SUMMARY OF CHANGES

A Pilot Study of Ibrutinib and R-da-EPOCH for Front Line Treatment of AIDS-Related Lymphomas

Version 9.0

NCI Protocol #: AMC-101
Local Protocol #: AMC-101

Protocol Date: 20DEC2024
NCI Version Date: 20DEC2024

I. Scientific and Substantive Changes

#	Section	Description of Changes
1.	What possible risks can I expect from taking part in this study?	The CAEPR risk profile for Ibrutinib (PCI-32765) Version 2.8, dated November 4, 2024 was added.

II. Administrative and Editorial Changes

#	Section	Description of Changes
2.	Global	Protocol version was updated to 9.0 and date was updated to 20DEC2024.

AMC-101 MODEL INFORMED CONSENT FORM

Study Title for Study Volunteers: **Testing Adding Ibrutinib to Usual Treatment for AIDS-Related Lymphomas**

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: **A Pilot Study of Ibrutinib and R-da-EPOCH for Front Line Treatment of AIDS-Related Lymphomas**

A Clinical Trial of the AIDS Malignancy Consortium (AMC)

WHY IS THIS STUDY BEING DONE?

You are being asked to take part in this study because you have B-cell non-Hodgkin lymphoma (NHL). Lymphoma is a cancer of infection-fighting immune system cells called B cells. NHL is a potentially curable condition with standard cancer treatment drugs (chemotherapy) and steroids.

This study is being done to develop better treatments for B-cell non-Hodgkin lymphoma for HIV-positive people. The purpose of this study is to test the safety of an oral drug, ibrutinib, added to the standard lymphoma treatment. The U.S. Food and Drug Administration (FDA) has approved ibrutinib alone to treat other types of lymphoma. It is experimental to treat the type of lymphoma that you have. Ibrutinib has not been used in combination with the chemotherapy that will be used in this clinical trial. Scientists think that adding ibrutinib may help how effective R-da-EPOCH is to treat your type of lymphoma. We will also study whether ibrutinib has a helpful effect against HIV and other viruses in our bodies that can cause lymphoma. Up to 54 people will take part in this study.

Standard lymphoma treatment includes chemotherapy, or cancer-fighting drugs, called etoposide, vincristine, cyclophosphamide, prednisone and doxorubicin (called EPOCH). These drugs are FDA approved for treatment of cancers such as lymphoma. The drugs are given over 5 days every 3 or 4 weeks, called a cycle. This combination of drugs is called dose-adjusted EPOCH (da-EPOCH) because the amount of drug given may be changed in later cycles to give you the highest dose possible and decrease any side effects. You may also be given a drug called rituximab if appropriate for you (R-da-EPOCH).

WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS STUDY?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach for your lymphoma
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for this cancer

WHAT ARE THE STUDY GROUPS?

The study will be conducted in two stages. The first stage, called the "Phase I" portion of the trial, will find what dose of ibrutinib may be safely combined with standard therapy In the Phase I portion of the study, study volunteers will be given different doses of the study drug ibrutinib and standard therapy. The first several study volunteers will receive the highest dose, since this dose has been safely used in other clinical trials. If there are serious side effects, the next study volunteers will receive a lower dose of ibrutinib. The dose of ibrutinib may decrease for every group of study volunteers until side effects related to treatment are acceptable. Once the accepted safe dose ibrutinib is found, the first stage of the study will be complete. Then, the second stage,

or "dose-expansion" portion of the trial will start. In the dose-expansion phase all study volunteers will get the same starting dose of ibrutinib.

HOW LONG WILL I BE IN THIS STUDY?

You will take ibrutinib with standard chemotherapy for a maximum of six cycles. Each cycle is 21 days long. If your treatment is delayed for any reason, then the total treatment time will be longer. After you finish the planned treatment, your doctor will continue to watch you for side effects and follow your condition for five years. This will include visits every 3 months for years 1-2, and then visits every 6 months for years 3-5.

WHAT EXTRA TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?

Most of the exams, tests, and procedures you will have are part of the usual approach for your care for your cancer. However, you will need some extra tests if you take part in this study. Listed below is an outline of the extra tests needed from you before, during and after the study.

