Study Title for Participants: A Study of the Combination of Immunotherapy and Targeted Chemotherapy in Relapsed Hodgkin Lymphoma

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: E4412: A Phase I Study with an Expansion Cohort/Randomized Phase II Study of the Combinations of Ipilimumab, Nivolumab and Brentuximab Vedotin in Patients with Relapsed/Refractory Hodgkin Lymphoma (NCT01896999)

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer.

We are asking you to take part in this research study because you have classical Hodgkin lymphoma which has relapsed after at least 2 kinds of standard chemotherapy, or has not shrunk in response to standard chemotherapy.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is This Study Being Done?

This study is being done to answer the following question:

What effects, good and/or bad, do two different combinations of multiple drugs: brentuximab vedotin, with either one or two immune activating drugs: ipilimumab, and nivolumab, have

on you and your relapsed or refractory Hodgkin lymphoma? Your disease is considered relapsed if it has come back after one or more chemotherapy treatments. Your disease is considered refractory if it did not respond to your previous therapy.

We are doing this study because we want to find out which combination approach is better or worse for your type of relapsed or refractory Hodgkin's Lymphoma.

What is the usual approach to my relapsed/refractory Hodgkin Lymphoma?

The usual approach for patients who are not in a study is treatment with standard chemotherapy, including some drugs that are Food and Drug Administration (FDA)-approved. If you have relapsed after at least 2 previous treatments, the usual approach may include either brentuximab vedotin given alone or nivolumab given alone. If a treatment gets rid of all your lymphoma and puts you in a remission, stem cell transplant may be used.

Sometimes, combinations of these treatments are used. Your doctor can explain which treatment may be best for you.

What are my choices if I decide not to take part in this study?

- You may choose to have the usual approach described above.
- You may choose to take part in a different research study, if one is available.
- You may choose not to be treated for cancer.
- You may choose to only get comfort care to help relieve your symptoms and not get treated for your cancer.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will either get 2 study drugs for up to 2 years or you will get 3 study drugs for up to 2 years

After you finish your study treatment, your doctor will continue to follow your condition for 5 years and watch you for side effects. Follow up include clinic visits every 3 months for the first year after treatment ends, every 4 months for the second year after treatment ends, and every 6 months for the rest of follow up.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

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

There is also a risk that you could have side effects from the study drugs. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

Some of the most common side effects that the study doctors know about are:

- Common side effects:
  - Rash
  - Itching
  - Diarrhea
  - Damage to the thyroid
  - Elevation of liver enzymes (liver inflammation)
  - Unknown risks exist with novel therapies and immunotherapies
- Rare, but serious side effects:
  - Damage to the lungs

There may be some risks that the study doctors do not yet know about.

Benefits

There is evidence that these drugs combinations are effective in shrinking your type of cancer. It is not possible to know now if the study drugs will extend your time without disease compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. This may mean slowly stopping the study drugs so that there is not a sudden unsafe change, risk to your health, etc. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your 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.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), or study sponsor (National Cancer Institute (NCI)). The study sponsor is the organization who oversees the study.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to compare the combination of brentuximab vedotin and nivolumab to the combination of brentuximab vedotin, nivolumab, and ipilimumab. Both brentuximab vedotin and nivolumab are FDA-approved as single drugs for patients who have relapsed or refractory Hodgkin's lymphoma. The combination of these drugs together, and with ipilimumab are not FDA-approved, so this therapy is considered an experimental treatment. The addition of ipilimumab to brentuximab vedotin and nivolumab may or may not shrink your cancer and keep it away for longer than the combination of brentuximab and nivolumab. It may also cause more side effects. Side effects for both treatments are are described in the risks section below.

This study will help the study doctors find out if this combination approach is the same or better than the usual approach of using these drugs alone. To decide if it is better, the study doctors will be looking to see if the study drugs shrink patients' cancer using both treatments, and which combination shrinks Hodgkin lymphoma better with reasonable side effects. There will be about 120 people taking part in this study.

What are the study groups?

This study has 2 study groups.

