PRINCIPAL INVESTIGATOR:	Mark Roschewski, M.D.
STUDY TITLE:	Phase 1 Study of Copanlisib with Dose-adjusted EPOCH-R in Relapsed and Refractory Burkitt Lymphoma and other High-Grade B-cell Lymphomas
STUDY SITE:	NIH Clinical Center
Cohort:	Standard Affected Subject
Consent Version:	04/24/2023

WHO DO YOU CONTACT ABOUT THIS STUDY?

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KEY INFORMATION ABOUT THIS RESEARCH

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

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

You are being asked to take part in this study because you have relapsed and/ or refractory highly-aggressive B-cell lymphomas (such as Burkitt lymphoma [BL] and certain types of diffuse large B-cell lymphoma [DLBCL]).

The main purpose of this research study is to learn if it is safe to give individuals with these cancers the drug copanlisib (Aliqopa®) together with a regimen called DA-EPOCH-R which includes rituximab as well as several chemotherapy drugs. This regimen stands for dose-adjusted (**DA**), etoposide (**E**), prednisone (**P**), vincristine (**O**), cyclophosphamide (**C**), doxorubicin (**H**), and rituximab (**R**). As not every drug in this regimen is a chemotherapy, throughout this document DA-EPOCH-R will be referred to as a "combination chemotherapy regimen". We also hope to get early information if this treatment combination is an effective treatment for highly-aggressive B-cell lymphomas.

Although each is approved and used either alone or in combination to treat types of lymphoma, the use and combination of the drugs in this study is investigational. An "investigational drug" is a drug or combination of drugs that is being tested and is not approved in the United States by the U.S. Food and Drug Administration (FDA). The reason that this combination needs to be studied is to ensure that copanlisib is safe to be given with this chemotherapy regimen and that

it will not be associated with any side effects that will require stopping of known effective treatment such as DA-EPOCH-R.

There are other drugs and treatments that may be used for your disease, and these can be prescribed by your regular cancer doctor, if you are not in this study. These drugs all work in different ways in the body as compared to the study drugs and with different side effects. If you would prefer other drugs or treatments, such as alternative chemotherapy regimens, radiation therapy, single-agent targeted therapy and/or approved forms of immunotherapy, you should consider not joining this study.

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

- In the first part of the study (dose escalation portion), we want to find out the highest dose of copanlisib that is safe to use with rituximab and combination chemotherapy regimen (DA-EPOCH-R). We will test increasing doses of copanlisib in small groups of patients. We also want to find out what kind of side effects these medications might cause. After the first part is done, we will enroll additional patients in a second part of the study (dose expansion portion) to learn more about whether these study medications can shrink your tumor(s).
- If you are eligible to receive treatment, the study drugs will be given as follows for up to 6 cycles of 21 days each. The treatment is similar in both parts. Copanlisib will be given by IV infusion on day 1 each cycle. The combination chemotherapy regimen you will receive, DA-EPOCH-R is standard chemotherapy treatment that is given over 5 days by intravenous (IV) infusion and one with one oral medication . Additional details are provided later in this consent.
- If you are at risk of your disease spreading to your central nervous system, you may also receive a drug known as methotrexate injected into your spinal fluid. Additional details are provided later in this consent.
- You may experience side effects from taking part in this study. Some can be mild or very serious, temporary, long-lasting, or permanent, and may include death. Examples of some of the side effects that you may have include: changes in blood counts (such as low red or white cells), gastrointestinal (such diarrhea, nausea, vomiting), rashes, fatigue, and infections. Since this is the first time that these drugs are being administered together, there may be side effects that we cannot predict. Some side effects may affect your ability to have children. You may also have side effects from some of the procedures (such as the spinal tap) and bone marrow tests. All of the possible side effects are described in more detail later in the consent form
- You will be seen regularly during the study. You will have clinical, laboratory, and imaging tests to see how you are doing and to see if the treatment is having any effect on your disease. We will also collect required samples from you (including blood, bone marrow, and tumor biopsies) for both clinical and research purposes. We may also collect saliva or cheek swabs for research.
- After the study treatment has ended, we will need to see you about 30 days after the last dose of study drugs at the NIH Clinical Center. We will continue to see you about every 3-6

months for about 5 years after treatment, and then at least yearly to see how you are doing and if your cancer gets worse (or comes back). After this time, we may contact you to see how you are doing for the rest of your life. If your disease worsens, or you start need to start a new anti-cancer we will continue to follow-up with you by phone to see how you are doing until we complete the main research goals of the study, which we expect will take 4-5 years.

Just as we do not know what side effects you might have, we cannot know if you may benefit from taking part in this study. If you do not benefit, this study and the results from our research will help others in the future.

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

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

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

WHY IS THIS STUDY BEING DONE?

The main purpose of this research study is to learn if it is safe to give the drug copanlisib (Aliqopa®) together with a combination chemotherapy regimen (DA-EPOCH-R), to patients with relapsed and/or refractory highly-aggressive B-cell lymphomas (such as Burkitt lymphoma [BL] and certain types of diffuse large B-cell lymphoma [DLBCL]). We also want to see if the study drug, copanlisib, in combination with rituximab and standard combination chemotherapy is an effective treatment for highly-aggressive B-cell lymphomas.

