permanently stopped, you choose to withdraw from the study, or your disease progresses.

Most side effects seen were mild and patients recovered with or without holding treatment with duvelisib. However, some side effects were severe, led to hospitalization, were life-threatening, or caused death. Side effects are listed later in this form.

1. Why is this study being done?

This research is being done because investigators are studying the use of a drug called nivolumab (OPDIVO®) in combination with a drug called duvelisib (COPIKTRA®).

Nivolumab has been approved by the United States Food and Drug Administration (FDA) for treating patients with other kinds of cancer such as lung cancer, melanoma (a type of skin cancer), and a specific sub-type of lymphoma called Hodgkin's lymphoma. Nivolumab is designed to allow the immune system to better recognize cancer cells and act against these cancer cells. Duvelisib has been approved by the United States Food and Drug Administration for treating adult patients with CLL or SLL lymphoma after at least two prior treatments. Duvelisib is designed to block a protein called PI3 kinase in order to stop cancer growth and cause changes in the immune system that may allow the immune system to better act against cancer cells. The use of nivolumab in combination with duvelisib is not FDA approved and is considered investigational. An investigational drug is one that has not been approved by the FDA.

The purpose of this study is to:

- Find the appropriate dose of duvelisib in combination with nivolumab for patients with aggressive lymphoma including Richter's syndrome
- Characterize the tolerability and safety of duvelisib in combination with nivolumab in patients with aggressive lymphoma including Richter's syndrome.
- Understand how well duvelisib in combination with nivolumab is working in patients with Richter's syndrome or transformed follicular lymphoma who are receiving the appropriate dose of duvelisib in combination with nivolumab (this is called efficacy)

Study Design

We are trying to identify the safest dose of duvelisib to give with nivolumab. All participants will receive both drugs and all participants will receive the same dose of nivolumab. The dose of duvelisib you receive will depend on when you are enrolled on the study, and will be based on how study participants before you tolerated the drug. Your doctor will tell you which dose of duvelisib you will receive. You will take duvelisib by mouth twice a day, every day, unless instructed to take at a lower dose or frequency due to side effects and you will receive nivolumab in clinic once every two

weeks intravenously for the first four cycles of treatment. Beginning with the fifth cycle of treatment the frequency may decrease to once every four weeks thereafter.

Correlative Studies: As part of this study, blood tests will be performed to determine the changes in the number and types of immune cells (white blood cells) in the blood during treatment. In addition, genetic testing of your cancer will be performed and if tumor mutations are found they will be tracked during treatment. As part of this testing genetic testing of normal cells taken from you cheeks will be performed to help to interpret possible genetic changes seen in the tumor cells.

2. How many people will take part in this study?

Participants in the study are referred to as subjects. At least six and as many as 24 subjects will take part in the Dose Escalation Phase of this study to determine the highest dose of duvelisib in combination with nivolumab which can be safely tolerated. About 20 additional subjects will take part in the Dose Expansion Phase of the study for patients with Richter's syndrome or transformed follicular lymphoma.

3. What will happen if I take part in this study?

Study Treatment

Duvelisib comes as a capsule and you will take duvelisib twice by mouth every day in 28-day cycles. Each period of 28 days is called one cycle of treatment. Nivolumab is given through an IV (intravenous) over about 60 minutes at the study site in the outpatient infusion center on day 1 and 15 of each cycle (every 14 days) for the first four cycles and then on day 1 beginning cycle 5. You do not stop taking duvelisib between cycles if you are eligible to continue treatment for more cycles.

If you have side effects which you cannot tolerate, your dose of duvelisib may be changed, your dose of duvelisib and/or nivolumab may be stopped temporarily, or you may be taken off of the study treatment. You should always take the dose that your study doctor tells you to take.

