Consent and Authorization Document

Phase II Neoadjuvant trial of Nivolumab in Combination with HF10 Oncolytic Viral Therapy in Resectable Stage IIIB, IIIC, IVM1a Melanoma (Neo-NivoHF10)

This document may contain words and information that you do not understand. Please ask your study doctor or study staff to explain anything that is not clear to you. You are being asked to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Ask the research doctor or staff if there is anything that is not clear or if you would like more information. Take time to decide whether or not to volunteer to take part in this research study.

Once you know about the study, you will make a decision about whether to take part. If you decide to take part, you'll be asked to sign this form. Your decision to take part in this study is voluntary which means you are free to decide to join this study or not to join this study.

BACKGROUND

You are being asked to take part in this study because you have been diagnosed with a type of skin cancer called Melanoma. Also, you have tumors that are able to be measured, and you have tumors that are located on your skin (cutaneous) or near the surface of the skin (superficial), and thus, they are able to be injected with the investigational study drug, HF10. You will also be given a drug called nivolumab. These will both be given to you prior to undergoing surgery to remove your tumors. Then just nivolumab will be given to you after surgery. Researchers want to find out if these drugs together can reduce the size of your tumors prior to surgery, while still being safe for you to take. They are also wanting to see how your cancer reacts after surgery.

Nivolumab is an anti-PD-1 (programmed cell death) antibody. It works by attaching to and blocking a molecule called PD-1. PD-1 is a protein that is present on different types of cells in your immune system and controls parts of your immune system by shutting it down. Antibodies that block PD-1 can potentially prevent PD-1 from shutting down the immune system, thus allowing it to recognize and help your body destroy the cancer cells.

Nivolumab has not been approved by the U.S Food and Drug Administration (FDA) for your type of melanoma so it is being considered "investigational" for use in this study. An investigational drug is a drug that is being tested and is not approved for sale in the United States by the U.S. Food and Drug Administration (FDA). OPDIVO® (nivolumab) is approved by the FDA for the treatment of multiple other tumor types and is available to be prescribed for patients with those diseases.

HF10 is an antitumor medicine consisting of a live, naturally occurring strain of the Herpes Simplex Virus Type 1 (HSV-1). HSV-1, the virus that can cause cold sores, is very widespread in the environment. In the United States, many people have been exposed to HSV-1. HF10 is a weakened strain of HSV-1 and is

believed to pose minimal health risk. HF10 is also an investigational drug and is available for research use only. HF10 will be administered by injection directly into a cutaneous or superficial tumor.
The study is being conducted by Dr. Robert Andtbacka at Huntsman Cancer Institute of the University of Utah.

NUMBER OF PARTICIPANTS
Approximately 20 patients are expected to be enrolled in this study from the Huntsman Cancer Institute/University of Utah.

STUDY PROCEDURES
If you decide you will take part in the study and you sign this informed consent form, you will have some screening tests and procedures done to make sure you are eligible to enroll.

Screening Period

- Medical history will be collected as well as details about what medications and vitamins you are currently taking
- You will have a physical exam and a measure of your vital signs
- You will have a CT (Computerized Tomography) scan. This is considered standard of care and would be done even if you were not participating in this study.
- If you are female with the potential of becoming pregnant, you will have a pregnancy test.
- You will have your blood drawn for standard lab testing to ensure you are healthy enough to take part. This will include thyroid function tests. If you are taking an anti-clotting medication such as warfarin, you will have a test called PT/INR which tests how fast your blood clots. You will also have tests done to check different components of your cancer and blood.

Treatment Period
Once it is decided that you are able to enroll into this study, you will begin study treatment. The treatments will be broken up into two different time periods: prior to surgery and after surgery. The study drug, nivolumab will be given to you in segments of time called “cycles”. Prior to surgery, a cycle will be 14 days. You will be given 240 mg of nivolumab on day 1 of each cycle, for a total of 7 cycles. It will be given to you as an intravenous (IV) infusion.