Copanlisib (Aliqopa®) has been shown to slow the growth of cancer cells and cause tumor cell death. It does this by inhibiting, or interfering, with several cell-signaling pathways that lymphoma cells use to grow. Rituximab is a type of drug called a "monoclonal antibody." It is believed that rituximab works by using the body's immune system to attack the cancer. Rituximab may work by attaching to the cancer cells and causing the cells to die or by telling your immune system to destroy the cancer cells. Rituximab together with standard combination chemotherapy regimens are known to get rid of aggressive lymphomas in many patients. However, these regimens do not work in everyone. Our hope is that adding copanlisib to standard combination therapy will be safe and will work even better than standard combination therapy alone; however, we do not know if this will be the case.

Copanlisib is approved by the Food and Drug Administration (FDA) for treatment of follicular

lymphoma that has relapsed (or progressed) after prior treatment, but is not approved for your type of lymphoma. Rituximab is approved by the FDA for several types of Non-Hodgkin's lymphoma, including types of DLBCL, and is commonly used to treat BL, both as a single agent or in combination with other chemotherapy. The standard combination chemotherapy regimen (DA-EPOCH-R) includes approved drugs by FDA that are commonly used to treat lymphoma. The use of copanlisib in this study is considered investigational, which means it has not been approved by the U.S. Food and Drug Administration (FDA) to treat your type of lymphoma. However, the FDA has given us permission to use copanlisib in this study. The combination of copanlisib with combination chemotherapy regimen (DA-EPOCH-R) for your cancer is investigational.

WHAT WILL HAPPEN DURING THE STUDY?

The screening process showed that you are eligible to participate in the study, and if you choose to be in it, you may need to have a few additional standard tests completed if not done recently. You will also have additional samples collected for research tests. If any of the screening tests need to be repeated, and show that you have become ineligible, you will not be able to continue with this study.

If you decide to take part in the study, you will be asked to:

- Receive study treatment at the NIH Clinical Center and be seen regularly in the clinic, to have tests and procedures during and after the study treatment in follow-up to see how you are doing and to assess your disease
- Provide specimens (such as blood, saliva, tumor and normal tissue, and bone marrow) for research studies.

Study Treatment

The treatment will be given in the outpatient setting at the Clinical Center. If there is a reason to give any part of the treatment and/or testing as an inpatient, your doctor will discuss this with you.

The treatments are given in cycles of treatment (each cycle is 21 days- 3 weeks) and may continue for up to 6 cycles. Treatment will be given as follows:

- **Copanlisib:** is given on Day 1 of each 21-day cycle, by intravenous (IV) infusion over about 60 minutes. Since copanlisib may elevate your blood sugar or may raise your blood pressure after the infusion, special precautions will be taken prior to each infusion. You must fast for at least 8 hours prior to your first dose of copanlisib on Day 1. Beginning on subsequent copanlisib dosing days, you may be asked to eat no more than a small, light meal that is low in carbohydrates (also called a "low glycemic index meal") within 4 hours before the start of the copanlisib infusion. The timing of these meals, including what and how much you will eat, will be discussed with you by the study team. If you have type 1 or type 2 diabetes, you will be asked to consult with an endocrinologist prior to starting the infusions. If your blood sugar remains elevated at times other than the first 5-8 hours after the infusion of copanlisib, you may be asked to monitor your blood sugar at home before and after meals. Your blood pressure will also be monitored right before each dose of copanlisib and in the middle of the infusion (mid-infusion, 30 minutes), and at the end of the infusion.

- **DA-EPOCH-R:** The drug regimen you will receive is a combination of medications called DA-EPOCH-R, which refers to dose-adjusted **(DA)** etoposide (**E**), prednisone (**P**), vincristine (**O**), cyclophosphamide (**C**), doxorubicin (**H**), and rituximab (**R**). Rituximab will be given by IV infusion on Day 1 of each cycle of treatment, after copanlisib, over several hours. When the rituximab IV infusion is complete, the drugs doxorubicin, etoposide, and vincristine will be mixed together in an IV bag and given by continuous IV infusion over the next 4 days (that is, continuously for a total of 96 hours). Cyclophosphamide will be given by IV infusion on Day 5 after you have received the previous chemotherapy drugs. Prednisone will be given by mouth (orally) each day on Days 1-5. "Dose adjusted" means that your drug doses with each cycle will be adjusted based on how your body responds (such as your blood counts) to the prior cycle.

In order to confirm the dose of copanlisib that is safe to give together with combination chemotherapy, patients will be enrolled and start treatment on the study in groups as follows:

Dose escalation part: First, a group of 3-6 study participants will receive copanlisib, at a low starting dose, together with DA-EPOCH-R (delivered at a standard dose during Cycle 1 and dose-adjusted as needed for Cycle 2 onward). The dose of copanlisib will be escalated (or increased) in a new group of 3-6 patients, as long as there were no safety issues in the first group. If there are no safety issues in the second group, the dose of copanlisib will be increased again in another group of 3-6 patients to see if this higher dose is safe. Each group of patients will be monitored closely for side effects by the study staff closely for at least 3 weeks before enrolling the next group and/or moving on to the next doses, until the best or highest dose of copanlisib planned for this study is found.