On days when you have a visit to the study site, you will take your duvelisib capsules at the study site. On all other days, you will take your duvelisib capsules at home. It is important to follow the instructions below when you take duvelisib:

- You must take duvelisib under appropriate conditions, as described on the study drug label.
- Only you should handle duvelisib, and you should wash your hands well after touching duvelisib capsules. Duvelisib should always be stored in its original packing. If a dose of duvelisib is missed by less than 6 hours, it should be made

up immediately, and then next dose taken as usual. If dose is missed by more than 6 hours, it should be skipped.

- You should always try to take each dose around the same time of day, each day, with or without food.
- Duvelisib should be swallowed whole with a glass of water (about 8 ounces or 240 mL)
- Do not drink grapefruit juice or eat grapefruits while you are taking study drug.
- Do not take herbal supplements including but not limited to St. John's wort during this study.
- Please discuss with the study doctor all medications (including any herbal supplements) that you are taking, as some medications may interfere with your study treatment.
- You must return all of your capsules that you did not take and any empty study drug blister pack(s) and tell the study doctor or study site staff of any doses that you did not take.
- You will be asked the specific time that you took your duvelisib dose.
- Taking duvelisib may increase the chance of getting an infection. You may be asked to take additional medication(s) (prophylactic treatment) to reduce the risk of getting an infection. The study doctor will tell you what these medication(s) are and when to take them.

Additional Potential Effects While on Treatment with Duvelisib

Exposure to Sun: Duvelisib has the potential for more sensitivity to the sun and getting sunburned in animal or preclinical studies. The effect of duvelisib on the skin, especially when in direct sunlight or with artificial UV light (e.g. tanning booths), is not known. As a general precaution, it is advised to use appropriate protective measures (e.g. long sleeve shirts and pants, hat, umbrella) to minimize exposure to direct sunlight during the treatment period and for at least 30 days after the last dose of duvelisib.

Vaccinations: Tell your study doctor if you have had a recent vaccination or are scheduled to receive vaccinations. You should not receive certain vaccines after starting duvelisib. Vaccinations while taking duvelisib may not work or could result in infection. Tell your doctor if anyone in your household is scheduled to receive a vaccination

Drug-Drug Interactions: If you start any new medications (prescriptions, herbal and/or over the counter), inform your doctor. Drug-drug interactions can decrease how well your medications work, may increase minor or serious unexpected side effects, or even increase the blood level and possible toxicity of a certain drug. Drug interactions with substances such as alcohol can also affect how your medications work. Therefore, you should always discuss the use of any new medications with your study doctor while you are participating in this study.

Tissue Samples: Your tissue samples, called specimens (such as blood and tumor), will also be used to study biomarkers to assess the influence of this treatment on the immune system and to assess for tumor markers which might predict better response. Biomarkers studied will include studying the immune function (blood cell functions), gene (DNA) mutations, and protein markers on the tumor. Because the genetic tests in this study are not used for regular medical care, you will not be told the results of the test(s), unless there any genetic changes found in your normal cells which may need your doctors to take action such as an inheritable cancer risk syndrome. If this were to happen your provider would be notified and provide the option of referral for genetic testing and counseling to confirm these findings. Otherwise, the test results will not be put in your medical record either.

Study Procedures

A list of study procedures appears on the following pages. Please note that you may be asked to repeat a procedure or test and/or have additional procedures performed if the study doctor feels it is needed to evaluate your condition. The study doctor may ask you to come in early for some procedures because of scheduling or because of how your body is responding to the drug.

At each visit, you study doctor and/or research coordinator will ask you questions concerning any medications you have been taking and any side effects (unusual or harmful reactions or illnesses) that you may have experienced. You must tell your study doctor or study staff about any side effects that you may have. If you are not honest about your side effects, it may not be safe for you to stay in the study. You must also tell your study doctor or study staff if you have made any visits to other doctors and/or hospitals.

