Certification of Completion of the Informed Consent

IRB #

Title:

I have discussed the "Informed Consent for Participation in Research Activities" in its entirety for the above referenced research study, with the research participant listed below (or the research participant's legally authorized representative). During the review of the consent form, the possible benefits, risks and discomforts involved in his/her participation on the study, as well as potential alternatives were reviewed.

The research participant has been encouraged to ask questions, and all questions asked by the participant have been answered. The research participant affirmed that he/she has received all information that he/she desires at this time, and a copy of the signed consent form has been provided to the participant.

PRINTED NAME of Person Obtaining Informed (Consenter)	SIGNATURE	TITLE	DATE	TIME

ADULT INFORMED CONSENT
PARENTAL PERMISSION / YOUTH ASSENT (16-18yrs)

COH Protocol # 18157
TITLE: A Phase 2 Front-Line PET/CT-2 Response-Adapted Brentuximab Vedotin and Nivolumab Incorporated and Radiation Free Management of Early Stage Classical Hodgkin Lymphoma (cHL)
Protocol Version date: 09/09/2022

PRINCIPAL INVESTIGATOR: Alex Herrera, M.D.

24-HOUR TELEPHONE NUMBER: (626) 256-HOPE (4673) ext. 85200
DAY TIME TELEPHONE NUMBER FROM THE HOURS OF 8:00 AM TO 5:00 PM: (626) 256-HOPE (4673) ext. 82405

EXPERIMENTAL PARTICIPANT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study, also known as an experiment or clinical trial. As a research participant, you have the following rights:

1. To be told what the research study is trying to find out.
2. To be told what will happen to you and whether any of the procedures to be used are different from what would be used in standard practice.
3. To be told about the discomforts, side effects and risks of the things that will happen to you as part of the research study.
4. To be told if you can expect any benefit from participating in the research study.
5. To be told of the other choices you have and how they may be better or worse than being in the research study.
6. To be told what medical treatment is available if any complications arise.
7. To be allowed to ask any questions concerning the research study, both before agreeing to be in the study and during the course of the study.
8. To refuse to participate in the research study or to change your mind about participation after the study is started. To be informed that this decision will not affect your right to receive the care you would receive if you were not in the study.
9. To receive a copy of the signed and dated research study consent form.
10. To be free of pressure when considering whether you wish to agree to be in the research study.

ADULT INFORMED CONSENT
PARENTAL PERMISSION / YOUTH ASSENT (16-18yrs)

COH Protocol # 18157
TITLE: A Phase 2 Front-Line PET/CT-2 Response-Adapted Brentuximab Vedotin and Nivolumab Incorporated and Radiation Free Management of Early Stage Classical Hodgkin Lymphoma (cHL)

PRINCIPAL INVESTIGATOR: Alex Herrera, M.D.

"If you are reading this form as the parent of a participant, "you" also refers to "your child."

INTRODUCTION

You are invited to take part in a clinical trial, a type of research study, because you have early stage classical Hodgkin lymphoma (cHL).

Standard treatments for early stage 1 or 2 Hodgkin's lymphoma are:

1) Chemotherapy with 2-4 cycles of chemotherapy called ABVD, obtain interim PET CT to assess the disease followed by involved field radiation, OR
2) To incorporate PET CT after 2 cycles of ABVD chemotherapy if your doctor plans to use only chemotherapy, then based on results of PET CT scan, your doctor can decide whether you can stop therapy at that point if there is no residual disease, OR 2 more cycles of ABVD if you still have residual disease, OR using more intensive chemotherapy regimen called BEACOPP if there are lot of disease left OR adding involved field radiation to additional cycles of chemotherapy.

In this study, we plan to incorporate new Investigational drugs brentuximab vedotin (antibody drug conjugate, targeted HL) and nivolumab (immunotherapy) with standard chemotherapy ABVD without using any form of radiation treatment at all. We hope to learn safety and effectiveness (how well the drugs work) of the Investigational drugs brentuximab vedotin and nivolumab.

This research study is sponsored by City of Hope. Bristol-Myers Squibb and Seattle Genetics are the companies that makes the drugs being tested. They provide funding to cover the costs of conducting this study.

Dr. Zain, Participating Clinician, is paid as a consultant for Seattle Genetics, Inc., the company that provides the drug, brentuximab vedotin, you will receive and supports this research. The City of Hope Conflict of Interest and Commitment Committee and IRB have reviewed Dr. Zain's relationship with Seattle Genetics, Inc. and found that this is very unlikely to affect how you will be treated or how the study results will be determined. If you have questions about this, please ask the Principal Investigator

or contact IRB at (626) 256-HOPE (4673) Ext. 62700. You may also contact the City of Hope Conflict of Interest Manager, at (626) 256-HOPE (4673).

Dr. Siddiqi, Participating Clinician, is paid as a consultant for Seattle Genetics, Inc., the company that provides the drug, brentuximab vedotin, you will receive and supports this research. The City of Hope Conflict of Interest and Commitment Committee and IRB have reviewed Dr. Siddiqi's relationship with Seattle Genetics, Inc. and found that this is very unlikely to affect how you will be treated or how the study results will be determined. If you have questions about this, please ask the Principal Investigator or contact IRB at (626) 256-HOPE (4673) Ext. 62700. You may also contact the City of Hope Conflict of Interest Manager, at (626) 256-HOPE (4673).

It is expected that about 155 participants will take part in this research study. 34 participants will be from City of Hope.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future. Please take as much time as you need to read the consent form. If you find any of the language difficult to understand, please ask questions. If you decide to participate, you will be asked to sign this form. We will give you a copy so that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

A. WHY IS THIS RESEARCH STUDY BEING DONE?

This research study is a Phase II clinical trial. Phase II clinical trials test the safety and effectiveness of an investigational (experimental) intervention to learn whether the intervention works in treating a specific disease. "Investigational" means that the intervention is being studied.

The FDA (the U.S. Food and Drug Administration) has not approved Nivolumab and Brentuximab vedotin for your specific disease but it has been approved for other uses.

The names of the study interventions involved in this study are:

- Administration of study drugs nivolumab (OPDIVO™) and Brentuximab vedotin (BV; ADCETRIS®)
- Correlative tumor tissue collection
- Blood collection
- Bone marrow collection

Brentuximab is an antibody attached to a chemotherapeutic drug targeted against Hodgkin lymphoma cells. Nivolumab is an antibody that enhances the immune system to better attack Hodgkin lymphoma cells. It has shown that both drugs induce high response rates in relapsed or refractory Hodgkin lymphoma.

B. WHAT IS INVOLVED IN THE STUDY?

If you decide to take part, this is what will happen:

Screening period and research procedures through PET/CT-2:
After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. Many of these tests and procedures are likely to be part of regular cancer care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **Medical history,** which includes questions about your health, current medications, and any allergies.
- **Positron-emission tomography (PET), computed tomography (CT) scan:**
  - Positron emission tomography (PET) is a nuclear medicine test based on imaging radioactive molecules with a special scanner. A radioactive atom (F-18) is chemically attached to glucose (sugar) which is then transported to the tumor and normal organs. FDG (F-18 glucose) is administered in a small amount into a vein. The FDG is taken up into cells and then trapped inside the cell. A series of scans are taken with the PET camera to visualize where the FDG has accumulated.
  - A CT scan is a computerized x-ray that shows cross-sectional images (slices) of the body. If a contrast dye is to be used for a CT scan, you must not drink or eat anything for 4 hours before the test and remove all jewelry. A tourniquet will be applied to your arm, a radioactive isotope will be injected, and you will wait 2-3 hours. During the scan, you will lie on your back on an x-ray table for 30-60 minutes. A strap will be placed across the body part to be scanned to prevent movement so that the scan will be clear. The table will then slide into a large, tunnel-shaped machine. When the CT scan is finished, you may immediately resume your usual activities and diet.
- **Quality of Life questionnaire,** designed to collect the patient's perspective on new treatments and thereby help clinicians manage side effects and also help patients understand both the short- and long-term consequences of the cancer and its treatment.
- **Tumor Tissue:** Archival tissue from diagnostic tumor biopsies will be retrieved
- **Blood tests** for research purposes (monitor response to therapy) (about 2 teaspoons of blood will be drawn from a vein in your arm)

A PET scan (PET/CT-2) will be used after your 2 cycles of standard of care therapy with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) for evaluation and classification into the main groups: PET/CT-2 positive and PET/CT-2 negative groups.
PET/CT positive are subjects who are scored 4-5 with the Deauville score, and PET/CT negative are subjects who are scored 1-3. The Deauville score is a five-point scale used for interpreting interim positron emission tomography scans for response assessment.