- Dose expansion part: Once the highest safe dose of copanlisib given together with DA-EPOCH-R is found, then the next part of the study will begin. In this part of the study, patients will receive the safest doses of the study drugs as determined in the dose escalation part of the study to learn more about this drug combination and its effect on the treatment of highly aggresive B-cell lymphomas.

All study participants will take the standard doses of the combination drugs comprising DA-EPOCH-R which may be dose-adjusted in Cycle 2 onward. Your dose of copanlisib will be assigned depending on what dose level is open at the time of your enrollment during dose escalation or the maximum tolerated dose during the dose expansion portion. Treatment in both groups will be given for a maximum of 6 (21-day) cycles as long as your disease does not get worse and you do not have any severe side effects.

The study drugs will be given by intravenous (IV) infusion (through a needle in a vein in your arm) or through a "central line," an IV catheter (or tube) surgically placed in the large vein under your collarbone or in your neck.

Copanlisib will be administered prior to DA-EPOCH-R on Day 1 of each cycle.

We will give you standard medications to try and prevent certain side effects. In addition to others, these may include medications to help prevent nausea and vomiting, and medication to prevent infection.

Certain medications need to be used with caution or avoided all together while you are participating on this study. If any physician other than the study team prescribes a medication for you for another condition, or you take any new over-the-counter medications, vitamins or herbal supplements, you must tell us and check with us prior to starting. This is important because the interaction of some medications may cause serious side effects and/or may still be unknown. You should also avoid grapefruit juice as this may affect how your body processes the study medications. Your study team will discuss what medications to avoid during your study participation.

Highly aggressive lymphomas can spread to your central nervous system (the brain, spinal cord and eyes). Your study doctor will tell if you if you are at risk of your disease spreading to your CNS, in which case you will receive a drug to help prevent this from happening. Treatment given to prevent lymphoma from spreading to your central nervous system is called 'CNS prophylaxis'. This treatment is considered standard of care and would therefore, if needed, be a part of your treatment even if you were not participating in this research study. If your study doctor determines that you are not at risk of your disease spreading to your central nervous system, then the information provided in the list below does not apply to you.

- If your study doctor determines that you have active disease in your spinal fluid (cerebrospinal fluid, CSF) then the following information applies to you: You will receive a drug known as methotrexate. Methotrexate will be injected into your spinal fluid. This method is called a lumbar puncture (also called a spinal tap).
- You will receive a minimum of 8 injections of methotrexate (twice a week) until at least 2 weeks after the disease in your spinal fluid has cleared, and then you will be given 1 injection a week for 6 weeks, and then 1 injection a month for the next 6 months.

Study Procedures

Similar to the tests done at the beginning of the study to determine eligibility, the following tests and procedures will be performed during the study, to see how you are doing and how the cancer may be responding to treatment. Unless otherwise noted, these will be done at least before starting treatment, before the start of every cycle, and at the end of treatment or when your disease progresses. If the procedures were done at screening, they will be done similarly unless otherwise noted.

Clinical Assessments and Procedures:

- History and physical exam, including vital signs, seeing how you function in your daily activities, any current symptoms of your condition and a review of all medications that you take.
- Standard blood and urine tests:
    - To measure your organ function, such as liver and kidney, and white blood cells, red blood cells and platelets, and blood electrolytes.
    - To measure your blood sugars (these will not be repeated until the end of treatment and in follow-up).

  - To check for Cytomegalovirus (CMV) viral load: Since there is a risk of copanlisib reactivating CMV, your blood will be tested for CMV before every cycle and for six months after stopping treatment.
  - Hepatitis B Testing and Prophylaxis: As part of our study, we will test you for infection with Hepatitis B. We will tell you what the results mean and if you will require more frequent testing for Hepatitis B and need to take medicine to prevent Hepatitis B reactivation while on the study. If you need to take medicine, you will take one, such as entecavir, by mouth every day until 12 months after your last chemotherapy.
  - To check to see if you are pregnant: If you are a woman able to get pregnant, you will also have a pregnancy test done before starting treatment and before the start of every cycle.
  - Standard urine tests: before starting treatment, and before the start of every cycle

- Bone marrow testing: A bone marrow aspiration and/or biopsy will be done: at the end of study treatment only if it was positive when you were screened to join this study, and may be repeated in follow-up to confirm response, if and only if other tests show a complete response.
- Imaging: Imaging to show all sites of disease, including CT scan of chest, abdomen and pelvis and FDG PET/CT scans will be done before starting treatment, after Cycles 1 (CT scan only, no FDG PET/CT), 3 and 6 (both CT and FDG PET/CT) and at the end of treatment (CT scan only no FDG PET/CT) or when your disease progresses (both CT and FDG PET/CT).
- Lumbar puncture: A lumbar puncture (spinal tap) will be done before starting treatment to confirm the stage and status of your disease, and will be repeated at the end of study treatment only if it was positive at the start of treatment. This procedure is when a needle is carefully inserted into the spinal canal low in the back (lumbar area). Some cerebrospinal fluid (CSF) is removed for testing.

