Informed Consent Form

WINSHIP4388-18: A Phase I/II Study of Gemcitabine, Bendamustine, and Nivolumab in Patients with Relapsed or Refractory Classical Hodgkin Lymphoma

NCT Number: NCT03739619

Document IRB Approval Date: 09/01/2021

You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University and Saint Joseph's Hospital
Consent to be a Research Subject / HIPAA Authorization

Title: Winship 4388-18: A Phase I/II Study of Gemcitabine, Bendamustine, and Nivolumab in Patients with Relapsed or Refractory Classical Hodgkin Lymphoma

Principal Investigator: Jonathon B. Cohen, MD MS

Investigator-Sponsor: Jonathon B. Cohen, MD MS

Study-Supporter: Bristol Myers Squibb, Inc. (BMS)

Introduction
You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:
- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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.

What is the purpose of this study?
The purpose of this study is to learn about the safety of the combination of gemcitabine, bendamustine, and nivolumab in patients with Hodgkin lymphoma that has returned after at least one treatment. We are also interested in learning about the effectiveness of this treatment.

What will I be asked to do?

If you participate in this study, you will complete a series of tests to determine if you are eligible to receive the study treatment. This will include a test of your lung function, blood oxygen levels and other blood tests. We will also complete a PET/CT or other scan through radiology to determine whether your lymphoma is active. Your physician and/or team will provide you with the results of these tests and will tell you whether you are able to receive treatment on the trial.

If you are eligible to participate, you will receive three drugs administered every 3 weeks for a total of 6 cycles. On the first day of each cycle, you will receive gemcitabine, bendamustine, and nivolumab. On day 2 of each cycle, you will receive only bendamustuine. You will receive an injection on days 3 or 4 after each cycle, called pegfilgrastim (neulasta), which will help your white blood cell count (your immune system) recover between treatments. You may choose to receive neulasta through an automated device placed on your arm after completing treatment. This can be decided on the day of each treatment. This treatment will repeat for up to 6 times.

After completing 6 cycles, or if your treatment team feels you are no longer able to take all three drugs, you will move to the maintenance phase where you will receive one infusion of nivolumab every 4 weeks for up to 2 years. You will not receive any additional chemotherapy during this time.

You will also have scans performed by your physician from time to time to see how the treatment is working. You will also have clinic visits throughout the study to ensure that you are tolerating the treatment. These will include lab evaluations, physical examinations, and questions about how you are feeling. If you are not feeling well or having other side effects related to the treatment, your study team may decide to lower your dose, delay your dose, or stop one or more drugs.

NOTE: There is no placebo or randomization in this study. All enrolled patients will receive all three drugs.

We plan to enroll up to 54 patients on this trial, 30 patients from Emory.

How will my medicine be provided?
The medicine that you will take will be dispensed by the pharmacy and delivered to the principal investigator or study team member. The principal investigator or health care providers on his/her research team will provide the medicine to you. If you have questions about the medicine, you should ask the principal investigator or study nurse. You may also call the pharmacy if you have questions about the medicine. The number for the pharmacy is included on your medicine package.

If you participate in this study, nivolumab will be provided to you at no charge. The costs of gemcitabine and bendamustine will be your responsibility and these charges will be billed to your insurance company.

Who owns my study information?
If you join this study, you will be donating your study information. You will not receive any compensation if your information are used to make a new product. If you withdraw from the study, data that were already collected may be still be used for this study. You may withdraw from the study at any time for any reason. However, if you choose to stop study therapy in the middle of a cycle, your doctor may ask you to return to clinic for a few weeks to make sure you have recovered from any side effects from the treatment. In this case, this follow-up would not be part of the study.

What are the possible risks and discomforts?
There may be side effects from the study drugs or procedures that are not known at this time. All three drugs utilized in this study are approved by the US Food and Drug Administration.