PET/CT-2 negative

Previously, patients with a PET negative scan were assigned to either Arm A, B1 or B2 as follows:

- Patients with initial tumor measurements larger than 7.5 cm were assigned to Arm B2.
- Patients with initial tumor measurements less than 7.5 cm were randomized between Arm A or Arm B1. Randomization means that you are put into a group by chance. It is like pulling a number out of a hat. The reason for randomization is that no one knows which option is better. Patients with tumors less than 7.5 cm will have an equal chance of being placed in any A or B1.

The design of the study has now been modified: all patients with a negative PET/CT-2 will be assigned to Arm A, and Arm B (B1/B2) is closed.

Treatment plan for each arm is as follows:

- **Arm A:** Three cycles of BV plus nivolumab
- **Arm B1:** Two cycles of chemotherapy (ABVD), followed by 6 cycles of nivolumab
- **Arm B2:** (For patients with tumors greater than 7.5 cm): Same treatment plan as in B1: Two cycles of chemotherapy (ABVD), followed by 6 cycles of nivolumab

PET/CT-2 positive

Patients with a PET positive scan will all be enrolled in Arm C and will get the dose escalation therapy involving BV plus AVD (doxorubicin, vinblastine, and dacarbazine). Patients in Arm C will not be randomized.

- **Arm C:** Four cycles of BV plus AVD, followed by 6 cycles of nivolumab. Patients in this arm must be PET-CT negative at the end of the 4 cycles of BV plus AVD in order to receive nivolumab.

The goal is to develop methods of care that decrease long term toxicities while preserving excellent outcomes for patients whose PET/CT-2 are negative. For participants whose PET/CT-2 is positive, the goal is to improve outcomes and minimize needs for future salvage therapies (treatment given after the cancer has not responded to other treatment).

Before you begin study therapy (pre-treatment):

Additional tests or procedures will be done just before the start of study therapy to find out if you can start study therapy. If you have had some of these tests or procedures done recently, they may not have to be repeated. Your study doctor can give you more information on what needs to be done.

- **Medical exam,** which evaluates your health, current medications, and any allergies.
- **Performance status**, which evaluates how you are able to carry on with your usual activities.
- **Blood tests** to check your blood counts and organ function (about 2 teaspoons of blood will be drawn from a vein in your arm)
- **Blood tests** for research purposes (monitor response to therapy) (about 2 teaspoons of blood will be drawn from a vein in your arm)

- **MUGA/echocardiogram (ECHO) scan:** (a picture of the heart using a small amount of radioactive material injected into the bloodstream through a vein) or echocardiogram (a picture of the heart in motion using ultrasound or sound waves) to evaluate how your heart is working.
- **Pulmonary function tests** to measure how well your lungs are functioning.
- **Pregnancy test:** If you are a woman of childbearing potential by drawing about ½ teaspoon of blood usually from a vein in your arm or urine sample.
- **Quality of Life questionnaire,** designed to collect the patient's perspective on new treatments and thereby help clinicians manage side effects and also help patients understand both the short- and long-term consequences of the cancer and its treatment.

If these tests show that you are eligible for study therapy, you will be enrolled into one of the arms mentioned above and begin the study treatment.

If these tests show that you are not eligible for study therapy, you will not be able to start study therapy and your participation in the study will end. In that case, any blood samples that were collected from you will be destroyed, and any tissue sample that was collected from you will be returned.

Research Study Calendars:

The frequency of all assessments may increase as clinically necessary.

Screening and research procedures through PET/CT-2

Protocol Activity	Screening	Standard of care ABVD			PET/CT-2
		C1D1	C1D15	C2D1	
Medical history	X				
Correlative Tumor Tissue	X				
Correlative Blood		X	X	X	X
QOL Assessment	X				X

QOL: Quality of life questionnaire.

Brentuximab vedotin plus Nivolumab- Maintenance (Mntc) Arm A

Treatment must start within 21-28 days post-C2D15 of standard of care ABVD.

Each cycle of BV+Nivo maintenance is 21 days. Total is 3 cycles.

Protocol Activity	Pre-treatment	BV plus Nivolumab Mntc			End of Cycle 3	Response Follow-Up (+/-1 month)
		C1D1 (+/- 3 days)	C2D1 (+/- 3 days)	C3D1 (+/- 3 days)		
Adverse events collection		X	X	X	X	
Current medication review	X	X	X	X	X	
Performance test	X	X		X	X	
Vital Signs	X	X	X	X	X	
Physical Exam	X	X	X	X	X	
Blood tests	X	X	X	X	X	
Pregnancy Test	X					
ECHO scan	(X)					
Pulmonary Function Test	(X)					
Brentuximab vedotin		X	X	X		
Nivolumab		X	X	X		
PET/CT					X	X*
CTs during Follow-Up						X*
Correlative Blood	X				X	
QOL Assessment	X				X	X

* CT or PET/CT will be performed during Response Follow-up.

ABVD <u>followed by</u> Nivolumab Maintenance (Mntc) Arm B1/B2 (This arm is now closed)
Treatment must start within 14-28 days post-C2D15 of standard of care ABVD.
Each ABVD cycle is 28 days (2 cycles of ABVD numbered C1 and C2).
Each Nivolumab maintenance cycle is 14 days. Total is 6 cycles of Nivolumab alone.

Protocol Activity	**Pre-treatment**	**Protocol ABVD**				**Nivolumab Mntc**	**End of Cycle 6 of Nivolumab**	**Response Follow-Up** (+/-1 month)
		C1D1 (+/- 3 days)	**C1D15** (+/- 3 days)	**C2D1** (+/- 3 days)	**C2D15** (+/- 3 days)	**C1 to C6** (+/- 3 days)		
Adverse events collection		X	X	X	X	X	X	
Current medication review	X	X	X	X	X	X	X	
Performance test	X	X		X		X	X	
Vital Signs	X	X	X	X	X	X	X	
Physical Exam	X	X	X	X	X	X	X	
Blood tests	X	X	X	X	X	X	X	
Pregnancy Test	X					X (Only on C1D1)		
ECHO scan	(X)							
Pulmonary Function Test	(X)							
ABVD		X	X	X	X			
Nivolumab						X		
PET/CT							X	X*
CTs during Follow-Up								X*
Correlative Blood	X						X	
QOL Assessment	X				X		X	X

* CT or PET/CT will be performed during Response Follow-up.

BV plus AVD <u>followed by</u> Nivolumab Maintenance (Mntc) Arm C
(For PET/CT-2 Positive patients)

Treatment must start within 21-28 days post-C2D15 of standard of care ABVD.

Each BV+AVD cycle is 28 days. Total is 4 cycles.

Each Nivolumab maintenance cycle is 14 days. Total is 6 cycles of Nivolumab alone.