- **Group 1 (Arm K)**

  If you are in this group, you will get brentuximab vedotin through a vein in the arm on day 1 of each cycle for cycles 1-16 and nivolumab through a vein in the arm on day 1 of each cycle for cycles 1-34. Each cycle lasts 21 days. This study has 34 cycles.

  There will be about 60 people in this group.

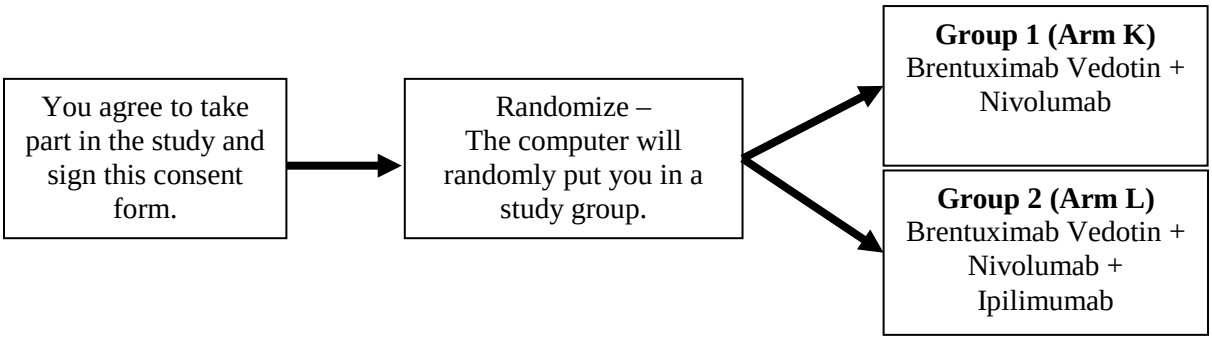
- **Group 2 (Arm L)**

  If you are in this group, you will get brentuximab vedotin through a vein in the arm on day 1 of each cycle for cycles 1-16, nivolumab through a vein in the arm on day 1 of each cycle for cycles 1-34, and ipilimumab through a vein the arm on day 1 every 4 cycles. Each cycle lasts 21 days. This study has 34 cycles.

  There will be about 60 people in this group.

We will use a computer to assign you to one of the study groups. This process is called "randomization." It means that your doctor will not choose and you cannot choose which study group you are in. You will be put into a group by chance. You will have an equal chance of being in Group 1 or Group 2.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Listed below are exams, tests, and procedures that need to be done as part of this study to monitor your safety and health, but may not be included in the usual care or may be done more often because you are in this study. We will use them to carefully follow the effects of the study treatment, including preventing and managing side effects.

- Pregnancy test. If you receive ipilimumab and you are a woman of childbearing potential, you will also be required to have a blood or urine pregnancy test prior to each treatment with ipilimumab. The blood or urine pregnancy test must be negative within 24 hours before every ipilimumab treatment.
- During the first cycle of treatment, you will be evaluated for side effects on a weekly basis.

- Physical examination and/or questions to evaluate for neuropathy every week during cycle 1 and then on the first day of every cycle of treatment.
- Follow-up tests of lung function. These tests measure how well your lungs work and measures how well you are able to breathe and how effective your lungs are at circulating oxygen to the other parts of your body. This test will be done before starting treatment and it may be repeated if the first test indicates any signs of dysfunction.
- Samples of your original tumor tissue and relapse tumor tissue (cancer that has returned) will be sent to be examined by a central reviewer. This review will be used to confirm the results of the local institutional review. This review will not affect your eligibility to participate in this trial. The results of this review will not be returned to the site and will not impact patient care.

What risks can I expect from taking part in this study?

General Risks

If you choose to take part in this study, there is a risk that the study drug combinations may not be as good as other study drug combinations for your cancer 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 study drugs used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 5 months (for female patients) or 7 months (for male patients who are sexually active with women of child bearing potential) after you have completed the study. This will be discussed later under "What are my responsibilities in this study?"