The most common risks and discomforts expected in this study are:

Nivolumab (Opdivo):

Fatigue (15%)
Diarrhea (9%)
Itching (8%)

Nausea (8%)
Rash (6%)
Fever (3%)
Lung injury/ difficulty breathing (2-3%)
Decreased appetite (6%)
Vomiting (3%)
Constipation (2%)
Headache (2%)
Muscle or joint aches (2-4%)
Colitis (1%)
Liver enzyme elevation (2-3%)
Increase amylase or lipase (pancreas enzyme; 1-2%)
Kidney toxicity (1%)

Other rare toxicities including endocrine (hormone) disorders and changes in electrolytes such as sodium and potassium.

Gemcitabine:
Anemia (low blood count; 68%)
Low neutrophil count (63%)
Low platelet count (24%)
Abnormal liver enzymes (67-68%)
Kidney toxicity (up to 45%)
Nausea/vomiting (69%)
Fever (41%)
Rash (30%)
Shortness of breath (23%)
Diarrhea (19%)
Bleeding (17%)
Infection (16%)
Hair loss (15%)
Mouth sores (11%)
Fatigue/tiredness (11%)
Numbness/tingling (10%)

Bendamustine:
Common blood related toxicities occurring > 15% of the time including low lymphocyte count, low red blood cells (anemia), low white blood cells, low platelet count, and low neutrophil count.

Common non-blood related toxicities occurring > 15% of the time include nausea, fatigue, vomiting, diarrhea, fever, constipation, poor appetite, cough, headache, decreased weight, shortness of breath, rash, and mouth soreness.

If you are a woman: to protect against possible side effects of the study drug, women who are pregnant or nursing a child may not take part in this study. If you become pregnant, there may be risks to you, the embryo, or fetus. These risks are not yet known. If you are a woman of childbearing ability, you must use an adequate birth control method or abstinence for the duration of the stud. If you think that you have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

If you are a man: the effect of the study drug on sperm is not known. To protect against possible side effects, if you are a man you should not get a sexual partner pregnant while taking the study drug and for two months after the last dose. You and the study doctor should agree on an adequate method of birth control to use throughout the study.

If you will be taking the study drug home, keep it out of the reach of children or anyone else who may not be able to read or understand the label. Do not let anyone else take the study drug besides you.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Radiation Safety Risks

You will be exposed to radiation from nuclear medicine and CT scans. These procedures are necessary for your medical care and will occur even if you do not participate in this study. The radiation dose estimate that you will receive is equal to or less than the radiation exposure allowed to be received by a radiation worker for 4 years. The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. Although the risk from radiation is cumulative it is not expected to adversely affect your condition or treatment. The Emory University Radiation Safety Committee has reviewed and approved the use of radiation in this research study.

Contrast Agents

Your PET-CT, CT or MRI procedure may require the use of a contrast agent, which is a substance that helps the radiologist interpret the images. The contrast agent will be injected by either a hand-held needle or a machine that does the injection. Most contrast agents stay in your body for only a few minutes, but some of them can remain for a few hours or days without any harm to you or anyone near you. Contrast agents are generally quite safe, but any injection involves some risks. The injection could harm a nerve, artery or vein, or cause infection. The contrast agent could affect kidney function or cause an allergic reaction, though these outcomes are rare. The contrast agent could also leak from your veins a little, causing swelling and discomfort, which is typically treated with ice packs.

PET-CT

For your PET-CT scan, a small amount of radioactive material will be injected by either a hand-held needle or a machine. Such injections are generally quite safe, but any injection involves some risks. The injection could harm a nerve, artery or vein, or cause infection. The radioactive material could also leak from your veins a little, causing swelling and discomfort. After injection and a waiting period for the drug to circulate within your body, you will be asked to lie very still for several minutes while the scan takes place.

Will I benefit directly from the study?