Protocol Activity	Pre-treatment	BV plus AVD								End of Cycle 4 of BV plus AVD	Nivolumab Mntc	End of Cycle 6 of Nivo	Response FU (+/- 1 month)
		Cycle 1		Cycle 2		Cycle 3		Cycle 4			C1 to C6 (+/- 3 days)		
		D1 (+/- 3 days)	D15 (+/- 3 days)	D1 (+/- 3 days)	D15 (+/- 3 days)	D1 (+/- 3 days)	D15 (+/- 3 days)	D1 (+/- 3 days)	D15 (+/- 3 days)				
Adverse events collection		X	X	X	X	X	X	X	X		X	X	
Current medication review	X	X	X	X	X	X	X	X	X		X	X	
Performance test	X	X		X		X		X			X	X	
Vital Signs	X	X	X	X	X	X	X	X	X		X	X	
Physical Exam	X	X	X	X	X	X	X	X	X		X	X	
Blood tests	X	X	X	X	X	X	X	X	X		X	X	
Pregnancy Test	X										X (Only on C1D1)		
ECHO scan	(X)												
Pulmonary Function Test	(X)												
BV		X	X	X	X	X	X	X	X				

AVD		X	X	X	X	X	X	X	X				
Nivolumab											X		
PET/CT										X		X	X*
CTs during FU													X*
Correlative Blood	X			X						X^r		X	X
QOL Assessment	X									X^r		X	X

FU: Follow-Up

* CT or PET/CT will be performed during Response Follow-up.

If you discontinue protocol therapy before completion of planned protocol therapy, you will proceed to "End of cycle" visits.

Planned Follow-up:

Patients will undergo follow-up for 3 years after completion of therapy.

- **Response Follow-up**- for those who have yet to have disease progression (Cancer that continues to grow or spread).

  Follow-up visits (including imaging) will be conducted at 6-month intervals from conclusion of treatment for a total of 3 in person follow-up visits (at 6, 12, and 18 months from end of treatment).

- **Survival Follow-up**- for participants who have progressed OR completed Response Follow-Up.

  Patients can either be seen in person or followed-up by phone for documentation of disease status and survival every 6 months until 3 years post-completion of therapy. Subsequent therapies will be collected when available.

If you enrolled in the study but did not start study treatment, you will not undergo any follow-up.

C. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be in this research study for up to 45 months.

D. WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

There are risks to taking part in any research study. One risk is that you may get a study drug that does not help treat your disease or that makes your condition or disease worse. Another risk is that there may be side effects.

All cancer treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different cancer treatments and between individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**

Everyone in the research study will be watched carefully for side effects. You will be monitored during the administration of study drugs to keep track of your blood counts and organ function, particularly your kidney and liver function. If you experience side effects, they may go away after you stop taking the study drug. You will be monitored closely for any severe, life-threatening side effects listed below. Some of these side effects may be permanent. Appropriate medical care will be provided, if necessary, including additional treatment, hospitalization and/or surgery.

Possible risks and discomforts you could experience during this study include:

Risks and side effects related to the Brentuximab Vedotin (when taken in combination with other cancer drugs):

Very common side effects of Brentuximab Vedotin. A lot of people who take this drug may have these side effects *(events occurring in more than 10 out of 100 research participants*)

- Stomach pain (abdominal pain)
- Hair loss (alopecia)
- Not enough red blood cells (anemia), which could make you feel tired or need a blood transfusion
- Pain in your joints (arthralgia)
- Back pain
- Bone pain
- Constipation
- Cough
- Not feeling hungry (decreased appetite)
- Diarrhea
- Feeling dizzy (dizziness)
- Feeling out of breath (dyspnea)
- Tiredness (fatigue)
- Very low white blood cells with a fever (febrile neutropenia). This makes it easier to get an infection and can be life-threatening
- Headache
- Low levels of potassium in your blood (hypokalemia). You may feel weak or tired. You could have muscle cramps, an abnormal heartbeat, or a hard time passing a bowel movement.

- Not being able to sleep (insomnia)
- Muscle pain (myalgia)
- Nausea
- Low levels of a type of white blood cell called neutrophils that help your immune system (neutropenia). You could have a higher chance of getting an infection.
- Numbness or tingling in the hands and feet, which can spread to the arms and legs (peripheral neuropathy). You might have problems with muscle weakness, balance, coordination, or feeling in your fingers or toes.
- Itching (pruritis)
- Fever (pyrexia)
- Swelling and sores in the mouth (stomatitis)
- Vomiting
- Weight loss

Common side effects of Brentuximab Vedotin. Some people who take this drug may have these side effects *(events occurring in more than 1 but less than 10 out of 100 research participants*)

- Bloating or swelling in your belly (abdominal distension)
- Belly pain (abdominal pain)
- Sudden and serious reaction to the injection of a drug (acute infusion related reaction). You could have a rash or itchy skin, swelling in your face or throat, wheezing, chills, or fever. You could feel faint or out of breath.
- High levels of liver enzymes (ALT/AST elevation). This may mean that there are problems with your liver. If this becomes serious, it can cause death.
- Painful swelling in your lungs (bronchitis). You could have a cough, a hard time breathing, or chest pain. You could cough up a thick liquid called mucus. You could feel tired, have a fever, or have chills. If this happens, get emergency medical help **right away**.
- Patchy redness on your skin (erythema)
- Your skin could get red and feel hot (flushing)
- Shingles (herpes zoster), which is a painful, blistering rash caused by a viral infection
- High blood sugar levels (hyperglycemia), which can cause serious health problems including diabetes. You could feel very thirsty, need to pee often, have blurry vision, feel tired, or have a headache.
- Seasonal flu (influenza). You could have fever, body aches, chills, sweats, headache, runny nose, or a sore throat. In some people, this infection can lead to death.
- Muscles feeling weak (muscular weakness). You may have a hard time doing normal daily activities.
- Swelling and redness in your throat and nose (nasopharyngitis). You may have throat pain, cough, or a runny nose, like the common cold.
- Infection in your mouth (oral candidiasis), sometimes called “thrush”
- Throat pain (oropharyngeal pain)

- Infection in your lungs (pneumonia). You could have a cough, fever, chills, pain in your chest, or trouble breathing. If this happens, get emergency medical help **right away**.
- Swelling of the lungs (pneumonitis). You could have trouble breathing, cough, feel tired, or feel less hungry. If this happens, get emergency medical help **right away**.
- Rash
- Blood infection (sepsis), which is serious and can cause death. You may have a fever, fast heartbeat, and fast breathing. If this happens, get emergency medical help **right away**.
- Sinus problems (sinusitis). You may have a stuffy nose, headache, or fever. You may feel pressure behind your eyes or pain at the base of your skull.
- Low levels of a type of blood cell called platelets (thrombocytopenia). This could make you have problems with your blood clotting, bruise easily, feel tired, or bleed longer than usual when you get cut.
- Infection that could cause you to pee more often or have pain when you pee (urinary tract infection).
- Hives (urticaria)
- Chills
- Upset stomach (dyspepsia)
- Pain in your arms or legs (pain in extremity)
- Infection in the nose, sinuses or throat (upper respiratory tract infection). You may have fever, pain, or a hard time breathing (upper respiratory tract infection)

Uncommon side effects of Brentuximab Vedotin. A few people who take this drug may have these side effects *(events occurring in more than 1 but less than 10 out of 1000 research participants)*

- Pain in the belly caused by swelling of the large intestine (enterocolitis).
- Bleeding in your throat or gut (gastrointestinal hemorrhage). You could vomit blood, have dark sticky bowel movements, or see red blood in your bowel movements. You could have problems breathing, belly or chest pain, or feel lightheaded or faint.
- Damage to your liver that makes it stop working (hepatotoxicity). This is serious and could cause death. You may have yellow eyes or skin, feel tired, sick to your stomach, or vomit. You could have belly pain, bleeding that doesn't stop, sudden weight gain, or swollen hands or feet. If this happens, get emergency medical help right away.
- Loss of the ability of your gut to move and digest food, which could block your intestines (ileus).
- Increased risk of infection.
- A hole in your gut (intestinal perforation), which can be serious and cause death. You may have belly pain and vomit blood. You may feel tired, weak, or out of breath. If this happens, get emergency medical help **right away**.
- Damage in your gut (neutropenic colitis). You could have a higher chance of getting an infection in your gut. This could happen suddenly. You could feel sick to your stomach, throw up, have pain in your belly, chills, a high fever, and watery bowel movements.