If you agree to be in this study, you will undergo some activities, tests, and evaluations to determine if you are eligible for this study. Such tests and evaluations are completed during a screening period that takes place before you begin treatment on the study. If you take part in this study, you will have the following tests and procedures:

<u>Screening</u>:

Within 28 days before starting treatment, you will visit the study site to have the following done to see if it is safe for you to be in the study:

- You will be asked to sign the consent form document
- Medical History (including questions regarding your health problems, list of prescribed and over the counter medications/ supplements that you are taking, details of your diagnosis and previous treatment)
- Physical exam and vital signs (including checking your heart rate, respirations, blood pressure, height, and weight)
- Performance status evaluation (what type of daily activities you are able to do)

- Tumor assessment by PET/CT scan or CT chest, abdomen, and pelvis (with possible exceptions if recently performed)
- Routine blood tests to check your blood counts (numbers of each type of blood cell), kidney and liver function, thyroid function, amylase, lipase and virus exposures (hepatitis B, HIV)
- Pregnancy (blood) test for women of child-bearing potential
- Blood tests to determine disease markers associated with your cancer
- EKG testing
- Cheek swab
- Echocardiogram to evaluate your heart function
- Bone marrow aspiration and biopsy

It is possible that after the results of these tests are reviewed, you will not qualify to be in the study. If you are not eligible to participate, the reasons why you cannot participate will be discussed with you by the study doctor or study staff.

Cycle 1 and 2
The following assessments will be done on day 1 and day 15 of Cycle 1 and Cycle 2, unless otherwise specified:

- Medical history
- Physical exam and vital signs
- Performance status evaluation
- Concomitant medication assessment
- Toxicity assessment
- Routine blood tests including blood count and tests of liver and kidney function
- Blood tests to examine disease markers and immune system
- Blood tests to determine immune cell number and function, presence of tumor DNA in plasma, and cytokine profile (correlative studies) (day 1 only)

Cycles 3 and Onward
The following assessments will be done at the start of each cycle unless otherwise specified:

- Medical History
- Physical exam and vital signs
- Performance status evaluation
- Concomitant medication assessment
- Toxicity assessment
- Routine blood tests including blood count and tests of liver and kidney function and thyroid function testing, and immunoglobulins
- Blood tests to determine immune cell number and function, presence of tumor DNA in plasma, and cytokine profile (correlative studies) on day 1 only

- PET/CT or CT chest, abdomen, and pelvis will be done before starting Cycle 3 and every 12 weeks thereafter until complete resolution of lymphoma activity at which time PET/CT or CT will be repeated every 24 weeks for 1 year and 48 weeks thereafter while on active treatment.

On day 15 of cycle 1-4, the following assessments will be performed prior to receiving nivolumab in the outpatient infusion center:

- Vital signs
- Toxicity assessment
- Routine blood tests including blood count and tests of liver and kidney function

End of Treatment
When treatment is stopped due to either side effects, decision to leave the study, or progression of disease the following assessments will be done:

- Toxicity assessment
- Concomitant medication assessment
- Medical History
- Physical exam and vital signs
- Performance status evaluation
- Routine blood tests including blood count and tests of liver and kidney function
- Blood tests to determine immune cell number and function, presence of tumor DNA in plasma, and cytokine profile (correlative studies) on day 1 only
- Bone marrow aspiration and biopsy

Follow-up
If you do not require other therapy or show signs of clinical progression after stopping study therapy due to side effects, you will be followed every 12 weeks to assess for resolution of side effects and to assess for possible disease progression until you begin another therapy for your cancer or have disease progression.

4. How long will I be in the study?

You will be treated on this study until either you experience side effects requiring the study medication to be permanently stopped, you choose to withdraw from the study, or your disease progresses.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first.

If you choose not to participate in the study or to leave the study, your regular care will not be affected nor will your relations with OSU Hospital, your physicians, or other personnel. In addition, you will not lose any of the benefits to which you are entitled.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

Withdrawal by investigator, physician, or supporting party
The investigators, physicians, or supporting party may stop the study or take you out of the study at any time should they judge that it is in your best interest to do so, if you experience a study-related injury, if you need additional or different medication, or if you do not comply with the study plan. They may remove you from the study for various other administrative and medical reasons. They can do this without your consent.