This study is not designed to benefit you directly, but it is being offered to you due to the fact that we think these drugs will be safe and effective for patients like you. Your lymphoma may improve while you are in this study but it may not, and it may even get worse. This study is designed to learn more about relapsed/refractory Hodgkin lymphoma and the safety of this combination of treatment. The study results may be used to help others in the future.

Will I be compensated for my time and effort?

You will not be offered compensation for being in this study.

What are my other options?

If you decide not to enter this study, there is care available to you outside of this research study. This would include common chemotherapy regimens or possible nivolumab by itself among others. The study doctor will discuss these with you. You do not have to be in this study to be treated for Hodgkin lymphoma.

Taking part in this study, however, may make you unable to participate in some other research studies, if they exclude people who have taken certain treatments. You should discuss this with the researchers if you have concerns. You may wish to research other study options at websites like clinicaltrials.gov and ResearchMatch.org.

How will you protect my private information that you collect in this study?
Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Storing and Sharing your Information
De-identified data from this study, may be shared with the research community at large to advance science and health. Data from this study may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Medical Record
If you have been an Emory Healthcare and Saint Joseph's Hospital patient before, then you already have an Emory Healthcare and Saint Joseph's Hospital medical record. If you have never been an Emory Healthcare and Saint Joseph's Hospital patient, you do not have one. An Emory Healthcare and Saint Joseph's Hospital medical record will be made for you if an Emory and Saint Joseph's Hospital provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory Healthcare and Saint Joseph's Hospital medical record you have now or any time during the study.

Emory Healthcare and Saint Joseph's Hospital may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory Healthcare and Saint Joseph's Hospital medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

Tests and procedures done at non-Emory and Saint Joseph's Hospital places may not become part of your Emory and Saint Joseph's Hospital medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury
If you believe you have become ill or injured from this research, you should contact Dr. Jonathon Cohen at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

If you get ill or injured from being in the study, Emory and Saint Joseph's Hospital will help you get medical treatment. Neither Emory, Saint Joseph's nor the study supporter will pay for your medical treatment. Your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurance does not pay, then you will have to pay these costs.

Emory, Saint Joseph's and the study supporter have not, however, set aside any money to pay you if you are injured as a result of being in this study or to pay for this medical treatment. For Emory and Saint Joseph's, the only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory or Saint Joseph's employee. "Negligence" is the failure to follow a standard duty of care. You do not give up any legal rights you may have by being in this study, including any right to bring a claim for negligence.

Costs

The study supporter will pay for certain items and services that you may receive if you take part in this study.

You will have to pay for the items or services for which the study supporter does not pay. The sponsor will not pay for your regular medical care. If you have insurance, Emory will submit claims to your insurance for items and services that the sponsor does not cover. Emory and Saint Joseph's Hospital will send in only those claims for items and services that it reasonably believes your insurance will pay and that the sponsor has not paid.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory and Saint Joseph's Hospital and the sponsor will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory and Saint Joseph's Hospital will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

Withdrawal from the Study

You have the right to leave a study at any time without penalty.

For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the study.

PHI that Will be Used/Disclosed:

The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory and Saint Joseph's Hospital may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- Dr. Cohen is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory and Saint Joseph's Hospital offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Office for Human Research Protections; Food and Drug Administration.
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.

- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at: 1365 Clifton Road, NE, Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information

Contact Dr. Jonathon Cohen at [redacted]:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at [redacted]:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent and Authorization

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in this research study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____

Name of Subject

_____ _____ _____ **am / pm**

Signature of Subject (18 or older and able to consent) **Date** **Time (please circle)**

_____ _____ _____ **am / pm**

Signature of Legally Authorized Representative with authority for research decisions **Date** **Time (please circle)**

_____

Authority of Legally Authorized Representative or Relationship to Subject

TO BE FILLED OUT BY STUDY TEAM ONLY

_____

Name of Person Conducting Informed Consent Discussion

_____ _____ _____ **am / pm**

Signature of Person Conducting Informed Consent Discussion **Date** **Time (please circle)**