Also prior to surgery, the other study drug, HF10 will be given to you as injections directly into your tumor lesion(s). All of your eligible lesions will be injected except for 1. The 1 that remains untreated will act as a control for comparison. A total of 9 administrations of HF10 (Study Days 1, 7, 14, 21, 28, 42, 56, 70 and 84) will be given by injection into one or more tumors per study day.

After you finish those treatments, you will have surgery to remove your lesions. After you have had surgery and recover from it, you will begin nivolumab again. Post surgery, a cycle will be 28 days. You will be given 480 mg of nivolumab on day 1 of each cycle, for one year.

Your doctor will give you more information about your treatment plan.

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You will come to the clinic on the days listed above for various procedures as well as for your treatments. Some of the procedures are being done as part of your standard cancer care. Some are being done because you are participating in this study. Post surgery, you will have to come to the clinic every 4 weeks. You will continue on the study treatment for a maximum of 1 year post surgery unless your disease gets worse, you have intolerable side effects, you decide to stop, your doctor decides it would be in your best interest to stop or the study ends.

Study Procedures during the Treatment Period both before and after surgery:

- You will have physical exams and measures of your vital signs during your clinic visits, including weight. You will also be asked about any changes in medications that you are taking and changes in how you are feeling to check for potential side effects.
- You will have a CT scan to check how your disease is responding to treatment. This will be done at Day 84 before surgery, and then every 12 weeks after surgery. This is considered standard of care and would be done even if you were not participating in this study.
- If you are female with the potential of becoming pregnant, you will have a pregnancy test.
- You will have your blood drawn for standard lab testing to ensure you are healthy enough to continue in the trial and to look how your body and cancer are reacting to the treatments. This will include thyroid function tests. If you are taking an anti-clotting medication such as warfarin, you will have a test called PT/INR which tests how fast your blood clots.
- Tumor biopsies – The researchers would like to collect fresh tumor tissue from you by performing a biopsy a few different times in the study. Some will be required and others will be optional. Your tumor tissue will be used to look at components of your tumor and your immune system and how that may relate to how your cancer reacts to the treatments.
    - Required biopsies - You will have a biopsy done to collect tumor tissue two different times in the study. These will be collected prior to beginning treatment with HF10 and then at surgery. These two biopsies are not optional and are required to be done for you to participate in this study.
    - Optional biopsies - If you consent, these will be collected at day 42 and then again if your cancer returns. See the end of this form for more information and to make your choice about participation.
- Optional blood samples – The researchers would like to collect additional blood for additional study related testing. These will be collected prior to every nivolumab injection throughout the study. The blood will be used to look at components of your cancer and your immune system and how that may relate to how your cancer reacts to the treatments. See the end of this form for more information and to make your choice about participation.

End of Treatment

- You will have a physical exam and measure of your vital signs, including weight. You will also be asked about any changes in medications that you are taking and changes in how you are feeling to check for potential side effects.
- You will have a CT scan. This is considered standard of care and would be done even if you were not participating in this study.
- You will have your blood drawn for standard lab testing for safety.

Follow-up

Once you complete your end of treatment visit, you will continue to be followed every 3 months for 1 year from your end of treatment visit. You will be followed per standard of care. You will also be asked about any new cancer treatment you may begin, to check changes in how you are feeling to check for potential side effects and to check if side effects you have been experiencing have gotten better. You will be asked for potential side effects for 90 after you stop taking nivolumab.

RISKS

You may have side effects while on the study. Some are listed below, but there are some that we cannot predict. If side effects occur, you may be given other drugs to make the side effects less serious and uncomfortable. Many side effects disappear shortly after the study drugs are stopped, but in some cases side effects can be serious, long-lasting or permanent, or, in rare cases, fatal. You should talk to your study doctor about any side effects that you have while taking part in the study.

Nivolumab

Nivolumab may cause one or more of the side effects listed below. This information is based on data from cancer 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 right away about any possible side effects you experience.