- Problems with your lungs caused by a drug or radiation (pulmonary toxicity). You could have trouble breathing on your own, feel tired, or have a dry cough.
- Serious painful rash that spreads to most of your skin (Stevens-Johnson syndrome/toxic epidermal necrolysis). This can cause death. Symptoms of this rash include widespread skin pain, blisters, hives, swollen tongue, red or purple rash that spreads, or skin peeling.
- Lots of cancer cells dying and breaking apart, which causes serious problems (tumor lysis syndrome or TLS). This usually happens 2-3 days after starting chemotherapy. If you start feeling sick and get worse over time, check with your doctor.

Rare side effects of Brentuximab Vedotin. Very few people who take this drug may have these side effects *(events occurring in more than 1 but less than 10 out of 10 000 research participants)*

- Belly pain caused by a sudden and serious problem with your pancreas (acute pancreatitis). You may have pain in your upper belly or back, fever, fast heartbeat, nausea, or vomiting

Very rare side effects of Brentuximab Vedotin. A very small number of people who take this drug may have these side effects *(events occurring in less than 1 out of 10 000 research participants)*

- Your body could have an immune response to the drug (drug-specific antibody).
- Block in your throat or gut that can cause serious problems and may need surgery (gastrointestinal obstruction). You may have throat or belly pain, feel like throwing up, be unable to have bowel movements, or feel very bloated. If this happens, get emergency medical help **right away**.
- A hole in your throat or gut (gastrointestinal perforation), which can be serious and cause death. You may have chest or belly pain and vomit blood. You may feel tired, weak, or out of breath. If this happens, get emergency medical help right away.
- Problems with the lining of your throat or gut, which can lead to sores (gastrointestinal ulcer). You could have pain in your chest or belly, feel sick to your stomach, or throw up.
- You could get sick from something that doesn't usually cause problems, like a virus or germ (opportunistic infection). This may happen because your immune system isn't as strong as usual.
- Brain damage caused by the John Cunningham virus (progressive multifocal leukoencephalopathy, PML). If you have a weakened immune system, you could get PML. You could become confused, clumsy, have weakness on one side of your body, or have problems with talking or seeing. This is a serious condition that can cause death or serious disability.

Patients Over 60 Years Old

Patients over 60 years old who got brentuximab vedotin for Hodgkin's lymphoma had similar side effects as younger patients. Most patients older than 60 had pain, weakness, or unusual sensations in their hands and feet (peripheral neuropathy). More older patients had serious cases of peripheral neuropathy than younger patients. This could be because of age. Or it could be because more patients

over 60 had diseases that are connected with neuropathy, like high blood sugar (diabetes) and low levels of thyroid hormones (hypothyroidism). Patients who already had some neuropathy symptoms before treatment didn't seem more likely to get serious cases of peripheral neuropathy.

Fertility risks

It is possible that treatment with brentuximab vedotin could lower your chances of becoming pregnant for several months after stopping treatment. When we tested a drug that is similar to brentuximab vedotin in female animals, we saw changes in the ovaries where eggs mature. We don't know if these changes will happen in people who get brentuximab vedotin.

The changes in the ovaries showed signs of reversing when treatment was stopped. You will need to use contraceptives during and after taking part in this study to prevent pregnancy.

The length of time you must use contraceptives is longer than the amount of time it took for most of the changes to reverse.

Risks and side effects related to the Nivolumab (BMS-936558)
Nivolumab may cause the side effects listed below. This information is based on data from subjects in other clinical trials with Nivolumab. In addition, there may be side effects that are not yet known that may occur. You should tell your doctor or nurse about any side affects you experience.

Side effects of nivolumab may happen anytime during treatment or even after your treatment has ended.

Very common side effects of Nivolumab *(events occurring in more than 10 out of 100 research participants)*

- Diarrhea
- Feeling tired or lack of energy
- Skin itching
- Skin rash

Common side effects of Nivolumab *(events occurring in less than 10 out of 100 research participants)*

- Abdominal pain
- Alkaline phosphatase increased: lab test result associated with liver or bone abnormalities
- Allergic reaction/hypersensitivity, a reaction related to infusion of the medicine. The symptoms may include but not limited to fever, rash, pain, swelling
- Alanine aminotransferase (ALT) increased: lab test result associated with abnormal liver function
- Amylase increased: lab test result associated with pancreas inflammation

- Aspartate aminotransferase (AST) increased: lab test result associated with abnormal liver function
- Bilirubin (liver function blood test) increased: lab test result associated with abnormal liver function
- Chills
- Constipation
- Cough
- Creatinine increased: lab test result associated with decreased kidney function
- Decreased appetite
- Dizziness or vertigo (feeling off balance which can lead to dizziness)
- Dry mouth
- Dry skin
- Fever
- Headache
- Increased blood sugar, a lab test result or diabetes, a disease that results in too much sugar in the blood
- Inflammation of the colon
- Inflammation of the mouth
- Lipase increased: lab test result associated with pancreas inflammation
- Loss of color (pigment) from areas of skin
- Low levels of sodium in the blood
- Low platelet counts (thrombocytopenia), this may increase your risk for skin bruising, nose bleeds, and bleeding from the gums
- Low red blood cell counts (anemia), this may make you feel weak and tired
- Lung inflammation (pneumonitis)**,** inflammation of the tissues of the lung. While many patients with X-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation. Symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue. These symptoms may require treatment with steroids, which may increase your risk of infections.
- Nausea
- Pain in the muscles, bones, ligaments, tendons, and nerves
- Shortness of breath
- Swelling, including face, arms, and legs (oedema)
- Thyroid gland function decreased/thyroid stimulating hormone increased (lab test associated with abnormal thyroid function)
- Thyroid gland function increased
- Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet

- Vomiting

Uncommon side effects of Nivolumab *(events occurring in less than 1 out of 100 research participants)*

- A common viral / bacterial infection that affects the nose, throat, and airways (upper respiratory tract infection)
- A condition in which not enough oxygen passes from your lungs into your blood, or when your lungs cannot properly remove carbon dioxide (respiratory failure)
- A skin disorder that is considered to be an allergic reaction to medicine or an infection. Symptoms may include symmetrical, red, raised skin areas that can appear all over the body, more noticeable on the fingers and toes. These patches often look like "targets" (dark circles with purple-grey centers) (erythema multiforme)
- Abnormally excessive sweating involving the arms, legs, hands and feet, underarms, and face, usually unrelated to body temperature or exercise
- Blistering of the skin or mouth caused by the immune system attacking healthy tissue (pemphigoid)
- Decreased secretion of hormones produced by adrenal glands, which may cause fatigue, weakness, loss of appetite and dizziness.
- Decreased thyroid stimulating hormone - a lab test result associated with abnormal thyroid function
- Dehydration
- Dry eye
- Flu like symptoms (which may include fever, chills, cough, sore throat, runny or stuffy nose, muscle or body aches · headaches, feeling tired)
- Hair loss
- Heart rate increased
- Heart rhythm abnormal
- High blood pressure
- Hives
- Inflammation of the eye
- Inflammation of the kidney
- Inflammation of the lining of bronchial tubes, which carry air to and from the lungs (bronchitis)
- Inflammation of the liver
- Inflammation of the muscle
- Inflammation of the pancreas
- Inflammation of the pituitary gland
- Inflammation of the stomach
- Inflammation of the thyroid gland
- Joint pain or stiffness
- Kidney function failure, kidney disease