6. What risks, side effects or discomforts can I expect from being in the study?

For trials of drugs, there may be risks. These risks will be discussed with you by the research doctor and/or your regular doctor.

Harmful reactions or side effects may occur in subjects participating in clinical trials. Some of these will be due to the subject's disease and some may be due to the drug being studied. Everyone taking part in the study will be watched carefully for any side effects. However, the doctors don't know all the side effects that may happen. In general, side effects can range from mild to very serious. Your health care team may give you medicines to help lessen side effects. Many side effects may go away after nivolumab and duvelisib have been stopped. Although numerous precautions are established to protect your health, it is possible that in some cases, side effects can be serious, long lasting, or may never go away.

Please let your study doctor know of any other medications or supplements you are taking. Some medications when taken together with the study medications may either increase the likelihood of side effects or lessen the effectiveness of the medications.

Tell the study doctor right away if you experience any side effects or discomforts.

<u>Risks and side effects related to duvelisib</u>

Subjects with advanced cancer have a risk of death due to their underlying cancer or as a complication of their cancer treatment. The risks and side effects related to duvelisib and the combination of duvelisib and nivolumab will be closely monitored.

The following lists of side effects are based on safety information from patients with blood cancer who have taken duvelisib alone as a single anti-cancer treatment (total daily doses range from 16 mg to 200 mg), with most patients with blood cancer having received

a total daily dose of 50 mg (25 mg 2 times a day). Most side effects seen were mild and patients recovered with or without holding treatment with duvelisib. However, some side effects were severe, led to hospitalization, were life-threatening, or caused death.

Likely (greater than 10%)

- Feeling tired (fatigue)
- Headache
- Fever
- Loose stool (diarrhea)
- Nausea and vomiting
- Decrease in number of white blood cells that helps fight infection
- Decrease in red blood cells which can cause tiredness and shortness of breath
- Decrease in platelet cells in the blood that help the blood to clot
- Infection in the lung (pneumonia) that could be caused by a bacteria, virus, or fungus
- Cough and shortness of breath
- Abnormally high level of enzymes produced by the liver meaning that it could affect your liver function
- Severe and/or serious skin rashes have been observed in patients with blood cancer. (A very small number of patients on duvelisib have experienced skin rashes that were life-threatening or led to death).

Less Likely (1-10%)

- Inflammation of the intestines which may cause diarrhea (frequent loose watery stools), you may require further medical attention and should immediately notify your doctor for further evaluation
- Infection that causes widespread inflammation resulting in poor blood supply to vital organs.
- Severe inflammation of lungs.
- Infection
    - Virus that causes shingles
    - Viruses that occur in patients with weakened immune system
    - Fungal infection in the mouth
- Dehydration (may be a result of diarrhea or vomiting)

Less Common Side Effects

- Infections that occur in people with decreased immune systems (such as patients with cancer)
    - Such infections may include infections with viruses such as Herpes simplex virus, Cytomegalovirus, or Epstein-Barr virus (a virus that can cause mononucleosis otherwise known as “mono”); and infections with fungus such as Aspergillus, Candida, or Pneumocystis.

If you have any new and concerning systemic symptoms (e.g. fevers, rigors, severe fatigue), respiratory symptoms (e.g. shortness of breath, persistent cough, chest pain), or gastrointestinal symptoms (e.g. diarrhea or blood in your stool), you should immediately notify your doctor for further evaluation.

Risks and side effects related to nivolumab

Subjects with advanced cancer have a risk of death due to their underlying cancer or as a complication of their cancer treatment. The risks of side effects or death related to nivolumab will be closely monitored.