Research Sample Collection

The following samples will be collected for research purposes only:

- Blood samples:
  - Blood samples (about 3 tablespoons): before starting treatment, at the end of every cycle, and the end of treatment or when your disease progresses.
  - Pharmacokinetic (PK) blood samples (about 1 teaspoon each) and cerebrospinal fluid samples (about 1 teaspoon each) will also be collected to look at levels of some of copanlisib in the body. The cerebrospinal fluid samples will be collected in all participants that have an Ommaya reservoir (a plastic device implanted under your scalp to deliver medication to your cerebrospinal fluid) and will be optional if you do not have one. These samples would be collected as follows:
    - Only during Cycle 1- on Day 1 before copanlisib infusion, and a few times after copanlisib infusion on Day 1 of Cycle 1 including once the next day, and on Day 5 of Cycle 1.

- Tissue samples: If tissue from your original diagnosis and/or from a procedure for your disease is available (taken either before or during the study), these may also be collected for the study.
- Saliva or Buccal swab samples: Sometime before the start of treatment, a saliva sample or buccal swab sample will be collected for the study to allow us to look at your normal DNA. In some cases, this might also be done by a blood sample.
- Biopsies:

  The biopsies are an optional part of the study and you will only be asked to do so if it is felt to be safe. We will ask you to undergo a tumor biopsy before starting treatment, and again if your disease should come back or progress during or after treatment on this study. The tissue is being collected for special research tests.

  Your doctor or the study team will discuss the biopsies with you. The optional biopsies to be performed are exclusively for research purposes and will not benefit you. They might help other people in the future.

  You may agree to biopsies now and change your mind later. If at any time you do not want to have a biopsy done, please tell us.

  A part of all biopsies done may be sent to the clinical laboratories for a standard of care evaluation to confirm the stage and grade of your disease, portions of the samples will also be used for research tests. Usually tissue can be obtained safely and comfortably with local anesthesia. If you require sedation before undergoing a biopsy, you will be informed of the risks and you will be asked to sign an additional consent prior to undergoing the procedure. Biopsies will NOT be done on this study if they require general anesthesia. We may ask that you have ultrasound and/or CT scan to help clearly locate your tumor when doing a biopsy.

The following sections describe studies to be done on your samples for research:

What tests will be done on my samples?

All of your samples collected for research purposes on this study (such as the tumor and normal tissue) may be used to check for levels of some of the study drugs in the body, to look at your body's immune response to treatment, and to look for specific changes in the DNA in tumors that could be used to develop new ways of diagnosing and treating cancer. DNA (also called deoxyribonucleic acid) in the cells carries genetic information and passes it from one generation of cells to the next – like an instruction manual. Normal tissue contains the DNA (instructions) that you were born with, DNA in tumor cells has changed – or mutated – and we think that change in the DNA is what causes tumors to form and to grow.

To look at your DNA, we may use do what is called "whole genome sequencing." This where we will do special tests in the lab to look at the entire sequence, or order, of how your DNA is put together. This is what makes you unique.

To determine which parts of the DNA have mutated, we will compare the DNA in your tumor cells to DNA from your normal cells. We will then analyze the results from similar tumors to see if there are any changes in the DNA that are common to a particular type of tumor. To examine the tumor and normal tissue we may use several different techniques depending on the type of tissue

we collect. These could include growing cell lines (cells which keep dividing and growing in the laboratory, sometimes for years allowing us to continually study those cells), xenograft studies (placing or growing cells in another animal, such as mice), and looking in detail at the parts of the genes that produce specific proteins.

However, you should know that the analyses that we perform in our laboratory are for research purposes only; they are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing or testing for routine clinical care. For these reasons, we will not give you the results of the research tests done on your research samples in most cases. There may be exceptions to what we share with you and this is described later in this consent form in the section for "Return of research results."

When you are finished taking the drugs (treatment)

When you finish the study treatment, we will ask you to come to the clinic for a safety check-up, about 30 days after the last dose of study drug to see how you are doing. If you stop the study drug and your cancer has improved or is stable at the time you stop, you will be followed every 3 months for the first 2 years after completion of treatment; every 6 months for years 2-5, and then once a year indefinitely. The tests and procedures to be completed at each visit include:

- Physical exam, including vital signs and weight
- Blood tests to check your organ function, including blood counts, blood chemistries and other tests to monitor your health
- CT scan of your chest, abdomen and pelvis (not at the 30 day safety check-up)
- Research blood samples for biomarkers and other research studies
- CMV viral load (for 6 months)
- Hepatitis B Testing and Prophylaxis for 12 months after your last chemotherapy, if applicable

If you stop the study drug and your cancer has worsened or you have started another anti-cancer therapy, you will be contacted about every 3 months by phone to get information on any new medications, treatments, or procedures you are currently taking or have recently received for the cancer and to see how you are doing. You will be followed on this study until the end of the study or your voluntary withdrawal from the study or your death (whichever is sooner).