Before you can be considered for the study, we need:

- Answers to questions related to the risk of getting HIV
- You may need to switch your HIV medications (antiretroviral regimen) or other medications if it could cause side effects when taken with ibrutinib. Your cancer doctor will review your medications to decide if your current HIV regimen or any other medications need to be switched. If needed, the study doctor will contact your HIV doctor to discuss these potential medication changes. In addition, we will send a letter to your HIV doctor to discuss what medicines are safe to take with ibrutinib
- Submission of your pathology slides used for the diagnosis of your lymphoma and any remaining lymphoma biopsy for further studies related to the study. Tests on your tumor sample will be performed for research.
    - To diagnose your lymphoma, all or some of your cancer was removed. This tissue went to the hospital's pathology department for testing and diagnosis. Any leftover tissue was stored in wax at the pathology department. This study requires that your tissue be reviewed by an expert panel of doctors. We will send your tissue and a copy of the report of your diagnosis to other AMC researchers for these studies. Your name will be removed from your sample and report and your study number put on them to protect your privacy. The results from these studies will not change your care for your lymphoma.
    - Your tissue will be sent to a central office (New York Presbyterian Hospital General Hospital, New York, NY). Doctors working with the AMC will review your diagnosis. You, the physician and the AMC will be given the results of this tissue review.
    - Your tissue will then be sent to a different facility (Mayo Clinic, Arizona). Researchers will test your samples for tumor genes and other factors to determine the origin of your lymphoma. You and your physician will not know the results of these tests.
- Blood tests for research studies studying:
    - *Levels of chemotherapy drugs and ibrutinib*
    - *Inflammatory markers*
    - *Amount of specific viruses which are associated with these particular lymphomas*
    - *Amount of particular proteins found in specific blood cells*
    - *If any tumor DNA is in your blood*

- If you are Hepatitis B or C positive, blood tests to check the amount of virus will be done from time to time
- Pregnancy test if you are female and can have a baby
- PET/CT imaging of your lymphoma
- Bone marrow biopsy (if deemed necessary by your physician)
- Lumbar puncture

You will need these tests and procedures during the study that are either being tested in this study or being done to see how the treatment is affecting your body.

- Complete blood count (CBC)
- Blood test for quantitative immunoglobulins, which measures different kinds of antibodies in your blood. Antibodies are proteins made by special white blood cells that aid in fighting infection.
- Blood test for HIV viral load and T cell subsets.
- Blood tests for effects of treatment other viruses.
- Blood tests for effects of treatment on blood cells.
- Blood tests to measure the amount of chemotherapy as well as ibrutinib in your blood (first cycle of chemotherapy only).
- If you are Hepatitis B or C positive, blood tests to check the amount of virus will be done from time to time.
- Medication diary at each visit.

The following will happen before/during Cycle 1 of your therapy and in future cycles of your therapy.

Participants in Phase I and dose-expansion portion of the study will receive combination chemotherapy with ibrutinib every 3 weeks. This 3 week period of time is called a cycle. The cycle will be repeated up to a maximum total of 6 times. After you complete cycle 4, we will look at how your lymphoma is responding to treatment. You may receive up to 6 cycles of treatment if your lymphoma is responding to treatment. Each cycle is numbered in order.

The following will happen after your therapy.

- Periodic blood tests to monitor your lymphoma or for research purposes
- Bone marrow biopsy immediately after study treatment is completed (if you had bone marrow disease prior).
- Blood tests for research studies studying:
  - Inflammatory markers
  - Amount of specific viruses which are associated with these particular lymphomas
  - If any tumor DNA is in your blood

A study calendar that shows how often tests will be done is attached.