- Low blood pressure
- Low white blood cell counts (neutropenia), these put you at higher risk for infection
- Skin disease with thickened patches of red skin, often silvery scales (psoriasis)
- Trouble falling and/or staying asleep (Insomnia)
- Underactive function of the pituitary gland situated at the base of the brain
- Vision blurred

Additional rare but serious side effects of Nivolumab can also occur

- A disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes (sarcoidosis)
- A disease that may affect your body's defense system, called immune system. Certain white blood cells may attack other blood cells. These abnormal blood cells collect in your spleen and liver, causing these organs to enlarge. The symptoms may include fever, rash, and low blood cell counts (hemophagocytic lymphohistiocytosis (HLH) syndrome)
- A malfunction of the immune system that produces autoantibodies, which attack red blood cells as if they were foreign substances to the body (autoimmune hemolytic anemia)
- A neuromuscular disease that may cause weakness of eye, face, breathing, and swallowing muscles (myasthenic syndrome, myasthenia gravis).
- A potentially fatal, severe skin disease characterized by blistering and peeling of the top layer of skin resembling a severe burn (toxic epidermal necrolysis).
- A swelling and irritation of the thin saclike membrane surrounding the heart (pericardium) (pericarditis)
- Acne-like skin condition resulting in redness of face (rosacea)
- An autoimmune disorder associated with progressive muscle weakness or paralysis (Guillain-Barre syndrome).
- An inflammatory disorder that causes muscle pain and stiffness, especially in the shoulders (polymyalgia rheumatica)
- Cranial nerve disorder
- Damage to the protective covering of the nerves in the brain and spinal cord
- Diabetes complications resulting in excess blood acids and diabetic coma
- Fulminant type 1 diabetes mellitus, a severe form of type 1 diabetes that is characterized by extremely rapid disease onset. Flu-like symptoms (fever, upper respiratory symptoms, etc) or gastrointestinal symptoms (upper abdominal pain, nausea and/or vomiting, etc) precede the disease onset.
- Disease caused by the body’s immune system attacking healthy organs (autoimmune disorder)
- Disorder of the lymph nodes which causes the lymph nodes to become enlarged, inflamed and painful, commonly affecting lymph nodes of the neck and possibly associated with fever or muscle and joint pains (histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis)
- Double vision
- Drug induced liver injury

- Inflammation of blood vessels
- Inflammation of the brain, potentially life-threatening or fatal
- Inflammation of the heart
- Inflammation of the lining of the brain and spinal cord
- Inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin (Stevens Johnson syndrome)
- Lung infiltrates, associated with infection or inflammation
- Muscle fiber released into the blood stream which could damage your kidneys (rhabdomyolysis)
- Rupture of the intestine/hole in the intestine or stomach
- Severe allergic reaction may include but not limited to high grade fever, rash, swelling, difficulty breathing or pain
- Vogt Koyanagi Harada syndrome; a disease that affects the pigmented tissue; this may affect the eye leading to swelling, pain and/or blurred vision; the ear leading to hearing loss, ringing in the ears and/or the skin leading to loss of skin color.

Solid organ and tissue transplant rejection has been reported in patients who have previously undergone transplantation and who were subsequently treated with therapy which affect immune system functioning, including Nivolumab. Treatment with Nivolumab may increase the risk of rejection in solid organ and tissue transplant recipients.

Rapid-onset and severe graft vs host disease (GVHD), some with fatal outcome, has been reported in patients who had undergone prior allogeneic hematopoietic stem cell transplant (HSCT) and subsequently received PD-1/PD-L1 inhibitors. Complications of allogeneic HSCT after treatment with PD-1/PD-L1 inhibitors including Nivolumab, administered before allogeneic HSCT, may be associated with an increased risk of transplant-related complications, including GVHD. Fatal cases have been reported in clinical studies.

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

As with any medication, allergic reactions are a possibility

Risks and Side Effects Related to ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine)

The study medications ABVD will each be administered as separate intravenous infusions. Your study doctor will let you know about how long each infusion will take.

It is very important that you try to avoid eating grapefruit or drinking grapefruit juice while receiving doxorubicin. Grapefruit has an ingredient that can potentially affect how the medication works in your body.

Common side effects of ABVD (events occurring in more than 10 out of 100 research participants) are:

- Increased risk of getting an infection from a decrease in white blood cells
- Tiredness and breathlessness due to a decrease in red blood cells (anemia)
- Bruising more easily due to a decrease in platelets
- Fatigue (tiredness) during and after treatment
- A hypersensitivity reaction happens to as many as half the patients treated with bleomycin, causing a high temperature (fever) and chills while you have the drug – if you have a high temperature the night after your treatment, tell your doctor or nurse when you go for your next dose
- Skin reactions – reddening, darkening or thickening of the skin or nails or dry, peeling skin at the fingertips. You are most likely to develop these side effects 2 to 3 weeks after you start your treatment
- Hair loss – almost everyone has complete head and body hair loss, which usually begins 2 to 5 weeks after the treatment starts. Your hair will grow back when the treatment ends
- Loss of appetite
- Feeling or being sick – doxorubicin and dacarbazine can cause severe sickness, which may begin a few hours after treatment and last for a few days
- A sore mouth – about 2 to 3 days after each treatment you may have red sore skin in your mouth and mouth ulcers. This gradually clears up within a couple of weeks
- Your urine may become pink or red for 1 or 2 days after treatment – this is due to the color of one of the drugs and is not harmful
- Black or brown discoloration in the skin creases
- Sensitivity to sunlight – don't sit out in the sun, and make sure you cover up or use sun block on exposed skin
- Watery eyes occur in about 1 in 4 people with doxorubicin (25%) and may last for several days after the beginning of each treatment
- Women may stop having periods (amenorrhea) but this may only be temporary
- Loss of fertility – you may not be able to get pregnant or father a child after treatment with this drug so it is important to talk to your doctor about your fertility before starting treatment
- ABVD may have a harmful effect on a developing baby

Occasional side effects (events occurring in less than 10 out of 100 research participants) are:

- Inflammation around the infusion site – if you notice any signs of redness, swelling or leaking at your infusion site, tell your chemotherapy nurse immediately
- An allergic reaction happens to 3 people out of 100 who have doxorubicin (3%) – you may have a sudden rash of pink, itchy bumps on your skin and a reddening of the skin along the veins, which should clear up within a few days
- Reddening of the skin in areas where you have had radiotherapy in the past, and the skin may get dry and flaky and feel sore and hot
- Damage to heart muscle from doxorubicin, which is usually temporary but for a small number of people may be permanent – your doctor will check your heart before and after your treatment
- Diarrhea – drink plenty of fluids and if the diarrhea becomes severe or continues tell your doctor or nurse because you could get dehydrated
- Constipation can be a problem with vinblastine, but this is usually well controlled with laxatives – tell your doctor or nurse if you are constipated for more than 3 days
- Taste changes – food may taste metallic
- Nails may become darker and white lines may appear on them
- Fever and chills
- Numbness or tingling in fingers and toes can cause difficulty with activities such as doing up buttons – this starts within a few days or weeks and usually goes within a few months of finishing treatment
- Inflammation of the lungs occurs in about 1 in 10 patients treated with bleomycin (10%) but is more common in people over 70 – you will have lung tests before and during treatment. Tell your doctor or nurse if you develop a dry cough or breathlessness, especially in cold weather
- Dacarbazine can cause flu like symptoms for a week after treatment in about 1 in 10 people (10%) – you may have a high temperature (fever), chills, muscle and joint aching, or weakness
- Sore eyes happen in some people

Risks and Side Effects Related to AVD (doxorubicin, vinblastine, and dacarbazine)

It is very important that you try to avoid eating grapefruit or drinking grapefruit juice while receiving doxorubicin. Grapefruit has an ingredient that can potentially affect how the medication works in your body.