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for at least 5 years. After this time, we may continue to contact you until we complete the main research goals of the study, which we expect will take an additional 4-5 years. We will continue to contact you to see how you are doing for the rest of your life or until the study is stopped.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 39 people participate in this study at the NIH.

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

If you choose to take part in this study, there is a risk that the study drugs may not be as good as the usual approach for your cancer or condition at shrinking or stabilizing your cancer.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

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

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important things to know about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, and some may never go away.
- Some side effects may make it hard for you to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects. The medications that you receive to try to prevent or treat side effects may also have risks that will be explained to you.
- Your study doctor may adjust the study drugs to try to reduce side effects.

Risks and side effects related to the treatment and the procedures on this study are identified below:

Risks from Study Treatment

Copanlisib

The copanlisib used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health. These risks are described in more detail below. There is also a risk that you could have other side effects from the study drug, including those below, or those that are not yet known.

COMMON, SOME MAY BE SERIOUS In 100 people receiving copanlisib, more than 20 and up to 100 may have:
• Diarrhea, nausea • Tiredness

COMMON, SOME MAY BE SERIOUS In 100 people receiving copanlisib, more than 20 and up to 100 may have:
• Infection, especially when white blood cell count is low • High blood pressure which may cause headaches, dizziness, blurred vision • High blood sugar (see additional information below) • Low white blood cells count (see additional information below)

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving copanlisib, from 4 to 20 may have:
• Anemia which may require blood transfusion • Low blood platelet counts (thrombocytopenia) • Dry mouth • Sores in the mouth which may cause difficulty swallowing • Vomiting • Bruising, bleeding • Loss of appetite • Muscle spasms • Changes in taste • Feeling of "pins and needles" in arms and legs • Damage to the lungs which may cause shortness of breath • Rash • Low blood sodium levels (hyponatraemia) which can lead to symptoms of headache, muscle cramps, low energy, confusion and nausea • Skin condition which causes shedding of the top layers of your skin (exfoliative dermatitis) • Inflammation of the colon (colitis)

RARE, AND SERIOUS In 100 people receiving copanlisib, 3 or fewer may have:
• Belly Pain • Inflammation of the pancreas (Pancreatitis)

Other risks and additional information about copanlisib:

You may have several side effects at the same time such as nausea, vomiting, diarrhea, high sugars, fever and poor appetite which may lead to the need for your doctor to change your medications or give you fluids. Call your doctor right away if you are losing fluids (such as vomiting) and are drinking or eating less than normal.

The most common toxicities that required the dose of copanlisib to be changed or stopped in prior studies were high blood sugar (hyperglycemia), low neutrophil count (a type of white blood cell; neutropenia), and high blood pressure (hypertension). It is common for high blood sugar and high blood pressure to happen without any noticeable symptoms. However, if you notice symptoms including dizziness, lightheadedness, headaches, frequent urination, excessive thirstiness, or excessive hunger, you should notify your doctor. Another serious risk is lung infection (pneumonia) and inflammation of the lungs that may happen without an associated infection (pneumonitis). Other changes in blood levels and infections have also been seen.

Call your study doctor if you have any diarrhea, even if it is mild. Close monitoring and early management of diarrhea is essential for successful treatment of patients with copanlisib. Early and appropriate intervention by your study team can prevent the development of more severe diarrhea.

There is also the possibility of an allergic reaction to copanlisib and it might be severe. We will monitor for symptoms and treat as appropriate.

There is also the possibility you may experience abnormal electrical conduction within the heart which may lead to an irregular heartbeat. You should notify your doctor if you experience abnormal heart sensations.

Cytomegalovirus (CMV) Reactivation: CMV is a common virus that infects most people worldwide. It is a member of the herpesvirus family. Other members of the herpesvirus family cause chickenpox, infectious mononucleosis ("mono"), fever blisters, and genital herpes. These viruses all share the ability to remain alive, but dormant, in the body for life. Dormant means the virus lives in the body silently without causing obvious damage or illness, but may reactivate such as when the immune system weakens during sickness or stress. Even upon reactivation, there are usually no symptoms produced and is detected only on a blood test. You will be monitored closely with a blood test each time you return to clinic for signs of this infection.

Rituximab and Combination Chemotherapy Regimen (DA-EPOCH-R)

The following risks are associated with combination chemotherapy regimen with DA-EPOCH-R (dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab):

Likely:

- Lowered white blood cell count* (neutrophil/granulocyte) that may lead to infection
- Lowered white blood cell count (lymphocytes) that may lead to infection
- Lowered platelets* which may lead to an increase in bruising or bleeding
- Lowered red blood cells* which may cause anemia, tiredness, or shortness of breath
- Constipation
- Fatigue or tiredness
- Tingling of fingers and/or toes
- Hair loss
- Nausea
- Fingernail discoloration

- Bony pain
- Time away from work
- Infusion reaction with rituximab including fever, chills and/or nausea which can be severe
- Vomiting

*Should this occur, it can be treated with blood products (transfusions), antibiotics, and there may be a reduction in the amount of drug given to you.