This study will use samples of your tissue. Generally, your hospital will keep some of your tissue. This tissue may be used to help treat your cancer in the future. Because this study will need to use some of this tissue, there is a small risk that it could be used up.

Side Effect Risks

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 let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study drugs.

Here are important things to know about side effects:

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

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.
- Your study doctor may adjust the study drugs to try to reduce side effects.

This study is looking at a combination of the usual drugs used to treat this type of cancer plus a study drug. This different combination of drugs may increase your side effects or may cause new side effects.

Drug Risks

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

Study Group 1 (Arm K) and Group 2 (Arm L) – Possible side effects of brentuximab vedotin and nivolumab are listed in the tables below. These drugs are part of the usual approach for treating this type of cancer:

Risks and side effects related to the brentuximab vedotin (SGN-35) include those which are:

(Table Version Date: February 13, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving SGN-35 (brentuximab vedotin), more than 20 and up to 100 may have:
• Diarrhea, nausea • Tiredness • Numbness, tingling or pain of the arms and legs

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving SGN-35 (brentuximab vedotin), from 4 to 20 may have:

- Anemia which may require blood transfusion
- Pain
- Constipation, vomiting
- Chills, fever
- Swelling of arms, legs
- Liver damage which may cause yellowing of the eyes and skin
- Infection, especially when white blood cell count is low
- Cold symptoms such as stuffy nose, sneezing, sore throat
- Bruising, bleeding
- Weight loss, loss of appetite
- Dizziness, headache
- Feeling of "pins and needles" in arms and legs
- Muscle weakness
- Worry
- Difficulty sleeping
- Cough, shortness of breath
- Hair loss, itching, rash
- Increased sweating

RARE, AND SERIOUS

In 100 people receiving SGN-35 (brentuximab vedotin), 3 or fewer may have:

- Damage to the pancreas which may cause belly pain and hospitalization
- Swelling of the bowels
- Bleeding from multiple sites
- Internal bleeding which may cause black tarry stool, blood in vomit
- Blockage of internal organs which may cause difficulty swallowing, inability to pass stool
- A tear or hole in internal organs that may require surgery
- Sores in the throat
- Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat
- Kidney damage which may require dialysis

RARE, AND SERIOUS In 100 people receiving SGN-35 (brentuximab vedotin), 3 or fewer may have:
• 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

Risks and side effects related to the nivolumab (BMS-936558) include those which are:

(Table Version Date: June 18, 2018)

Special precautions
Side effects of BMS-936558 (nivolumab, MDX-1106) may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when BMS-936558 (nivolumab, MDX-1106) is used in combination with ipilimumab. **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse**

COMMON, SOME MAY BE SERIOUS In 100 people receiving BMS-936558, more than 20 and up to 100 may have:
• Tiredness

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving BMS-936558, from 4 to 20 may have:
• Anemia which may require blood transfusion • Swelling and redness of the eye • Pain • Diarrhea, nausea • Dry mouth • Fever • Swelling and redness at the site of the medication injection • Bruising, bleeding • Pain or swelling of the joints • Loss of appetite • Reaction during or following a drug infusion which may cause fever, chills, rash BMS-936558 (nivolumab, MDX-1106) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving BMS-936558, from 4 to 20 may have:

- Lung problems (pneumonitis and pleural effusion). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.
- Skin: itching; rash, blisters including inside the mouth; loss of skin pigment
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly
- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior; decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting

RARE, AND SERIOUS

In 100 people receiving BMS-936558, 3 or fewer may have:

- Dry eyes
- Sores in the mouth which may cause difficulty swallowing

BMS-936558 may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to:

- Visual disturbances which may cause double vision, blurred vision, or loss of vision with a chance of blindness
- A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
- Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body.
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine
- Swelling of the brain (meningitis/encephalitis) which may cause: headache, stiff neck, confusion, sleepiness, seizures or injury to the brain which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome)
- Problem of the nerves that can cause paralysis. Signs and symptoms may include:

RARE, AND SERIOUS In 100 people receiving BMS-936558, 3 or fewer may have:
numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut damage), and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received BMS-936558 therapy, since the risk and severity of transplant-associated complications may be increased.