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss
- The addition of ibrutinib to standard chemotherapy in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. To prevent dehydration, for example, you should consume at least 2 liters (about ½ a gallon) of fluid orally, on a daily basis, in particular during the days that they are being treated with ibrutinib. The study doctor will be testing 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. Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

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

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

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

1. Ibrutinib- Risk Profile for Ibrutinib (PCI-32765) (CAEPR Version 2.8, November 4, 2024)

COMMON, SOME MAY BE SERIOUS In 100 people receiving ibrutinib (PCI-32765), more than 20 and up to 100 may have:
• Diarrhea

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving ibrutinib (PCI-32765), from 4 to 20 may have:
• Anemia which may require blood transfusion • Abnormal heartbeat which may cause fainting • Pain • Constipation, nausea, vomiting • Sores in the mouth which may cause difficulty swallowing • Swelling of arms, legs • Tiredness, fever • Infection • Bruising, bleeding • Loss of appetite, dehydration • A new skin growth that is not cancerous • Dizziness, headache • Cough, shortness of breath • Rash • High blood pressure which may cause headaches, dizziness, blurred vision

RARE, AND SERIOUS In 100 people receiving ibrutinib (PCI-32765), 3 or fewer may have:
• Blood clot which may cause swelling • Death • Liver damage which may cause yellowing of eyes and skin, swelling • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Prior liver infection that returns which may cause yellow eyes and skin, tiredness • Hepatitis • Fungal infection of the lungs or central nervous system which may cause cough, shortness of breath, fever, confusion, headache or stiff neck • Kidney damage which may require dialysis • A new cancer resulting from treatment of earlier cancer • Damage to the lungs which may cause shortness of breath • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body • Low blood pressure

2. Rituximab (MoAb C2B8 anti CD20, chimeric)

COMMON, SOME MAY BE SERIOUS In 100 people receiving rituximab, more than 20 and up to 100 may have:
• Nausea • Chills, fever • Reaction during or following infusion of the drug • Infection, especially when white blood cell count is low • Anemia which may require blood transfusions • Numbness and tingling of the arms and legs • Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving rituximab, from 4 to 20 may have:
• Bruising, bleeding • Abnormal heartbeat • Heart attack or heart failure which may cause shortness of breath, swelling of ankles, and tiredness • Sores in eye • A tear or a hole in the bowels that may require surgery • Diarrhea, vomiting • Pain • Swelling of the body • Hepatitis, or liver damage which may cause yellow eyes and skin • Dizziness, headache • Kidney damage which may require dialysis • Cough • Scarring of the lungs • Stuffy nose • Blockage of internal organs which may cause shortness of breath, wheezing, vomiting • Increased sweating • Itching, rash, blisters on the skin • Severe skin rash with blisters and peeling which can involve mouth and other parts of the body • Low blood pressure which may cause feeling faint

RARE, AND SERIOUS In 100 people receiving rituximab, 3 or fewer may have:
• Damage to the brain caused by a virus which may result in tiredness, weakness, changes in thinking, and disability. This is called progressive multifocal leukoencephalopathy (PML). • Heart stops beating

3. Rituximab treatment risks in when taken with chemotherapy

Other events have occurred in patients receiving rituximab. The following have occurred in patients receiving rituximab in combination with chemotherapy:

* In some patients who have hepatitis B virus (HBV), rituximab has caused the infection to worsen by reactivating the virus. Severe and sudden hepatitis inflammation of the liver, very serious liver disease (including liver failure) and death can occur during, or within several months after rituximab treatment. HBV diagnosis in most patients has occurred approximately 4 months after their first dose of rituximab. Seek immediate medical attention if you develop persistent stomach/abdominal pain, dark urine, extreme fatigue, or yellowing eyes and/or skin. Treatment with antiviral medication is usually given to control HBV.
* Other viral infections, including JC virus (a virus responsible for an infection of the brain and spinal cord), cytomegalovirus (a member of the herpes virus group, which also includes herpes simplex virus and varicella-zoster virus [virus that causes chickenpox]), parvovirus B19 (a virus that can decrease or halt the body's production of red blood cells), West Nile virus (a virus causing an inflammation to the brain), and hepatitis C have been found in patients who have received rituximab in combination with chemotherapy.
* Patients have also experienced abdominal pain, bowel obstruction (blockage) and perforation (tearing), in some cases leading to death, after receiving rituximab in combination with chemotherapy for NHL and diffuse large B-cell lymphoma (DLBCL).