Very common side effects of nivolumab are: [may affect more than 1 in 10 people]

- Diarrhea
- Fatigue
- Itching
- Rash

Common side effects of nivolumab include: [may affect more than 1 in100 people to less than 1 in10]

- Abdominal (stomach) pain
- Alkaline phosphatase increased: lab test result associated with liver or bone abnormalities
- ALT increased: lab test result associated with abnormal liver function
- Amylase increased: lab test result associated with pancreas inflammation
- AST 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
- Dry mouth
- Dry skin
- Fever

- Headache
- Inflammation of the colon
- Inflammation of the mouth
- Infusion related reaction
- Itching
- Joint pain or stiffness
- Lipase increased: lab test result associated with pancreas inflammation
- Loss of color (pigment) from areas of skin
- Lung inflammation (pneumonitis - see details below)
- Musculoskeletal pain
- Nausea
- Redness
- Shortness of breath
- Sodium levels in blood low
- Swelling, including face, arms, and legs
- Thyroid gland function decreased
- Thyroid gland function increased
- Thyroid stimulating hormone increased: lab test result associated with abnormal thyroid function
- Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet
- Vomiting

Uncommon side effects of nivolumab include: [may affect more than 1 in 1,000 people to less than 1 in 100]

- Adrenal gland function decreased
- Allergic reaction/hypersensitivity
- Bilirubin (liver function blood test) increased
- Bronchitis
- Cranial nerve disorder
- Diabetes
- Dry eye
- Hair loss
- Heart rate increased
- Heart rhythm abnormal
- High blood pressure
- Hives
- Inflammation of the eye
- Inflammation of the kidney
- Inflammation of the pancreas
- Inflammation of the pituitary gland
- Inflammation of the stomach

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- Inflammation of the thyroid gland
- Liver inflammation
- Low blood pressure
- Lung infiltrates, associated with infection or inflammation
- Pituitary gland function decreased
- Psoriasis: characterized by patches of abnormal, scaly skin
- Renal (kidney) failure or kidney injury
- Respiratory failure
- Upper respiratory tract infection
- Vertigo (feeling off balance which can lead to dizziness)
- Vision blurred

Rare side effects of nivolumab include: [may affect more than 1 in 10,000 people to less than 1 in 1,000]

- Anaphylactic reaction (severe allergic reaction)
- Damage to the protective covering of the nerves in the brain and spinal cord
- Diabetes complications resulting in excess blood acids and diabetic coma
- Erythema multiforme: skin inflammatory reaction
- Guillain-Barre syndrome, an autoimmune disorder associated with progressive muscle weakness or paralysis
- Inflammation of blood vessels
- Inflammation of the brain, potentially life-threatening or fatal
- Inflammation of the heart
- Muscle inflammation
- Myasthenic syndrome (neurologic syndrome characterized by muscle weakness) including myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles.
- Polymyalgia rheumatica, an inflammatory disorder causing muscle pain and stiffness
- Rhabdomyolysis: muscle fiber released into the blood stream which could damage your kidneys
- Rosacea: acne-like skin condition resulting in redness of face
- Sarcoidosis, a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes
- Stevens Johnson syndrome: inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin
- Toxic epidermal necrolysis: a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn
- Histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis: 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.
- Vogt Koyanagi Harada syndrome; a disease that affects the pigmented tissue; ths 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.

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Lung Inflammation (pneumonitis): It is possible that nivolumab may cause inflammation of the tissues of the lung. This side effect has been reported infrequently in patients treated with nivolumab. 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. Signs and 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.

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 lung 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.

Complications, including fatal events, have occurred in patients who received allogeneic hematopoietic stem cell transplantation (HSCT) after nivolumab.

Please inform your study doctor or nurse AT ONCE if you experience any of the following:

- Any new or increased shortness of breath;
- Any new or increased chest pain;
- Any new or increased pain/difficulty while breathing;
- Any new or increased cough or any significant change in your type of cough; for example any new or increased mucous or blood in your cough;
- Any change in the amount of oxygen you require;
- Any fever, fatigue, or other symptoms that occur at the same time as any changes to your breathing or other lung symptoms.