Study Group 2 (Arm L) - In addition to side effects listed above, people who are in Group 2 may also have some side effects from ipilimumab. These side effects are listed below.

Risks and side effects related to the ipilimumab (MDX-010) include those which are:

(Table Version Date: March 29, 2019)

Special precautions Side effects of ipilimumab (MDX-010) may happen anytime during treatment or even after your treatment has ended. Some of these problems may happen more often when ipilimumab (MDX-010) is used in combination with BMS-936558 (nivolumab). **Call or see your healthcare provider right away if you develop any problems listed below or the symptoms get worse.**

COMMON, SOME MAY BE SERIOUS In 100 people receiving ipilimumab (MDX-010), more than 20 and up to 100 may have:
• Diarrhea, nausea • Tiredness Ipilimumab (MDX-010) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • Skin: itching; rash, blisters including inside the mouth (can be severe); hives

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving ipilimumab (MDX-010), from 4 to 20 may have:
• Abnormal heartbeat • Hearing loss

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving ipilimumab (MDX-010), from 4 to 20 may have:

- Swelling and redness of the eye
- Pain
- Difficulty swallowing, eating
- Constipation, vomiting
- Weight loss, loss of appetite
- Fever
- Dehydration
- Pain or swelling of the joints
- Reaction during or following a drug infusion which may cause fever, chills, rash
- Low blood pressure which may cause feeling faint

Ipilimumab (MDX-010) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to

- Lung problems (pneumonitis). Symptoms may include: new or worsening cough, chest pain, shortness of breath.
- Intestinal problems (colitis) that can rarely lead to tears or holes in your intestine. Signs and symptoms of colitis may include: diarrhea or increase in bowel movements, blood in your stools or dark, tarry, sticky stools, severe belly pain or tenderness.
- Kidney problems, including nephritis and kidney failure requiring dialysis. Signs of kidney problems may include: decrease in the amount of urine, blood in your urine, ankle swelling.
- Problem of the muscle, including swelling, which can cause muscle pain and severe muscle weakness sometimes with dark urine.
- Problem of the nerves that can cause paralysis. Signs and symptoms may include: numbness, tingling of hands and feet; weakness of the arms, legs and facial muscle movement.
- Liver problems (hepatitis) which can cause liver failure. Signs and symptoms of hepatitis may include: yellowing of your skin or the whites of your eyes, severe nausea or vomiting; drowsiness; pain in the right upper belly.
- Hormone gland problems (especially the thyroid, pituitary and adrenal glands, and pancreas). Signs and symptoms may include: headaches that will not go away or unusual headaches, extreme tiredness or changes in mood or behavior decreased sex drive; weight loss or weight gain; excessive thirst or urine; dizziness or fainting

RARE, AND SERIOUS In 100 people receiving ipilimumab (MDX-010), 3 or fewer may have:
• Bleeding • Blockage of the bowels which may cause constipation • Fluid around heart • Severe illness with multiorgan failure • Confusion Ipilimumab (MDX-010) may cause your immune system to attack normal organs and cause side effects in many parts of the body. These problems may include but are not limited to: • A condition with high blood sugar which leads to tiredness, frequent urination, excessive thirst, headache, nausea and vomiting, and can result in coma • Heart problems including swelling and heart failure. Symptoms and signs of heart problem may include: Shortness of breath, swelling of the ankle and body. • Complications associated with stem cell transplant using donor stem cells (allogeneic stem cell transplant). These complications are caused by attack of donor cells on the host organs (inducing liver, skin and gut), and can lead to death. If you are considering an allogeneic stem transplant after participating in this study, please tell your doctor that you have received ipilimumab therapy, since the risk and severity of transplant-associated complications may be increased • Swelling of the brain (meningitis/encephalitis), which may cause: headache, confusion, sleepiness, seizures, and stiff neck

Getting medical treatment right away may keep these problems from becoming more serious.