Some patients have developed new serious viral infections or had a worsening of chronic viral infection. Most, but not all, of these patients had cancer and they were on other anticancer treatments which made them more at risk. In some cases these infections occurred over one year after rituximab treatment and resulted in death. A rare and severe viral infection called PML (progressive multifocal leukoencephalopathy), which can cause brain damage such as memory loss, trouble thinking and blindness, and is almost always fatal, has occurred in patients who received rituximab. The majority of these patients received rituximab in combination with chemotherapy (drugs to treat cancer) or as part of a bone marrow transplant.

Some patients with systemic lupus erythematosus (lupus) who received rituximab developed PML, which resulted in death. It is uncertain whether treatment with rituximab increased the risk for this infection. Tell your doctor immediately if you, your family members, or healthcare provider notices any new or worsening medical problems, such as a new or sudden change in thinking, walking, strength, vision, or other problems that have lasted over several days.

4. Rituximab treatment risks in other disease areas

Rituximab is also used in studies to treat rheumatoid arthritis (RA), a disease characterized by inflammation of the joints. Patients with RA are at increased risk for cardiovascular (heart) events compared with the general population. Three cardiovascular deaths have occurred in RA patients treated with rituximab.

5. Chemotherapy (EPOCH)

May cause suppression of the immune system, which could lead to infections. The chemotherapy drugs used in the regimen are cyclophosphamide, etoposide, vincristine, and doxorubicin. Their side effects are listed below.

Likely side effects (these effects occur in more than 9% of patients taking EPOCH):

- Low white blood cell count that may lead to infection
- Low red blood cell count (also called anemia) that may require blood transfusions and can cause tiredness, weakness and shortness of breath
- Low platelet cell count that may lead to increased bruising or bleeding
- Fever and/or chills
- Infection that could be life-threatening
- Nausea and/or vomiting
- Mouth sores
- Numbness or tingling of the fingers or toes
- Loss of hair, which may include eyebrows, eyelashes, underarm and pubic hair.
- Constipation or diarrhea
- Stopping of menstrual periods, which may be permanent
- Stopping of sperm production

Less likely side effects (these effects occur in 3-9% of patients taking EPOCH):

- Elevated blood sugar
- Bleeding
- Change in taste or metallic taste
- Pink or red discoloration of the urine
- Bladder irritation

Rare but serious side effects:

- Congestive heart failure or weakening of the heart muscle
- Allergic reaction, which can cause shortness of breath, difficulty breathing, throat swelling or low blood pressure
- Low blood pressure
- Irritation of the skin or vein
- Blockage of the intestine
- Kidney damage
- Some people who have received cyclophosphamide or etoposide have developed other cancers of the urinary tract or bone marrow (like myelodysplasia or leukemia). This may happen years after the treatment has stopped.

6. Prednisone

COMMON, SOME MAY BE SERIOUS In 100 people receiving prednisone, more than 20 and up to 100 may have:
• In children and adolescents: decreased height • Loss of bone tissue • Mood swings • Skin changes, acne • Swelling of the body, tiredness, bruising • High blood pressure which may cause headaches, dizziness, blurred vision • Pain in belly • Increased appetite and weight gain • Weight gain in the belly, face, back and shoulders

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving prednisone, from 4 to 20 may have:
• Cloudiness of the eye, visual disturbances • Glaucoma • Infection • Non-healing wound • Diabetes • Damage to the bone which may cause joint pain and loss of motion • Kidney stones • Heartburn

RARE, AND SERIOUS In 100 people receiving prednisone, 3 or fewer may have:
• Bleeding from sores in the stomach • Broken bones

7. Reproductive risks

You should not become pregnant or father a baby while on this study or for 12 months after the last dose of rituximab and 90 days after the last dose of ibrutinib, whichever comes last, because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that both men and women need to use an approved birth method while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

Some of the drugs used in the study may make you unable to have children in the future. You may want to discuss this and your options with your doctor before starting treatment.

For more information about risks and side effects, ask your study doctor.

WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

Taking part in this study may or may not make your health better. While doctors' hope that chemotherapy with ibrutinib will be more useful against cancer compared to the usual treatment (chemotherapy without ibrutinib), there is no proof of this yet. We do know that the information from this study will help doctors learn more about using ibrutinib with chemotherapy as a treatment for cancer. This information could help future cancer patients.

CAN I STOP TAKING PART IN THIS STUDY?