Based on safety information from the patients already treated with nivolumab alone or in combination with other medicines, the most frequent side effects may include, but are not limited to:

Likely (greater than 10%)

- Feeling tired (fatigue)
- Weakness
- Skin problems: including rash, itchiness, redness, or dry skin
- Loose stools (diarrhea)
- Loss of appetite
- Feeling sick to your stomach (nausea)
- Throwing up (vomiting)
- Joint pain or inflammation
- Fever and chills

Less Likely (1-10%)

- Decreased white blood cells which may affect your ability to fight infections
- Shortness of breath
- Headache
- Cough
- Lung inflammation (see below for details)
- Bowel inflammation (diarrhea, blood or mucous in the stool, abdominal pain)
- Dry mouth
- Allergic reaction during infusion of study drug
- Muscle pain
- Arm or leg pain
- Post nasal drip
- Abdominal pain
- Heartburn
- Sensation of lightheadedness or vertigo (spinning sensation) (dizziness)
- Constipation
- Nerve numbness, pain, or weakness (peripheral neuropathy)

Less common side effects

- Back pain
- Swelling of the arms or legs
- Fluid collection in the abdomen
- Injection site reactions
- Trouble sleeping
- Night sweats
- Excessive sweating
- Hair loss
- Altered taste
- Irritability
- Kidney failure
- Muscle spasm
- Brain inflammation (meningitis or encephalitis)
- Hemophagocytic lymphohistiocytosis, a life-threatening immunodeficiency which causes fevers, enlarged spleen, low blood counts, and liver abnormalities
- Nerve associated muscle weakness (myasthenia gravis)
- Loss of nerve function (Guillian-Barre syndrome)
- Muscle inflammation and breakdown (polymyositis and rhabdomyolysis)
- Cardiac inflammation (myocarditis)
- A syndrome associated with muscle pain and stiffness in the neck, shoulders, and hips

Lung inflammation: It is possible that nivolumab may cause inflammation of the tissues in the lung. This adverse effect has been reported infrequently in subjects treated with nivolumab. While many subjects with x-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases death has occurred as a result of their lung inflammation. Symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, or fatigue. These symptoms may require treatment with steroids, which may increase your risk for infection.

Your study doctor and nurse will watch you closely for changes in your ability to breathe and for other signs or symptoms that might show you are developing this type of severe inflammation and will perform regular tests including physical exams, measurement of oxygen levels through noninvasive testing (i.e., pulse oximeter), and blood tests as well as chest x-rays and CT scans if warranted by symptoms.

At each visit, the study doctor will ask you about any usual symptoms and other treatments you may have started. Should a serious side effect occur, the study medication will be stopped. You will be checked regularly for the improvement of the side effects. This may require extra visits and examinations including blood and urine tests as well as

cardiac function tests. The study medication may be re-started after the side effects improve or disappear, depending on the severity and the duration of the events.

You will be told if any new side effect is found as a result of this study or any other study using nivolumab that could affect your participation in the study. If you are concerned about your health between visits and because of the trial, emergency telephone numbers are provided at the end of this document. You will be given any new information on nivolumab that may affect your willingness to start or continue in the study as it becomes available.

Risks Related to the Combination of Nivolumab and Duvelisib
The risks related to the combination of nivolumab and duvelisib are not known and the purpose of this study is to determine the safety of this combination. As both drugs act to effect the immune system there is potential when both drugs are combined for more frequent or more severe occurrence of immune related toxicities including inflammation of the intestines, colon, or the lungs, or liver injury or damage beyond what is seen with either nivolumab or duvelisib alone. The purpose of this study is to determine the safety of this combination.

Risks of Study Procedures
Possible Risks from Blood Drawing:
Likely:

- Slight discomfort of bruising at the site where the needle is inserted

Less likely, but serious:

- Lightheadedness and fainting
- Infection
- Excessive (too much) bleeding

Possible Risks from Electrocardiogram (ECG):
Rare side effects from ECG electrode placement include skin irritation, chafing, or redness.