Less Likely:

- Loss of appetite
- Headaches
- Joint, muscle or back pain
- High blood sugar levels
- High or low blood pressure
- Mouth & throat sores. Temporary irritation to the mouth may lead to mouth ulcers (similar to canker sores). Medications to numb the mouth may ease the mouth discomfort
- Stomach ulcers
- Irritation to skin and veins from the chemotherapy drugs that could cause tissue damage if drugs leak out of a vein.
- Skin rashes or hives
- Itching
- Muscle weakness
- Cough or wheezing
- Lung inflammation which can cause difficulty breathing and difficulty getting oxygen
- Swelling of the arms and legs
- Diarrhea
- Seizures
- Pain in the area of the tumor
- Back & neck stiffness/pain (if treatment for central nervous system disease is needed, following spinal fluid chemotherapy).
- Sensitivity to sunlight (in those patients who receive methotrexate because they are at risk of their lymphoma spreading to their central nervous system).
- Urine colored red for a day or two after the doxorubicin infusion
- Infection
- Low blood potassium
- Decreased blood supply to the heart/heart attack
- Abnormal fast heartbeat
- Abdominal pain

- Allergic reaction that may cause fever, aches and pain in the joints, skin rash and swollen lymph glands.
- Flushing
- Excess sweating
- Stuffy or runny nose, sneezing
- Swelling of the lips, eyes, tongue and throat which can be severe
- Dizziness
- Bladder irritation with bleeding
- Severe hepatitis (liver infection) in those patients who are carriers of the hepatitis virus. Your doctor will screen you for the hepatitis virus before beginning treatment on this study. If you test positive for the virus, you will receive medication to prevent reactivation and will be closely monitored for signs of the infection.
- Some other viral infections may be worsened or reactivated from a "sleeping state" in patients taking rituximab.

Rare, But Serious:

- Another viral infection, like those mentioned above, cause a serious brain condition called progressive multifocal leukoencephalopathy (PML). PML can be serious, causing severe disability or death.
- Severe constipation may result in abdominal pain and cramping
- Damage to the heart muscle leading to heart failure
- Tumor lysis syndrome, a rapid decline in the number of tumor cells that can lead to kidney failure and/or chemical imbalances that may have an effect on other organs like your heart. If this were to occur, you would receive close monitoring and blood tests, as well as appropriate medical treatment.
- Severe lung dysfunction resulting in an inability to breathe which can be life-threatening
- Skin rash that may be serious (R-CHOP and EPOCH-R)
- Severe reactions during rituximab infusions or severe allergic reactions: A fast heart rate, wheezing, low blood pressure, sweating, swelling of the throat and face rash may occur within a few minutes of starting treatment. They can be handled with medications and sometimes by slowing the rate of infusion. The reactions are more common during the first infusion of rituximab. You will be given medications to decrease the likelihood that the reactions may occur and decrease the severity if they should occur.
- Potentially life-threatening condition affecting less than 10% of the skin in which skin cell death causes the epidermis (outer layer) to separate from the dermis (middle layer).
- Life threatening condition affecting greater than 30% of the skin in which skin cell death causes the epidermis (outer layer) to separate from the dermis (inner layer).

Other possible treatment side effects (DA-EPOCH-R)

- Secondary Malignancy: A number of established chemotherapy agents have an inherent risk of causing another cancer (known as a "secondary malignancy"). Certain drugs in use

today, not currently known to be associated with this risk may be shown at a later time to result in the development of these secondary malignancies.

- Reproductive risks: Many of the drugs used in this treatment program are toxic to the cells in the ovary and testicle and may produce sterility. Recovery of normal fertility is not well studied although we know that some patients treated with this combination have remained fertile after the therapy has been completed. For this reason, men who are about to receive this treatment should, if they wish to have children in the future, consider sperm banking before start of the treatment. These drugs may also be very toxic to an unborn child. Therefore, adequate birth control measures (such as the contraceptive pill, condoms, diaphragm with contraceptive foam or ointment, contraceptive sponge, etc.) should be used by participants or their sexual partners while receiving treatment on this study. Women of childbearing age will have a pregnancy test, which must be negative at the time of study entry. The results of the pregnancy test will be made available to you prior to the initiation of the study. Women should not breastfeed a baby while participating in this study. See also "What are the risks related to pregnancy?" below.
- Infection risks: It is important to emphasize that when you have a decreased white blood cell count from the chemotherapy, you are at risk of infection. Such infections can be very serious and can even cause death if not quickly and properly treated. Therefore, if you have a temperature greater than 38.3°C (101°F), you must call your doctor immediately. If your temperature is higher than 38.0°C (100.4°F) two times in a 24-hour period, you must call your doctor immediately. Chemotherapy may also cause your platelets to fall; since platelets are the blood elements that permit blood to clot, this may place you at increased risk of serious bleeding. It may be necessary to give you transfusions of platelets if your platelet counts reach very low levels. There is a small chance that damage to the normal bone marrow may eventually result in bone marrow failure, leading to a serious shortage of one or more kinds of cells in the blood, or to leukemia. It is always possible that unanticipated side effects may occur, including death.