Yes. You can decide to stop at any time. Your choices include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment, with care to help you feel more comfortable

If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

WHAT ARE MY RIGHTS IN THIS STUDY?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number).*

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. 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 will not be responsible for the costs of the laboratory studies related only to research (blood samples and review of tissue for research purposes).

The NCI will supply ibrutinib at no charge while you take part in this study.

Even though it probably won't happen, it is possible that the manufacturer may not continue to provide ibrutinib to the NCI for some reason. If this would occur, other possible options are:

- You might be able to get ibrutinib from the manufacturer or your pharmacy but you or your insurance company may have to pay for it.
- If there is no ibrutinib available at all, no one will be able to get more and the study would close.

If a problem with getting ibrutinib occurs, your study doctor will talk to you about these options.

There will not be any monetary compensation for participation in this study.

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.

WHAT HAPPENS IF I AM INJURED OR HURT BECAUSE I TOOK PART IN THIS STUDY?

It is important that you tell your study doctor, _____ *[investigator's name(s)],* if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at _____ *[telephone number].*

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. No funds have been set aside to compensate you in the event of injury. You or your insurance company will be charged for continuing medical care and/or hospitalization. However, you are not giving up your right to seek to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research.

WHO WILL SEE MY MEDICAL INFORMATION?

Your privacy is very important to us and the researchers will make every effort to protect it. 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. 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.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The AIDS Malignancy Consortium (AMC)
- The Pharmaceutical Collaborator, Pharmacyclics LLC, or any drug company supporting the study.
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S.

Trained staff from the AMC may review your records. Access to your medical information will be limited to those listed in the Research Authorization Form, which is a part of the informed consent process.

WHERE CAN I GET MORE INFORMATION?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

For information on the AMC and its clinical trials, go to: http://www.amcoperations.com.

WHO CAN ANSWER MY QUESTIONS ABOUT THIS STUDY?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

OPTIONAL SAMPLE COLLECTIONS FOR LABORATORY STUDIES AND DONATION OF LEFTOVER TISSUE SAMPLES TO THE AIDS AND CANCER SPECIMEN RESOURCE (ACSR)

This section is about optional studies you can choose to take part in. You can still take part in the main study even if you say "no" to this study.

Researchers are trying to learn more about cancer, HIV/AIDS, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part in this study, the study doctor for the main study would like to collect these specimen types:

- **Donation of left over study specimens to the ACSR for all study participants:** If you choose to take part in this clinical trial, the researchers would like to collect unused blood and biopsy tissue left over after the study is done. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking." The Biobank is being run by the **AIDS and Cancer Specimen Resource** and is supported by the National Cancer Institute.

What is involved?

If you agree to take part, here is what will happen next:

1) **Donation of left over study specimens to the ACSR for all study participants:** Your sample and some related health information will be stored in the ACSR Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record may be updated after the study is over.
2) Qualified researchers can submit a request to use the materials stored in the ACSR. A science committee at the ACSR will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
3) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
4) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

What are the possible risks?

1) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
2) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
3) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

How will information about me be kept private?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. The ACSR and AMC staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom the ACSR and the AMC send your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

What are the possible benefits?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments?

There are no additional costs to you or your insurance for these optional studies. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What if I change my mind?

If you decide you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

What if I have more questions?

If you have questions about the use of your samples for research, contact the study doctor, _____, *(insert name of study doctor for main trial)*, at _____ *(insert telephone number of study doctor for main trial)*.

Please check your answer to show whether or not you would like to take part in each option:

Samples for future research studies:

My samples and related information may be donated to ACSR Biobank for use in future health research.

☐ YES ☐ NO

My donated samples and related information may undergo genetic testing to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.

☐ YES ☐ NO

This is the end of the section about optional studies.

MY SIGNATURE AGREEING TO TAKE PART IN THE MAIN STUDY

I have read the consent form or had it read to me and understand the information above. I have discussed it with the study doctor and my questions have been answered I understand that I will be given a signed and dated copy of this consent form. I agree to take part in the main study and any additional studies where I circled 'yes.' My signature below indicates that I understand my rights and want to take part in this study as a research participant.