Commonly Occurring Side Effects (events occurring in more than 10 out of 100 research participants)

- Low white blood cell count that may lead to infection
- Low platelet count that may lead to an increase in bruising and bleeding

- Low red blood count (anemia) that may cause tiredness or shortness of breath
- Hair loss
- Nausea
- Vomiting
- Fever
- Increased skin sensitivity to sunlight
- Time away from work

Occasional Side Effects (events occurring in less than 10 out of 100 research participants)

- Diarrhea
- Flu-like symptoms
- Abdominal cramps
- Loss of appetite
- Constipation
- Shortness of breath
- Skin rashes
- Skin or tissue damage (like a burn) if some of the chemotherapy drugs leak from the
- intravenous (IV) line
- Mouth and throat sores
- Metallic taste
- Numbness or tingling in the fingers and toes
- Abnormal liver function tests
- Urine discoloration – doxorubicin is red in color and small amounts may get into the urine and change its color. This is not harmful.

Rarely Seen Side Effects (events occurring in more than less than 1 out of 100 research participants)

- Heart damage
- Severe skin or tissue damage if doxorubicin leaks from the intravenous (IV) line
- Very high fever with sweating and dehydration

Since the effect of the study drug(s) taken with other medications may not be known, it is important that you tell the research doctor about all prescription and non-prescription drugs, herbal preparations and nutritional supplements that you are taking or planning to take. There may also be some foods that you should avoid while on this research study and your research doctor will review this information with you.

Risks Associated with Blood Draw

Risks of blood draws include mild pain or discomfort, bruising and swelling around the puncture site, dizziness or fainting, or infection (rare).

Cancer research often includes biopsies, scans, x-rays that are also provided as routine care. The following describes the side effects of procedures done only for the purposes of research.

Risks Associated with Biopsies:

Biopsies are normally performed under the guidance of an imaging technique. Each procedure requires a separate consent prior to the biopsy. The risks may include:

- Pain and discomfort. The amount of pain and discomfort will vary, depending on the location of the biopsy site. These risks can be discussed with the study doctor.
- Minor bleeding at the biopsy site.
- Tenderness at the biopsy site.
- Scarring at the biopsy site.
- Rarely, an infection at the biopsy site.

Uncommonly, complications from biopsies can be life threatening. As with any interventional procedure, other potentially serious complications from bleeding or organ damage may occur. These might require additional surgical intervention.

Risks Associated with Bone Marrow Biopsies:

For this procedure, a numbing drug is injected into the skin over one of your hipbones. A needle is then inserted into the hipbones and a small piece of bone is removed. The risks may include:

- Moderate pain and discomfort
- Bleeding at the biopsy site
- Scarring at the biopsy site
- Rarely, an infection at the biopsy site
- Rarely, nerve injury at the biopsy site

Risks Associated with Bone Marrow Aspiration:

For this procedure, a numbing drug is injected into the skin over the same hipbone. A needle is then inserted into the hipbone and a sample of bone marrow fluid is removed. Risks of this procedure are small, but may include:

- Pain from the needle sticks
- Pain from aspirating the bone marrow with a syringe
- Bleeding
- Infection
- Local nerve damage

Risks Associated with Intravenous Catheter Placement:
Prior to beginning the experimental therapy, your doctor may want to insert an intravenous (IV) catheter for the delivery of chemotherapy/study drugs and to take blood samples. IV catheters can be placed in a hand, arm or leg. These are known as "peripheral" IVs. IVs placed in the central circulation, like the internal jugular vein (neck) or subclavian vein (just beneath the collar bone), are known as "central lines". You should discuss this with your doctor. Complications of central venous catheters include blood clots and infection. Clotting may require removal of the catheter or treatment of the clot by injecting a medicine that dissolves blood clots. If you develop an infection, you will require treatment with antibiotics. If the catheter is placed under the collarbone, uncommon side effects include swelling of the face and arm and/or lung collapse. If the lung collapses, it may be necessary to place a tube between the ribs to allow the lung to re-expand.

Radiation Risks Associated with Scans and X-Rays:
While you are in this research study, CT scans, PET/CT scans, and/or other scans utilizing radioactivity may be used to evaluate your disease. The frequency of these exams is slightly greater than what you would receive as standard care. In the long term, over many years, there is a very low risk of developing a new cancer as a result of the radiological evaluation and treatment for your cancer.

The imaging CT scans and PET/CT scans that you may receive in this study will expose you to low amounts of radiation. Every day, people are naturally exposed to low levels of radiation that come from the sun and the environment. This type of radiation is called “background radiation”. No one knows for sure whether exposure to low amounts of radiation is harmful for your body. However, scientists believe that being exposed to too much radiation can cause harmful side effects, including the potential to cause a new cancer.

Risks Associated with MRI Scans:
When having an MRI (Magnetic Resonance Imaging) scan, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your research doctor. Your doctor may give you a medication to make you feel more comfortable. As images are taken, a loud banging noise will be produced. Earplugs or headphones will be available if needed. The MRI can be stopped at any time at your request, but the scan may not be complete.

Incidental Findings:
It is possible the research procedures could find a medical problem unrelated to the purpose of this study that you did not know about before. If during the research procedures we learn information that may be important for you to know about, such as the possibility of a previously unknown medical condition, we will tell you. You may authorize the release and communication of the findings to your personal doctor. These findings may require additional testing or treatment. You will be responsible for the cost of any additional tests or related treatment.

Reproductive Risks:
We do not know whether the study drug(s) might hurt an unborn child. While participating in this research study, you should not become pregnant or father a baby, and should not nurse a baby. We can provide counseling about preventing pregnancy for either male or female study participants. Let your doctor know immediately if you become pregnant or find out that you are going to be the father of a child.

In the event that partner becomes pregnant, it may be critical to share information regarding your participation in this research study with that person. Your research doctor should also be told if this happens. The study sponsor may want to collect data on your partner's pregnancy.

If you are pregnant or nursing a baby and do not want to stop, you cannot take part in this study. If you are a woman who can become pregnant, a urine pregnancy test will be obtained before treatment is started. If you are sexually active and capable of bearing or fathering a child, both you and your partner must agree to use a medically effective form of birth control while you are on this study and for at least 6 months following the last dose of brentuximab vedotin (for both women and men), and for at least 5 months after the last dose of nivolumab (for women only). The investigational drug(s) may involve risks to you (or to the embryo or fetus, if you or your partner become pregnant), which is currently unforeseeable.

You must use birth control while on this study. Acceptable medically effective forms of birth control are:

- Abstinence,
- Surgical sterilization (tubal ligation or hysterectomy for women, or vasectomy for men),
- Double-barrier methods (i.e. condoms, diaphragm, cervical cap, or sponge used with spermicidal gel or foam),
- Intrauterine device (IUD) (i.e. Progestin, Copper),
- Hormonal Contraceptives (Birth control patches, implants, pills, rings, or injections)

Other Risks:
Because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

Risks Associated with Questionnaires: The questionnaires used in this study may be upsetting. If you find the questionnaires upsetting, you may speak with the research doctor or ask to be referred for additional emotional support. Some of the questions may make you feel uneasy or embarrassed. You can choose to skip or stop answering any questions that make you uncomfortable.

Risks associated with Breach of Confidentiality*:*
There is a small risk that people who are not connected with this study will learn your identity or your personal information.

Risks associated with Highly Sensitive Information:
You are providing highly sensitive, personal information in this study. If people not connected with the study learn this information, you could have problems getting a new job, keeping your current job, and finding housing, or getting insurance (health, disability, or life insurance). In highly unlikely situations, you could be charged with a crime.

E. WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

F. HOW WILL YOUR INFORMATION BE KEPT CONFIDENTIAL?

Any information learned from this study in which you might be identified will be confidential and disclosed only with your permission. Every effort will be made to keep any information collected about you confidential. However, it is impossible to guarantee that information about you will not be mistakenly released. If, despite our best efforts, identifying information about you is released, it could negatively impact you or your family members. This risk is small.

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 study sponsor City of Hope and drug companies Bristol-Myers Squibb, Seattle Genetics 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.
- Regulatory agencies such as the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and the National Cancer Institute (NCI) in the U.S., and similar ones if other countries are involved in the study as required by law.

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.

G. WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS RESEARCH STUDY?

Taking part in this study may or may not make your health better. While doctors hope the treatment will be more useful against classical Hodgkin lymphoma (cHL) compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help doctors learn more

about this combination of drugs as a treatment for cancer. This information could help future cancer patients.

H. WHAT OTHER OPTIONS ARE THERE?

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 cancer, described on page 2.
- You may choose to take part in a different study, if one is available, or
- You may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

I. ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?

You will not be paid for participating in this study.

Possible Commercial Products
We may use your samples and information to develop a new product or medical test to be sold. The sponsor and hospital may benefit if this happens. Donors of blood, tissue and other biological materials do not retain any property rights to the materials. Therefore, you would not share in any money or other benefits that any entity might receive for these inventions or discoveries.

J. WHAT ARE THE COSTS?

Taking part in this research study might lead to added costs to you or your insurance company.

The investigational drug(s), Brentuximab Vedotin and Nivolumab will be provided to you at no cost by Seattle Genetics and Bristol-Myers Squibb while you take part in the study. You and your health plan/insurance company will need to cover the cost of the infusion/injection of the study drug. The commercially available drugs, doxorubicin, bleomycin, vinblastine, dacarbazine will be the responsibility of you and/or your insurance carrier. It is possible that Brentuximab Vedotin and Nivolumab may not continue to be supplied while you are on the study. If this occurs, the research doctor will talk to you about your options.

Most of the tests, procedures, and/or drugs provided to you as part of this study are routinely used to treat your illness. You would receive these tests, procedures, and/or drugs even if you were not participating in this study. You or your health plan/insurance company will need to pay for this routine care. You will also be responsible for any co-payments or deductibles required by your health plan/insurance company. Some health plans/insurance companies will not pay the costs associated with these tests, procedures, and/or drugs because you are in a research study. If your health plan/insurance company will not pay these costs, you will have additional expenses from being in this study, such as the costs associated with treating side effects.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services are:

- City of Hope Financial Support Services: 626-256-HOPE (4673), extension: 80258.

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

K. WHAT HAPPENS IF YOU GET INJURED AS A RESULT OF THIS STUDY?

If you think you have been hurt by taking part in this study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

City of Hope will offer you the care needed to treat injuries directly resulting from taking part in this research. This care will be billed to you or your health plan/insurance company. You will be responsible for co-payments, deductibles, and any other costs required by your health plan/insurance company. There are no plans to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

L. WHAT ARE YOUR RIGHTS IF YOU TAKE PART IN THIS STUDY AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE?

Your participation in this research study is voluntary. You are free to withdraw your consent for participation in this study without any loss of benefits, penalty, or interference with any future treatment at City of Hope.

You can decide to stop at any time and you may still be treated at your hospital or clinic. Tell your study doctor if you are thinking about stopping or decide to stop. You should talk to the doctor about leaving the study before you decide so that he/she can find out if you are having any side effects from study treatment. Another reason to tell your doctor that you are thinking about stopping is so that he/she can talk to you about any other treatments that could be helpful to you.

If you decide to stop being in this study, you will still be asked to come back to the hospital or clinic for the end of treatment tests described above. You may also be asked to take part in the follow-up phone calls and/or visits. This information is important to make sure that there are no lasting side

effects from the study treatment and to see if your cancer got better, stayed the same, or got worse after treatment.

M. CAN YOU BE REMOVED FROM THE STUDY?

You may be removed from this study without your consent for any of the following reasons: you are not eligible to start study treatment, you do not follow the investigator's instructions, at the discretion of the investigator or the sponsor, your disease gets worse, or the sponsor closes the study. If this happens, the investigator will discuss other options with you.

N. WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

The principal investigator, Dr. Alex Herrera or a colleague, Dr. _____, responsible for your care or treatment, has offered to and has answered any and all questions regarding your participation in this research study. If you have any further questions or in the event of a research related injury, you can contact Dr. Alex Herrera at (626) 256-HOPE (4673) ext. 82405 or Dr. _____ at (626) 256-HOPE (4673) ext. _____.

This study has been reviewed and approved by the Institutional Review Board (IRB). If you have any questions regarding your rights as a research participant, you may contact a representative of that Board, from the Office of Human Research Subjects Protection, at (626) 256-HOPE (4673) ext. 62700.

O. ADDITIONAL STUDIES SECTION:

This section is about optional studies you can choose to take part in. You will make your selection at the end of this section. You will not get health benefits from any of these studies. 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.

You will not be billed for these optional studies. You can still take part in the main study even if you say "no" to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

At the end of the document, circle your choice of "yes" or "no" for each of the following studies.

Optional Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer, diabetes, 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, left over blood and/or tissue will be saved. 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".

WHAT IS INVOLVED?

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

1) Your sample, and possibly specimens left over from diagnostic and clinical tests and some related health information may be stored in the Biorepository (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 will be updated from time to time.
2) Qualified researchers can submit a request to use the materials stored in the Biorepository (Biobank). An ethics committee review will be done 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. Any Biorepository (Biobank) staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom City of Hope sends 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.

Some of this research may result in new inventions or discoveries that may be of potential commercial value and may be patented and licensed for the development of new products. Donors of blood, tissue and other biological materials do not retain any property rights to the materials. Therefore, you would not share in any money or other benefits that any entity might receive for these inventions or discoveries. Your decision not to allow storage or future use of your tissue or specimens will not affect your ability to participate in this study.

WHAT IF I CHANGE MY MIND?

If you agree to allow your specimens to be used for future research, you can change your mind later. If you change your mind, please ask for the "Withdrawal of Informed Consent to Continue in Participation in Research Activities" for IRB #18157 – A Phase 2 Front-Line PET/CT-2 Response-Adapted Brentuximab Vedotin and Nivolumab Incorporated and Radiation-Free Management of Early Stage Classical Hodgkin Lymphoma (cHL). Please sign the section of this this withdrawal form named "Biological Specimen Withdrawal of Consent" and send it to the principal investigator of this study at City of Hope. Once City of Hope processes your signed withdrawal of informed consent, your specimens will not be used in any new research. At that time, any of your existing specimens will be destroyed.

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the use of your samples for research, contact the study doctor, Alex Herrera, M.D., at (626) 256-HOPE (4673) ext. 82405.

Please circle 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 kept in a Biorepository (Biobank) for use in future health research.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

P. SIGNATURE SECTION

SIGNATURE FOR CONSENT: By signing this consent form, you are making a decision to participate in this research study. Your signature on this informed consent form indicates that you:

1. Have read and understood the information in this form.
2. Have had the information in this form explained to you.
3. Have had a chance to ask questions and these questions were answered to your satisfaction.
4. Have been informed that you will receive a copy of this signed consent form, which includes the "Experimental Subject's Bill of Rights."