If you start to develop symptoms, your study doctor will ask you to return to the clinic for additional tests, which could include a physical exam, measurement of oxygen levels, blood tests, chest x-rays, and/or CT scans. You will be monitored very closely for changes in your overall lung symptoms, monitoring may require hospitalization. You may require specific treatment in order to control pneumonitis. You may also be seen by a special doctor called a pulmonologist, who has special training to be an expert in how your lungs work.

Prolonged treatment with medicines that suppress inflammation, sometimes needed to manage the side effects of nivolumab treatment, may lower your body's ability to fight off certain infections (i.e., opportunistic infections). These infections may require treatment with antibiotic or antifungal medications and may be fatal.

HF10-associated Side Effects and Risks

Potential risks of HF10 may include the following side effects which have been observed in volunteers receiving HF10:

- Occurring in more than 10% (1 in 10) volunteers - chills
- Occurring in 1%-10% (1 in 100 people to 1 in 10) of volunteers - injection site reactions (skin

redness, tenderness, swelling, changes in skin color), tiredness, weakness, fever, nausea, dehydration (low water level in the body), itching, and/or low blood pressure
- One patient with anal and scrotal tumors injected with HF10, experienced swelling in the genital area, skin breakage and scab formation in the area on/or near the scrotum

Risks associated with treatment of cancer with viral anti-cancer agents like HF10:
- In other clinical trials using viruses to treat cancer, some patients have reported flu-like symptoms (e.g., fever, chills, fatigue, nausea/vomiting, headache, diarrhea, and low blood pressure).
- The extent to which these side effects might occur following HF10 treatment is unknown.

Side effects following HF10 treatment in Phase I clinical trials in Japan and the United States:
Few HF10-related side effects have been reported in any of the trials and are similar across the trials. They include: flu-like symptoms such as fever, chills, fatigue, nausea/vomiting and hypotension (low blood pressure). Such events are consistent both with symptoms of viral infections and side effects reported in trials of other investigational oncolytic (cancer destroying) viruses (see above). No HF10-related serious side effects have been reported in these trials.

If you experience unexpected viral toxicity that your doctor believes is caused by the HF10 treatment, you may be treated by the antiviral drugs acyclovir, famciclovir, or valacyclovir, to which HF10 is sensitive.

Information presented below addresses questions that some patients may have regarding risks that the HF10 virus may pose to people with whom they come in contact.

The association of HF10 with any human illness has not been established. However, given the investigational nature of this therapy, your study doctor believes that it is appropriate to take some precautions to minimize the exposure to HF10 in persons with whom you have close contact.

After the injection of HF10 into your tumor, the virus may appear in your saliva and/or other body fluids (e.g., urine). This can begin within a few hours of the treatment and may persist for several days. It is currently not established how long HF10 may be found in these fluids following your treatment. However, evaluation of blood, saliva, and urine samples of the patients that have been treated with HF10 has indicated that the virus is either not present, or is present only briefly following injection of HF10. Nevertheless, your study doctor believes it is wise for you and your family to take steps to reduce their exposure to HF10, and especially, to minimize exposure to persons beyond your immediate family.

To minimize the exposure of others to HF10, the following steps are recommended for the one week period following HF10 injection, unless otherwise indicated (based on review of laboratory results for detection of HF10 virus in your blood, saliva, or urine):

- Avoid close contact with possible exposure to body fluids (e.g., kissing and sexual activity) to minimize exposure to your partner. It is also important that patients (or their partners) avoid becoming pregnant during this time.
- Do not share towels or eating utensils with others.

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- Isolate your toothbrush from those of others.
- Wash your hands frequently, especially after coughing, blowing your nose, or using a restroom.
- If a surface comes in contact with body fluids, the area should be cleaned using chlorine bleach.
- Avoid contact with persons who may have decreased immunity, such as:
    - Children 6 years old or younger
    - Elderly persons
    - Anyone who has had an organ or tissue transplant
    - Other cancer patients and people with weakened immune systems.
- Be sure to wear a mask when visiting the treatment clinic.