Participant's signature: _____

Date of signature: _____

Signature of person(s) conducting the informed consent discussion: _____

Date of signature: _____

ATTACHMENT 1: AMC CERTIFICATE OF CONFIDENTIALITY STATEMENT

The NIH has given the AMC a Certificate of Confidentiality. The Certificate does not mean that the NIH or the U.S. Government recommend that you take part in this study. This Certificate helps us keep your health information private.

Your records for this study will have information that may identify you. This Certificate lets us turn down legal demands for your study records. We can use the Certificate to turn down demands for records from a U.S. court. The Certificate can be used in any federal, state, or local legal matters. We will use the Certificate to turn down any demands for your study records. The cases where we cannot use the Certificate are explained below.

We cannot use the Certificate to turn down a demand from the U.S. Government for study records. This applies to audits or reviews of the AMC. This also applies to study records that we have to report to the FDA.

The Certificate does not stop you or your family members from sharing your health information. It does not stop you from talking about taking part in this study. You may give written permission for an insurer, employer, or other person to get copies of your study records. If you give permission, we cannot use the Certificate to say no to a request for your study records.

ATTACHMENT 2: STUDY CALENDAR

CYCLE 1	
Day	**What you do**
Within 4 weeks before starting the study (unless specified)	• Get routine blood tests. • Get a Computed Tomography (CT) scans (an imaging test to measure your cancer. You may also have a scan called a PET/CT scan or another imaging test called a MRI • Get a bone marrow biopsy (within 6 weeks). • Get a lumbar puncture. • Get an echocardiogram or MUGA and EKG. • Get insertion of a Port-A-Cath or central venous catheter as decided by your doctor. • Review your medical history, allergies and drugs you are taking with your doctor. • Get a physical examination, which includes measurement of your weight, height, blood pressure, heart and breathing rate, and temperature. * If needed, switch to an antiretroviral treatment regimen that is safe to use with the study drug ibrutinib. Other medications may need to be changed. * Answer questions about how much your lymphoma affects your daily life and ability to do such things as bathing, dressing, and taking care of yourself. * Answer questions about risks related to getting HIV * Submit tissue block and pathology slides for central review and further research studies
Before starting study	• You and your doctor may decide to have the chemotherapy in the hospital and you will check-in to the evening before or the day of starting the study. This chemotherapy may also be given as an outpatient on a case-to-case basis. • We will take routine blood tests. • Pregnancy test if you are female and can have a baby. • We will take some blood samples for research purposes. The blood samples will test for inflammatory markers, as well as a specific virus levels in the blood (total 15ml, or about 3 teaspoons of blood). We will also collect blood to see if there is any tumor DNA in your blood. This blood draw will require an additional 30 mL of blood (about 1.5 tablespoons). These samples will be tested to see whether ibrutinib changes the amount of HIV found in specific cells. If you do not agree to provide this sample, you may still participate in the study.

CYCLE 1	
Day	**What you do**
Days 1 to 21	• You must record in a drug diary when you take oral ibrutinib and prednisone or prednisone alone.
Day 1	• Begin taking prednisone once a day for 5 days. • We will take some blood samples for research purposes. These samples will be tested to see whether ibrutinib changes the amount of specific proteins found in specific blood cells. Before receiving any treatment, we will collect 25ml, or about 5 teaspoons, of blood. • You will begin taking ibrutinib once a day. It should be taken at the same time every day. • Start chemotherapy. Chemotherapy will be given through a vein over 96 hours (R-EPOCH). • After starting chemotherapy and ibrutinib, we will take some blood samples to check for levels of ibrutinib, chemotherapy, and proteins affected ibrutinib. This blood draw will require 20 mL of blood (4 teaspoons). • Take medicine to prevent a kind of pneumonia called *Pneumocystis jiroveci* pneumonia that commonly occurs in people with weak immune systems. This medicine will be taken as long as you are receiving treatment and then for as long as your doctor feels it is necessary. • Other medicines will be given to you to prevent side effects from the treatment. Some of these medicines will be given only during Cycle 1 and others will need to be taken the entire time you are receiving treatment. Your doctor will decide which medicines you need to take and will tell you exactly how and when to take them. • You may need to receive chemotherapy given directly into the central nervous system (CNS) as a preventive treatment. This is done to kill small numbers of cancer cells that may be in the brain and spinal cord. The drugs are injected into the fluid surrounding the brain and spinal cord and is called intrathecal chemotherapy. Your study doctor will talk with you about whether or not you will need this and how often.
Day 2-3	• Blood samples will be drawn for research purposes during the first cycle of chemotherapy in order to measure the levels of chemotherapy in your bloodstream. This will result in a total of 30 ml (about 2 tablespoons) of blood being drawn over 2 days.