I hereby agree to be a research participant in this research study:

_____ _____ _____

Research Participant's Signature | Date | Time

(For paper consent only, date and time must be in research participant's handwriting)

_____

Print Research Participant's Name

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)/PARENT/GUARDIAN SIGNATURE

_____ _____ _____

Legally Authorized Representative (LAR)/Parent/ Guardian's Signature (If applicable) | Date | Time

_____

Print Name of Legally Authorized Representative (LAR)/ Parent/Guardian and indicate relationship to participant

_____ _____ _____

Parent/Guardian's Signature (If applicable) | Date | Time

_____

Print Name of Parent/Guardian and indicate relationship to participant

INDIVIDUAL OBTAINING CONSENT SIGNATURE

_____ _____ _____

Signature of Individual Obtaining Consent | Date | Time

_____

Print Name of Individual Obtaining Consent

FOR USE WITH IRB APPROVED TRANSLATED SHORT/LONG CONSENT FORMS FOR NON ENGLISH SPEAKING PARTICIPANTS ONLY

NOTE: To determine who should sign below, review the guidance document, *Consenting Non English Speaking Research Participants (Pediatric or Adult) – Who Signs What?*

Interpreter: By signing here, I attest that I have acted as interpreter and facilitated this consent process.

_____ _____ _____

Interpreter's Signature Date Time

_____

Print Interpreter's Name

FOR USE WHEN A WITNESS IS REQUIRED:

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

_____ _____ _____

Witness' Signature Date Time

_____

Print Witness' Name

COH IRB# 18157: A Phase 2 Front-Line PET/CT-2 Response-Adapted Brentuximab Vedotin and Nivolumab Incorporated and Radiation-Free Management of Early Stage Classical Hodgkin Lymphoma (cHL)

AUTHORIZATION TO USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION (PHI) FOR PURPOSES OF THIS STUDY:

I. **Purpose of this Authorization**: The information about your health is something that is protected by law and cannot, except for certain purposes, be disclosed (shared) without your permission. As part of this research, you are agreeing to allow City of Hope to use and share with others your protected health information ("PHI"), as needed for the research. If you agree to participate in the study named above (called the "Study"), you must sign this authorization in addition to the *Study Consent Form*.

II. **The Information About You that is Covered By this Authorization**: PHI refers to information that we maintain about you that identifies you and includes the information contained in your medical record. Your medical record consists of information related to your health and the treatment we provide to you, such as your medical history, the results of physical exams, blood tests, x-rays and other diagnostic and medical procedures. If you sign this authorization, you are allowing City of Hope and the individuals indicated below to use and share any PHI we maintain about you that is required for your participation in the Study.

Certain information about you that is highly confidential is needed for the Study. If you sign this form, you are allowing City of Hope and the individuals indicated below to use and disclose the following highly confidential PHI about you: information about HIV/AIDS testing or treatment (including the fact that an HIV test was ordered, performed or reported, regardless of whether the results of such tests were positive or negative).

III. **Purposes for Uses and Sharing of your PHI; Who Will Use, Share and Receive your PHI**: Your PHI will be used and shared with others for the purpose of doing this research as described in the *Study Consent Form*. Your PHI will also be used to keep the research sponsor informed about this Study, for reporting to those

individuals and authorities responsible for overseeing our research activities to make sure that the activities are properly conducted, and to report to regulatory agencies as required by the Study.

The people authorized to use and share your PHI for purposes of the Study include the Principal Investigator and the research staff supporting the Study; your City of Hope physicians and the health care team; and the Health Information Management Services Department (i.e., Medical Records Department). This also includes any agents or contractors used by these individuals or groups for purposes of conducting or managing this Study. At the City of Hope, the Institutional Review Board ("IRB"), and other City of Hope research regulatory committees will have access to your PHI as necessary to monitor research.

You are also allowing your PHI to be shared with the Office for Human Research Protections ("OHRP") and with any person or agency as required by law. In addition, certain other regulatory agencies, including, the Food and Drug Administration ("FDA"); the National Cancer Institute ("NCI"), and the North American Hodgkin Lymphoma Consortium (NAHLC) will have access to your PHI.

Use and disclosure of your PHI may also continue for as long as the sponsor needs to maintain the PHI for purposes of obtaining approval of the Brentuximab Vedotin and Nivolumab from the FDA or for other FDA reporting.

Your information will also be shared, with City of Hope, the "Research Sponsor" and its employees, agents or contractors who are involved in the administration of the Study.

This study also involves tissue banking (storing your specimens such as blood or tumor tissue). The tissue banked as part of this study will be sent to City of Hope IRB approved biorepository. The banked blood and tissue will be stored indefinitely.

This authorization will allow us to use and share your PHI for the Study. No other additional uses and disclosures other than for the purposes of the Study is

included in this authorization. City of Hope's Notice of Privacy Practices will continue to protect your non-Study information. If necessary, another separate permission will be obtained from you for any non-Study uses or sharing of your PHI.

IV. **Expiration of this Authorization**: This authorization to use and share your PHI will expire twenty-five (25) years from the date that you sign this authorization.

V. **Further Sharing of Your PHI**: Your privacy is important and this is the reason for having rules which control who can use or see your PHI. City of Hope maintains control over your PHI at present, but once we share this information with a third party (for example, an individual or agency outside of the City of Hope), then it is no longer possible to maintain the same level of protection. The persons outside our control may not be governed by federal or state privacy laws and it is possible that they could share your PHI with others for whom you have not given permission.

The information from this Study may be published in scientific journals or presented at scientific meetings but your identity will be kept confidential.

VI. **Your Rights Under this Authorization**: You may cancel this permission to use and share your PHI at any time by contacting City of Hope's Privacy Officer at (626) 256-HOPE (4673) ext. 64025. You should ask for the form, *Revocation (Cancellation) of Authorization for Use of Protected Health Information for Research*. Fill this form out and return it as the form instructs. Your cancellation begins when the Health Information Management Department of City of Hope receives this form. If you cancel this authorization to use and share your PHI, you will no longer be able to participate in the Study. This is because the research under this Study cannot be conducted without your PHI.

Once you cancel your permission to use and share your PHI, the researchers and others involved in conducting the Study will no longer be able to use or share your PHI for this research. PHI already used and shared up to this point as part of this Study will continue to be used for purposes of this research. This means that any uses of your PHI and any PHI shared about you by City of Hope prior to

receiving your cancellation (revocation) form cannot be taken back. While no further PHI about you will be shared for the Study, your PHI already shared will continue to be used in the overall Study.

VII. **<u>Signing this Authorization is Your Choice</u>:** Your ability to obtain care at the City of Hope will not be affected by your decision to sign this authorization form. You will be able to continue to receive health care at City of Hope if you choose not to sign this authorization form or if you sign this form and later cancel your permission to use and share your PHI.

If you agree to the use and sharing of your PHI, please sign below. You will be given a copy of this authorization form.

_____ _____ _____

Research Participant's Signature Date Time

(date and time must be in research participant's handwriting)

_____

Print Research Participant's Name

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)/PARENT/GUARDIAN SIGNATURE

_____ _____ _____

Legally Authorized Representative (LAR)/Parent/ Guardian's Signature (If applicable) Date Time

_____

Print Name of Legally Authorized Representative (LAR)/ Parent/Guardian and indicate relationship to participant

_____ _____ _____

Parent/Guardian's Signature (If applicable) Date Time

_____

Print Name of Parent/Guardian and indicate relationship to participant

INDIVIDUAL OBTAINING CONSENT SIGNATURE

_____ _____ _____

Signature of Individual Obtaining Consent Date Time

_____

Print Name of Individual Obtaining Consent

FOR USE WITH IRB APPROVED TRANSLATED SHORT/LONG CONSENT FORMS FOR NON ENGLISH SPEAKING PARTICIPANTS ONLY

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_____ _____ _____

Interpreter's Signature Date Time

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Print Interpreter's Name

FOR USE WHEN A WITNESS IS REQUIRED:

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

_____ _____ _____

Witness' Signature Date Time

_____

Print Witness' Name