You may need to continue to carry out these precautions based on the results of laboratory testing of your saliva, blood, and urine for the detection of HF10 virus DNA. If you have any questions or concerns about any of the precautions listed above, please ask your healthcare providers.

There may be risks with the combination of HF10 and nivolumab that are unknown at this time. Please ask your study team/doctor for any questions about these risks.

REPRODUCTIVE RISKS
Nivolumab has been studied in laboratory and animal experiments to see if it causes problems with pregnancy or birth defects. However, even when the results are all normal it is still not possible to say that nothing bad will happen when a woman gets pregnant while taking nivolumab.

Information about birth defects:
No information is available at the present time

Information about harm to developing babies:
No information is available at the present time

Information about harm that may result from breastfeeding:
Because many medicinal products, including antibodies, can be secreted in human milk, a risk to newborns/infants cannot be excluded.

Human Pregnancy Outcomes with nivolumab:
The use of nivolumab in pregnant women has not been formally studied in clinical studies. One case has been identified of a nivolumab treated male patient with a female partner who became pregnant. The pregnancy was uneventful and at birth, the infant was slightly underweight.

Laboratory & Animal Reproductive Toxicology Findings:
No studies have been conducted to determine if nivolumab causes damage to genetic material (DNA). Because nivolumab is an antibody, the risk of damage to DNA is believed to be low.

Laboratory and animal studies have not been conducted using nivolumab to determine if nivolumab may cause cancer. One study in monkeys has been conducted to evaluate the effects of nivolumab on

pregnancy. The preliminary findings revealed an increase in late stage pregnancy loss as well as deaths in premature infants. These animal study findings suggest a potential risk to human pregnancy if there is continued treatment with nivolumab during pregnancy.

Findings with Similar Drugs in the Class:
There is no data/information for similar drugs in this class that may be under evaluation in other clinical trials.

Requirements for birth control
Your study doctor is familiar with the different forms of acceptable birth control (see table below) and will be able to give advice about which method might be best for you.

Any birth control method used must be highly effective with a failure rate less than 1% per year, and must be discussed with your doctor if it is started during the course of the study. You must not be pregnant or breastfeeding, and you should not become pregnant or breastfeed while you are taking the study treatments. Females should not breastfeed while receiving nivolumab and up to 7 months from the last dose of nivolumab. You must use an adequate method(s) to avoid pregnancy for the duration of this study and for up to 7 months after the last dose of study drug. Male subjects who are sexually active with a woman of child bearing potential should also use an adequate method(s) of birth control to avoid pregnancy of their partner for up to 7 months after the last dose of study drug. You should immediately contact your study doctor if there is a change in your method(s) to avoid pregnancy or if you start any prescription drug or other medication (including over-the-counter drugs and herbal supplements) not prescribed by the study doctor.

Female Subjects:
Women of child bearing potential are expected to use one of the highly effective methods of contraception listed below.

Male Subjects:
Male subjects must inform their female partners who are women of child bearing potential of the contraceptive requirements and are expected to adhere to using contraception with their partner. Female partners of male subjects, who are women of child bearing potential, are expected to use one of the highly effective methods of contraception listed below. In addition, male subjects are expected to use a condom as noted in the list below.

Highly Effective	Progestogen only hormonal contraception associated with inhibition of ovulation
	Hormonal methods of contraception including oral contraceptive pills (combination of estrogen and progesterone), vaginal ring, injectables, implants and intrauterine devices (IUDs)
	Non-hormonal IUDs such as ParaGard®
	Bilateral tubal ligation
	Vasectomized Partner

	Intrauterine hormone-releasing system (IUS)
	Complete abstinence
Other Methods	Condom
Unacceptable Methods	Vaginal sponge
	Progestin only pills
	Cervical cap with spermicide
	Periodic abstinence (calendar, symptothermal, post-ovulation methods)
	Withdrawal (coitus interruptus)
	Spermicide only
	Lactation amenorrhea method (LAM)
	A male and a female condom must not be used together

Information for Women of Child-bearing Potential:

While you are taking the study treatments you must not be pregnant or breastfeeding, and you should not become pregnant or breastfeed while receiving nivolumab and for up to 7 months from the last dose of nivolumab. You must use an adequate method(s) to avoid pregnancy for the duration of this study and for up to 7 months after the last dose of study drug. The reason is that at this time there is not enough information to know if nivolumab will cause birth defects or otherwise harm a developing baby. We also do not know whether the small amounts of nivolumab that may be present in breast milk would make it unsafe for mothers to breastfeed. There may be unknown risks to you, your unborn baby or nursing infant if you are or become pregnant during this study or are breastfeeding during this study.