Your doctor(s) will watch you closely for side effects. The treatment may need to be stopped if any side effects become a serious threat to your life or well-being. Your doctor(s) will also stop the treatments if it becomes clear that the treatment is not successfully controlling your disease. For more information about risks and side effects, ask your study doctor.

Risks from tests and procedures

- Blood draws: The possible side effects of drawing blood include pain, bleeding, bruising, dizziness, light-headedness, fainting and, on rare occasions, local blood clot formation or infection with redness and irritation of the vein.
- Bone marrow: The bone marrow aspiration and biopsy may cause pain, bruising, bleeding and infection. Soreness near the site may last for a couple of days after the procedure. You may have more pain, risk of bleeding and bruising if you complete both aspiration and biopsy rather than just the aspiration. If your pain is severe or you develop a fever, please contact the study team immediately
- Tumor biopsy: The likely side effects include discomfort or pain, redness, swelling, and/or bruising at the site of the needle insertion. Bleeding from the site of the needle insertion is

a less likely risk. Rarely, significant infection or bleeding from this procedure, allergic reaction to the anesthetic, or formation of a scar at the site of needle entry occurs. If you will have conscious sedation with the procedure, the most common risks last up to a few hours and can include drowsiness, feeling slow or sluggish, low blood pressure, headache, and nausea. If you will have sedation with the procedure, these risks will be discussed with you prior to the procedure. You will be asked to sign a separate consent form prior to any biopsy procedure.

- Lumbar puncture: The lumbar puncture may cause pain at the site where the needle goes in and the spinal fluid is taken. There is a small risk of infection or bleeding. After the lumbar puncture you may get a headache. About a third of adults report a headache after an LP. To minimize the risk of a headache, the doctor will use a small needle and may prescribe bed rest for one or more hours after the procedure. If a headache occurs, it is usually mild and can be controlled by bed rest, drinking lots of fluids and a pain pill, such as acetaminophen. Rarely, the headache is severe and may require additional treatment with a "blood patch". In this procedure, a small amount of your own blood is injected into the lumbar puncture site. This procedure is generally effective in stopping the headache. A rare but serious complication of a LP, if it is done when the pressure inside the head is higher than normal (such as when a brain tumor is present), is known as medullary herniation which can result in death. Increased intracranial pressure is very unlikely to be present. The LP will not be done if there are any clinical indications that you have increased intracranial pressure, a skin infection in the lower back area, or bone malformation of the lower back (including severe scoliosis) which would make a LP difficult.
- Imaging as applicable:
    - CT and PET scans: There is a chance of developing an allergic reaction from the contrast material, which may cause symptoms ranging from mild itching or a rash to severe difficulty breathing, shock or rarely, death. The contrast material may also cause kidney problems. The study doctors will do a blood test prior to the test to confirm that it is safe you to receive the contrast.

      For IV contrast: You may feel discomfort when the contrast material is injected. You may feel warm, flushed, get a metallic taste in your mouth or, rarely, may make you vomit or feel sick to your stomach.

      For oral contrast: You may experience vomiting, nausea, cramping, bloating, constipation or diarrhea after drinking the contrast.

      See also risks from radiation below.
- Other: There are no known risks or discomforts with other tests and procedures (e.g., urine or saliva collection, cheek/ buccal swabs).

What are the risks related to pregnancy?

Both copanlisib and DA-EPOCH-R may be very toxic to an unborn child (also called embryo-fetal harm). There may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus.

If you are able to become pregnant, we will ask you to have a pregnancy test before starting this study. You will need to use a highly effective form of birth control before starting study treatment (from the time of signing this consent document) until at least 1 month after your last dose of copanlisib. Please discuss with your study doctor the most appropriate birth control method for you.

Examples of highly effective forms of birth control include:

- Total abstinence
- Intrauterine device (IUD)
- Contraceptive rod implanted into the skin
- Vasectomy (of your partner)

If you are able to become pregnant, you will need to continue to use birth control until at least 12 months after your last dose of rituximab. While you may continue to use a highly effective method, effective methods of birth control may be used during this time and include:

Effective Methods (requires the use of TWO of the following):

- Diaphragm with spermicide (cannot be used in conjunction with cervical cap/spermicide)
- Cervical cap with spermicide (option for women who have never been pregnant only)
- Contraceptive sponge (option for women who have never been pregnant only)
- Male condom or female condom (cannot be used together)
- Hormonal (birth control pills, skin patch, vaginal ring, injections)

Women should not breastfeed a baby while participating in this study. You must tell the study doctor if your birth control method fails during the restricted period (during treatment and 1 month after the last dose of copanlisib and 12 months after the last dose of rituximab). If you think or know you have become pregnant during the restricted period, please contact the research team as soon as possible.

You and your partner must agree to use birth control if you want to take part in this study. If you are a sexually active person with a female partner of childbearing potential, it is important that your partner not become pregnant during the restricted period. Men must agree to use a condom unless their female partner is surgically sterile, and ask their female partners to be on highly effective birth control (IUD, contraceptive rod, abstinence) during the restricted period. If you think your partner has become pregnant during the restricted period, please contact the research team member identified at the top of this document as soon as possible. If you and your partner plan for your partner to become pregnant after the restricted time period, please discuss this with the study team.