While receiving treatment with ipilimumab, you may be at risk of side effects that occur during or shortly after the infusion (within 24 hours), or later after the infusion has finished. In isolated cases, some ipilimumab-related side effects may occur many months after the last dose of ipilimumab.

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.

Imaging Study Risks

Procedures such as PET/CT scans will be used during this research study to see how you are doing. All of the scans are what you would normally undergo with your disease. The cumulative radiation exposure from these tests is considered small and is not likely to adversely affect you or your disease. However, the effects of radiation add up over a lifetime. It is possible that having several of these tests may add to your risk of injury or disease.

When deciding to enter this study, think about your past and future contact with radiation. Examples of contact with radiation include x-rays taken for any reason or radiation therapy for cancer treatment.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:

- Keep your study appointments.
- Tell your doctor about:
  - all medications and supplements you are taking
  - any side effects
  - any doctors' visits or hospital stays outside of this study
  - if you have been or are currently in another research study.
- If you plan to have a routine vaccination, such as the seasonal influenza vaccination, it should be given at least 2 weeks before starting study treatment.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 5 months (for female patients) or 7 months (for male patients who are sexually active with women of child bearing potential) after your last dose of study drug.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:

- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the costs of getting the brentuximab vedotin ready and giving it to you.
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You or your insurance provider will not have to pay to get, prepare, or administer the ipilimumab or nivolumab while you take part in this study.

You or your insurance provider will not have to pay for the research tumor biopsies if they are considered not part of your normal cancer care.

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

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

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. Contact information for your study doctor is listed on the consent cover page. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

No funds have been set aside to compensate you in the event of injury.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

The ECOG-ACRIN Cancer Research Group is conducting this study. ECOG-ACRIN is a cancer research group that conducts studies for the National Cancer Institute. Your doctor is a member of ECOG-ACRIN or another group that is participating in this study.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- Montana Cancer Consortium
- The study sponsor and any company supporting the study agents now or in the future.
- The IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The FDA and the groups it works with to review research.
- The NCI and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research including the Imaging and Radiation Oncology Core.

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

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.

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 information for your study doctor is listed on the consent cover page.

For questions about your rights while in this study, you may contact the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

Optional studies that you can choose to take part in.

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading this optional study hope the results will help other people with cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in this optional study is your choice. You can still take part in the main study even if you say "no" to this study. There is no penalty for saying "no." You and your insurance company will not be billed for this optional study. If you sign up for, but cannot complete this study for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for (*the following study / each of the following studies*).

Optional sample collection for known laboratory studies and unknown future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies

If you choose to take part in this optional study, we are requesting that you allow the collection and submission of additional tumor tissue biopsies, blood, and stool samples for research. These studies will be performed to understand the differences in the way the body handles certain drugs and how your disease responds to the treatment.

Unknown future studies

If you choose to take part in this optional study, we are requesting that you allow the storage of your tumor tissue biopsies, blood, and stool samples leftover after the research studies for future research projects. The research that may be done is unknown at this time. Storing samples for future studies is called "Bio-banking." The biobank is being run by ECOG-ACRIN and is supported by the National Cancer Institute (NCI). Also, any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use.

We don't know what research may be done in the future using your samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- Future research studies may include sequencing of all or part of your DNA called genomic sequencing. All your genetic information makes up your genome. Genomic sequencing is a test that records all or part of the pieces of DNA that are in your genes, piece by piece. This is usually done to look for changes in your genome that may cause health problems.
- You will not get reports or other information about any research that is done using your samples.

The samples will be sent to laboratories where tests will be performed. Researchers will perform these tests in order to understand the differences in the way the body handles certain drugs and how your disease responds to the treatment. These studies may help explain why some people respond to a treatment and why others do not. In addition, the researchers hope to understand more about lymphoma and why certain lymphomas are more resistant to treatment while others are not.

What is involved in this optional sample collection?