It is important to contact your study doctor if:

- you have difficulty following the study doctor's contraception advice.
- your normal period is late or is missed.
- you think for any other reason you might be pregnant.
- you start to take any medication or non-prescription supplements (including over-the-counter drugs and herbal supplements) without the study doctor's approval.
- there is a change in your method(s) to avoid pregnancy.

If you become pregnant during this study, suspect pregnancy or if you missed your period or it is late, or if you have a change in your usual menstrual cycle (e.g., heavier bleeding during your period or bleeding between periods), you should immediately contact your study doctor.

1. You will discontinue nivolumab immediately. You will be instructed about continued use of other medications.
2. The study doctor will help you understand how nivolumab might affect your pregnancy. This will be based on all the information available at that time.
3. You will be referred to other doctors for pre-natal medical care. Your study doctor will be available to counsel other doctors about how nivolumab might affect your pregnancy.

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4. The study doctor will ask for your permission to follow the progress of your pregnancy, provided it is safe for you and your unborn baby to do so. This information will be used to advise other women who might become pregnant while taking the study medication.

In case of a pregnancy, your pregnancy and its outcome will be reported to the drug manufacturer.

Your doctor will discuss this with you, as well as options for additional appropriate care for your cancer. The sponsor has not set aside any funds to pay for any aspects of obstetric, child or related care and does not plan to pay for them.

Information for Men with Partners of Childbearing Potential

Sexual partner(s) of a male study participant can be exposed to the study drug because small amounts of investigational compounds may be present in seminal fluids. For this reason you must communicate your participation in this clinical trial to any sexual partner(s) you may have. You must promise to use an acceptable form of contraception (see table above) for up to 7 months after the last dose of study drug.

You must also tell the study doctor if your partner becomes pregnant during the clinical trial, and you and your partner will be asked to provide information about the pregnancy outcome. The drug manufacturer has not set aside any funds to pay for any aspects of obstetric, child or related care and does not plan to pay for them.

The effects that HF10 may have on an unborn baby are not known, but following the guidelines above will ensure you and a potential unborn child's safety.

Other Risks and Inconveniences

There are also non-physical risks associated with taking part in this study, such as the risks associated with a breach of privacy or confidentiality. For example, if your identity as a participant in research or your identifiable genetic or health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers. The risks of such improper disclosure are very small because Huntsman Cancer Institute has adopted strict privacy and confidentiality procedures for this research.

Blood draws or IV: Risks associated with drawing blood or putting a needle in your vein might include pain from the puncture, bruising, bleeding, infection, or fainting. Every effort will be made to minimize discomfort.

Risk of Biopsy: Tumor biopsies may cause pain, bruising, bleeding, redness, low blood pressure and/or feeling faint, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

UNFORESEEABLE RISKS
Problems or side effects that are not known could also occur. Most side effects are expected to go away after treatment is stopped or interrupted; however in some cases the side effects may be serious, long-lasting, permanent or lead eventually to death. You will be given any new information when it becomes available that may affect your willingness to start or continue in the study.

BENEFITS
There may not be any benefit to you from your being in the study. The information gained in this study will aid in the understanding of cancer and help in the development of new approaches to its treatment in the future.

ALTERNATIVE PROCEDURES
You do not have to be in this study to get help for the type of cancer you have. The study doctor will talk to you about other things you can do for this type of cancer, including the important risks and benefits.

Some other things you might do are:
- Use other approved chemotherapy regimens.
- Use other investigational treatments.
- Get supportive care.
- Choose to have no further treatment.