Possible Risks from Blood Pressure and Heart Rate Measurement:
Mild discomfort in your arm while the inflatable cuff is inflated

Possible Risks from CT scan and FDG-PET Scan:
Exposure to radiation. The risk associated with the amount of radiation exposure that you will receive from this study is considered to be low and comparable to everyday risks. Public policy is to keep exposure levels as low as possible.

Contrast dye may be used, which has a small possibility of severe allergic reaction and may also cause kidney problems, especially if you are dehydrated or have poor kidney function.

Risk of Bone Marrow Biopsy:
During a bone marrow aspiration procedure, a needle is inserted into the marrow of certain bones. This is done after the skin surface has been injected with a numbing solution. Once the needle is in place, a small amount of the marrow is withdrawn for testing. There is a risk of experiencing pain, pressure, and/or bleeding as a result of having a bone marrow aspirate procedure.

Possible Risks of Medications Used for Prevention and Treatment of Infection:
Your study doctor can explain what side effects to expect from medication(s) taken for prevention and/or treatment of infection.

Possible Risks and Implications of Genetic Testing:
It is possible that the genetic testing performed as part of this study will detect incidentally a possible inheritable genetic condition. In the event that this occurs, your provider will notify you and offer you the opportunity to confirm this finding with genetic testing and to speak with a genetic counselor. Please note that a federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions about your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this federal law. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under Ohio law, health insurance companies cannot ask about the results of a genetic test or use any information obtained from genetic testing to make decisions about providing coverage or benefits for health care services.

Risk to Reproduction, Unborn Babies, and Nursing Infants

General Statement

You must not be pregnant or breastfeeding, and you should not become pregnant or breastfeed while you are taking the study treatments. Urine or serum pregnancy tests are to be done at screening and then anytime thereafter that pregnancy is suspected or possible. For women of childbearing potential, if on cycle 1 day 1 greater than 7 days has

elapsed since the last negative result, a serum pregnancy test must be repeated and be negative on C1D1 for patient to remain eligible. Pregnancy test will be repeated every 12 weeks while on study for women of childbearing potential and must remain negative to remain on study. Female subjects of child bearing potential should be willing to use two methods or birth control, be surgically sterile, or abstain from heterosexual activity for the course of the study through 5 months following the last dose of nivolumab and at least 30 days after the last dose of duvelisib. The use of nivolumab or duvelisib in pregnant women has not been formally investigated in clinical studies. In animal studies, nivolumab lead to an increase in fetal loss and neonatal mortality, the cause of this could not be determined but may be due to an autoimmune reaction toward the fetus. In animal studies, high doses of duvelisib lead to reduced fetal weights and increased rates of pregnancy loss.

Male subjects who are sexually active with a woman of child bearing potential should also use an adequate method of birth control to avoid pregnancy of their partner for up to 7 months after the last dose of nivolumab and up to 30 days after the last dose of duvelisib. Male subjects should not donate sperm within the first 7 months after the last dose of nivolumab or 30 days after the last dose of duvelisib.

You should immediately contact your study doctor if there is a change in your method to avoid pregnancy or if you start any prescription drug or other medication (including over-the-counter drugs and herbal supplements) not prescribed by the study doctor.

Unforeseeable Risks

There may be unknown risks to you, your unborn baby or nursing infant if you are or become pregnant during this study or are breastfeeding during this study.

Occurrence of Pregnancy or Suspected Pregnancy

If you become pregnant, suspect pregnancy or if you missed your period or it is late, or if you have a change in your usual menstrual cycle (e.g., heavier bleeding during your period or bleeding between periods), you should immediately contact your study doctor.

Discontinuation from the Study

Should you become pregnant during this study, you will immediately have the study medication permanently discontinued and be referred for obstetric care. You will continue to be followed for any side effects or potential benefits of the study treatment, provided it is safe for you and your unborn baby to do so. Your doctor will discuss this with you, as well as options for additional appropriate care for your cancer. The study has not set aside any funds to pay for any aspects of obstetric, child or related care and does not plan to pay for them.