1. If you agree to take part, here is what will happen next:
   a. About four (4) tablespoons of blood will be collected from a vein in your arm before you begin treatment, before cycle two (2) of treatment, at the first restaging PET/CT scan (which will follow cycle five [5]), every three [3] months during treatment for up to two (2) years, any time you present with grade three [3] or greater toxicity, and after completion of treatment or if you go off treatment. The blood will usually be collected at the same time as the blood collected for your clinical tests to monitor your health. In most cases, an additional needle stick will not be required to collect blood.
   b. Tumor tissue leftover after the central review (described above) will be sent to the Biobank for research. Additional tumor tissue from procedures performed as part of your care while you are participating in this study may also be sent to be used in research studies.
2. If you agree that stool samples may be used for known research studies, stool samples will be collected before you begin treatment, at time of your first restaging, at 9 months, and when your treatment on the protocol ends.
3. If you agree to allow biopsies to be done to collect tissue samples for research, additional tumor tissue biopsies will be done before cycle two (2) of treatment at the time of your first restaging, and at the end of treatment. These tumor tissue collections are optional and not considered part of your standard care and will be performed only if you give your

consent below, if the risks from the biopsy are low, and the institution treating you has approved to allow the biopsies to be done. You or your insurance company will not be responsible for these biopsies.

4. Your samples and some related health information will be sent to researchers for use in the studies described above and remaining samples stored in the Biobank, along with samples and information from people who took part in this or other research studies. The samples will be kept until they are used up. Information from your medical record will be updated from time to time.
5. Only qualified researchers can submit a request to use the materials stored in the Biobanks. A committee of experts at ECOG-ACRIN, and/or the National Cancer Institute, will review each request to use the samples for research. All research projects using these samples will also be reviewed by an ethics or institutional review board 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.
6. 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.
7. Results from the research may be placed in centralized storage systems called databases. It is possible that some of your genetic information and your health information may be placed in these databases. It is also possible that some of these databases may be public.

What are the risks in this optional sample collection?

1. The most common risks related to drawing blood from your arm are brief pain and maybe a bruise. Rarely, an infection can happen where the needle was placed. Feeling dizzy or fainting can also happen, but should only last a few minutes after blood is drawn.
2. Common risks involved in collecting a new tumor biopsy could include bleeding, pain, and/or infection. Before having this procedure, you will be asked to indicate that you understand the nature of the surgical procedure to be performed, it will be determined that the risks for you are relatively small, and that you give your permission before the procedure.
3. Generally, hospitals will keep some of your tissue. This tissue may be used to help treat your cancer in the future. There is a small risk that when this tissue sample is submitted to the biobank for research, your tissue could be used up.
4. Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
5. In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic

information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

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

1. They will remove identifiers, such as your initials, from your samples and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your samples and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

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 to this optional sample collection?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?

If you decide you no longer want your samples to be used, you can call the study doctor, who will let the biobank know. Contact information for your study doctor is listed on the consent cover page. Then, any samples that remain in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?

If you have questions about the use of your samples for research, contact the study doctor. Contact information for your study doctor is listed on the consent cover page.

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for known research studies:

May we have samples of your tumor tissue and blood for laboratory research studies?

I agree that my samples and related health information may be collected and used for the laboratory studies described above.

YES NO

May we have samples of your stools for laboratory research studies?

I agree to provide additional samples for research.

YES NO

May biopsies be performed to collect tissue for research studies? These biopsies will be done only if it is considered that the procedure may only have small risks, as described above, and the institution has agreed that the biopsies may be done

I agree biopsies may be done to obtain research samples.

YES NO

Samples for unknown future studies:

May we keep any tumor tissue, blood, and stools leftover after the central review and laboratory research studies for future research?

I agree that my samples and related health information may be kept in a biobank for use in future health research.

YES NO

This is the end of the section about optional studies.

Signature:

This study has been explained to me, and I have been told what my enrollment in the study involves. I have read all pages of this consent and have had my questions answered to my satisfaction at this time. I consent to participate in this study and any additional studies where I circled 'yes'. I understand that by signing this form I have not given up any of my legal rights. I will be given a copy of this consent form. I may also request a copy of the protocol (full study plan).

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)
(Required for initial consent only)