What are the risks of radiation from being in the study?

During your participation in this research study, you will be exposed to radiation each year and maximum is in the first year from up to 7 CT scans of the chest, abdomen and pelvis, 5 ^{18}F-FDG PET scans, and 2 CT-guided biopsies. The amount of radiation exposure you will receive from these procedures is equal to approximately 13 rem per year. A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans, and ^{18}F-FDG PET scan that you get in this study will expose you to roughly the same amount of radiation as 43.3 years' worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 0.9 out of 100 (1.3%) and of getting a fatal cancer is 0.5 out of 100 (0.7%).

You may not participate in this study if you are pregnant. If you are able to become pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

Other risks

Privacy risks associated with genetic testing

It may be possible that genetic information from you could be used by law enforcement agencies or other entities to identify you or your blood relatives.

Psychological or social risks associated with return of incidental or secondary findings

As part of the research study, it is possible that you could learn that you have genetic risks for another disease or disability. This may be upsetting and, depending on what you learn, might create a need to make challenging decisions about how to respond.

Although your genomic information is unique to you, you share some genomic similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, learning your research results could mean something about your family members and might cause you or your family distress. Before joining the study, it may be beneficial to talk with your family members about whether and how they want you to share your results with them.

Protections against misuse of genetic information

This study involves genetic testing on samples. Some genetic information can help predict future health problems of you and your family and this information might be of interest to your employers or insurers. The Genetic Information Nondiscrimination Act (GINA) is a federal law that prohibits plans and health insurers from requesting genetic information or using genetic information. It also prohibits employment discrimination based on your health information. However, GINA does not address discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed condition or disease that has a genetic component.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

The aim of this study is to see if this combination of treatment is safe to give to patients with B-cell lymphoma. We also hope to learn more about how effective or not this combination of medications may be in treating patients. We do not know if you will receive personal, medical benefit from taking part in this study. These potential benefits could include shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer.

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

In the future, other people might benefit from this study because the knowledge gained from this study may help others in the future who have cancer.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

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

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

DISCUSSION OF FINDINGS

New information about the study

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

Return of research results

When we are examining your DNA, it is possible that we could identify possible changes in other parts of your DNA that are not related to this research. These are known as "incidental medical findings".

These include:

- Changes in genes that are related to diseases other than cancer
- Changes in genes that are not known to cause any disease. These are known as normal variations.
- Changes in genes that are new and of uncertain clinical importance. This means that we do not know if they could cause or contribute to a disease or if they are normal variations.

Since the analyses that we perform in our laboratory are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing, the genetic changes that we find may or may not be valid. Therefore, we do not plan to inform you of all of the genetic results of testing on your tissue and blood that is performed in our research lab. However, in the unlikely

event that we discover a finding believed to be clinically important based on medical standards at the time we first analyze your results, we will contact you. This could be many years in the future. We will ask you to provide another sample to verify the findings we have seen in our lab. If the results are verified, you will be re-contacted and offered a referral to a genetic Healthcare Provider To Discuss The Results.

EARLY WITHDRAWAL FROM THE STUDY

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

- if he/she believes that it is in your best interest
- if your disease worsens or comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if you become pregnant
- if any of the study drugs may become unavailable
- if new information shows that another treatment would be better for you
- if you do not follow the study rules
- if the study is stopped for any reason

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

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

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

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Bayer or designated representatives.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

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

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

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

_____ Yes _____ No

Initials Initials

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

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

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

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

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

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

Will your genomic data be shared outside of this study?

As part of this research study, we will put your genomic data in a large database for broad sharing with the research community. These databases are commonly called data repositories. The information in this database will include but is not limited to genetic information, race and ethnicity, and sex. If your individual data are placed in one of these repositories, they will be labeled with a code and not with your name or other information that could be used to easily identify you, and only qualified researchers will be able to access them. These researchers must receive prior approval from individuals or committees with authority to determine whether these researchers can access the data.

Summary information about all of the participants included in this study (including you) is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.

NIH policies require that genomic data be placed in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

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

Your specimens and data may be stored by the NIH as long as the study is open. When this study is closed, we may keep the data and any samples that are leftover for future research indefinitely.

Risks of storage and sharing of specimens and data

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

PAYMENT

Will you receive any type of payment for taking part in this study?

You will not receive any payment for taking part in this study.

REIMBURSEMENT

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

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

COST

Will taking part in this research study cost you anything?

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

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

CONFLICT OF INTEREST (COI)

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

The NIH and the research team for this study are using a drug developed by Bayer Pharmaceuticals through a collaboration between your study team and the company. The company also provides financial support for this study.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

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

Will your medical information be kept private?

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

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

- Qualified representatives from Bayer Pharmaceuticals, the pharmaceutical company who produces copanlisib.

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

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

Certificate of Confidentiality

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

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

The Certificate does not protect your information when it:

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

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

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

Privacy Act

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

reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

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

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Mark Roschewski, M.D., at mark.roschewski@nih.gov or 240-760-6183. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

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

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

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

Signature of Witness	Print Name of Witness	Date

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

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

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