Unknown/ Other Risks
There may also be side effects, other than those listed above, that we cannot predict. Other drugs may be given to make side effects that occur less serious and less uncomfortable. Many side effects go away shortly after the study drug is stopped, but in some cases side effects can be serious, long lasting or permanent.

For more information about risks and side effects, ask the study doctor and/or the research staff.

7. What benefits can I expect from being in the study?

Taking part in this study may or may not make your health better. While doctors hope the combination of drugs used in this study, duvelisib and nivolumab will be an effective form of treatment for aggressive lymphoma, there is no proof of this. We do know that the information from this study will help doctors learn more about duvelisib in combination with nivolumab as a treatment for aggressive cell lymphoma/ Richter's syndrome. This information could help future cancer patients.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment

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

9. What are the costs of taking part in this study?

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study, including the cost of study drug and administration, tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are being done at no charge. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment. You are responsible for any co-payments, coinsurance, and deductibles that are standard for your insurance coverage or as required by your insurance company or charges your insurance company does not pay.

You WILL NOT have to pay for:

- Duvelisib. This medication will be provided by the study and will not be billed to you or your insurance while you are taking part in this study. However, you or your health plan will be billed to pay for costs of the supplies and personnel who give you the agents.
- Extra blood work being done to examine blood markers and the effect of duvelisib and nivolumab on the immune system
- Research tissue samples (taken from original biopsy)

You WILL have to pay for:

- Nivolumab. This medication will NOT be provided by the study and will be billed to you and/or your insurance while you are taking part in this study.
- All doctor's visits, including physical exams and medical histories
- Routine blood test to check your health
- All standard imaging done while on the study (CT scans, PET scans, etc.)

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at
http://cancer.gov/clinicaltrials/understanding/insurance-coverage

You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

10. Will I be paid for taking part in this study?

You will not be paid for taking part in this study.

11. What happens if I am injured because I took part in this study?

If you suffer an injury from participating in this study, you should notify the researcher or study doctor David Bond, MD, (614) 688-7942, immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

If you are injured as a result of your participation in this study, you may obtain immediate care at the Ohio State University Medical Center. The cost for this treatment will be billed to you or your medical or hospital insurance. Your health insurance company may or may not pay for treatment of injuries as a result of your participation in this study. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

13. Will my de-identified information be used or shared for future research?

No.

14. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The Ohio State University Data Safety Monitoring Committee
- Secura Bio and/or their representatives will have access to your files; and
- Your insurance company (if charges are billed to insurance).

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

15. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
  HIV / AIDS
  Hepatitis infection
  Sexually transmitted diseases
  Other reportable infectious diseases
  Physical exams
  Laboratory, x-ray, and other test results
  Diaries and questionnaires
  The diagnosis and treatment of a mental health condition; and
- Records about any study drug you received

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office record;
- Others: Secura Bio and/or their representatives will have access to your files.

IV. Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;

- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

16. Who can answer my questions about the study?

For questions, concerns, or complaints about the study, or if you feel you have been harmed as a result of study participation, you may contact:

David Bond, M. D.
1140A Lincoln Tower
1800 Cannon Dr
Columbus, Ohio 43210
Phone: (614) 688-7942 or 614-293-8000 (24 hours).

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact:

HIPAA Privacy Officer
Suite E2140
600 Ackerman Road
Columbus, Ohio 43201
Phone: 614-293-4477

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact**:**

David Bond, M. D.
1140A Lincoln Tower
1800 Cannon Dr
Columbus, Ohio 43210
Phone: (614) 688-7942 or 614-293-8000 (24 hours)

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form**.**

Printed name of participant	**Signature of participant** **AM/PM** **Date and time**
Printed name of person authorized to consent for participant (when applicable)	**Signature of person authorized to consent for participant (when applicable)**
Relationship to the participant	**AM/PM** **Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent** **AM/PM** **Date and time**

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness** **AM/PM** **Date and time**
Printed name of witness	**Signature of witness** **AM/PM** **Date and time**