CYCLE 1	
Day	**What you do**
Day 5 or 6	• You will need to take medicines to help increase your white blood cell number. White blood cells are important to prevent or fight infections. Your study doctor will discuss the specific treatments with you. This type of medicine is given by injection under the skin to try to prevent the lowering of white blood cells which commonly occurs with chemotherapy. The clinic staff will teach you how to give yourself the injections.
Day 8	• Before you take your eighth dose (on day 8) of ibrutinib, 5 ml (about 1 teaspoon) of blood will be obtained to test for the level of ibrutinib. If there are more than expected drug side effects from ibrutinib during days 1-7, additional blood may be drawn to determine the level of ibrutinib (total 35 ml, less than 3 tablespoons).
Day 9	• Get routine blood test (CBC). • You will take medicine to prevent infection. Your study doctor will tell you which medicine to take and for how long.
Day 12	• Get routine blood test.
Day 15	• Get routine blood test.
Day 22	• Get routine blood test.
Day 22	• Return to your doctor's office for your next exam and to begin the next cycle of treatment. Bring your medication diary and pill bottles with you to each appointment.

FUTURE CYCLES	
Day	**What you do**
Days 1-22	• Keep taking oral medications and doing the injections as prescribed by your doctor if you have no bad side effects and the cancer is not getting worse. Call the doctor at _____ *[insert phone number]* if you do not know what to do. • Get routine blood tests on days 1 and 15 (more if your doctor tells you to). • Get routine blood tests and exams every cycle (more if your doctor tells you to). • Get routine PET/CT, CT scans, or MRIs after cycles 4 and 6 (more if your doctor tells you to). • You must record in a drug diary when you take oral ibrutinib and prednisone or prednisone alone.

FUTURE CYCLES	
Day	**What you do**
Day 22	• Return to your doctor's office at for your next exam and to begin the next cycle of treatment. Bring your medication diary and pill bottles with you to each appointment.
After Cycle 1	• If you were not taking antiretroviral therapy to treat your HIV infection, then you will start taking it now. Your doctor will tell you what medicines to take and how to take them.
After Cycle 2	• Get blood tests to measure your HIV viral load, CD4 and CD8 cells, other viruses and quantitative immunoglobulins. • We will take some blood samples for research purposes. The blood samples will test for inflammatory markers and tumor DNA. This requires 35 ml of blood, about 2 tablespoons.
After Cycle 4	• Get blood tests to measure your other viruses, if needed. • Scans as ordered by your physician (CT scans or PET/CT scan) • We will take some blood samples for research purposes. The blood samples will test for tumor DNA. This requires 30 ml of blood, about 1.5 teaspoons.

AFTER TREATMENT	
Day	**What you do**
4-8 weeks after the beginning of cycle 6, or within a month if stopping treatment early	• Review any side effects from therapy. • Review your medical history, allergies and drugs you are taking with your doctor. • Get a physical examination, which includes measurement of your weight, blood pressure, heart and breathing rate and temperature. • Routine blood work. • Get blood tests to measure your HIV viral load, CD4 and CD8 cells, other viruses and quantitative immunoglobulins. • Get blood samples for research (4 weeks after treatment). The blood samples will test for inflammatory markers, tumor DNA, as well as a specific virus levels in the blood (total 30 ml, or about 1.5 tablespoons of blood). • Get PET/CT, CT scans, or MRIs after cycles 4 and 6 (more if your doctor tells you to).
6 and 12 months after stopping treatment	• Blood samples for research. We will be again looking at inflammatory markers. Each blood draw will require 5ml of blood (about 1 teaspoon).