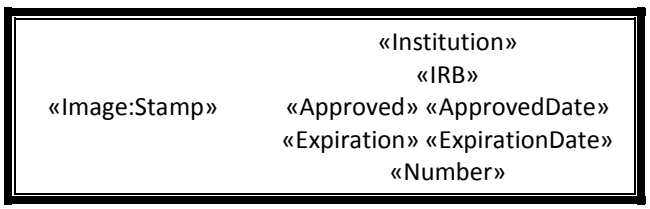
PERSON TO CONTACT
The principal investigator for this study is Dr. Robert Andtbacka, and he is responsible for its overall conduct. He and/or his research staff are able to answer any questions, complaints, concerns you have about the study or about a research-related illness or injury. You may contact **Dr. Andtbacka at** 801-585-0255, Monday through Friday from 8:00 AM to 5:00 PM.

At all other times, call the University of Utah Hospital operator at 801-581-2121, 24 hours a day, seven days a week, and ask for the hematologist/oncologist on call.

Institutional Review Board: Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Research Participant Advocate: You may also contact the Research Participant Advocate (RPA) by phone at (801) 581-3803 or by email at participant.advocate@hsc.utah.edu.

RESEARCH-RELATED INJURY
If you are injured from being in this study, medical care is available to you at the University of Utah, as it is to all sick or injured people. The University of Utah has not set aside any money to pay the costs for such care. The University will work with you to address costs from injuries. Costs would be charged to you or your insurance company (if you have insurance), to the study sponsor or other third party (if



applicable), to the extent those parties are responsible for paying for medical care you receive. Since this is a research study, some health insurance plans may not pay for the costs. By signing this consent form you are not giving up your right to pursue legal action against any parties involved with this research.

The University of Utah is a part of the government. If you are injured in this study, and want to sue the University or the doctors, nurses, students, or other people who work for the University, special laws may apply. The Governmental Immunity Act of Utah is a law that controls when a person needs to bring a claim against the government, and limits the amount of money a person may recover. See sections 63G -7-101 to -904 of the Utah Code.

VOLUNTARY PARTICIPATION

Taking part in this research study is voluntary. You may decide not to take part or you may leave the study at any time. Refusal to take part or the decision to withdraw from this study will involve no penalty or loss of benefits to which you are otherwise entitled.

Tell the study doctor if you are thinking about stopping or decide to stop, as it may be necessary to do certain tests in order to ensure your safety. If you choose not to return for an assessment, we may ask for medical records from your current general practitioner in order to continue to monitor your health.

If you decide not to continue in the study at any time, your study doctor will arrange for you to receive alternative treatment and any necessary assessments or procedures according to standard of care.

RIGHT OF INVESTIGATOR TO WITHDRAW

Your study doctor may decide to take you off this study at any time without your consent for any of the following reasons:

- if your disease becomes worse and is not responding to the study drug,
- if he or she believes it is in your best interest,
- if you do not follow the study rules,
- if you miss study visits and/or procedures,
- if you have serious side effects,
- if you become pregnant,
- you do not later consent to any future changes that may be made in the study plan; or any other reason.

There is also the possibility that the investigator, may close the study before your participation is complete and without prior warning. If any of these events were to happen, your study doctor would assist with arrangements for your continued care as appropriate.

COSTS AND COMPENSATION TO PARTICIPANTS

Some of the procedures and treatments you'll have while you are on the study are considered "standard of care" for your type of illness. Even though you will be a part of the study, these types of procedures and treatments will be billed to you and/or your insurance company just like regular medical care. Some

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procedures and treatments you'll have while you are on the study are considered "study related" and are not billed to you and your insurance company. You should ask your study coordinator and treating physician for details about the specific procedures you or your insurance company will be financially responsible for.

Nivolumab will be provided to you free of charge by Bristol-Myers Squibb (BMS), the drug maker. HF10 will also be provided to you free of charge by Takara, maker of HF10.

NEW INFORMATION
You will be given any new information about the study drugs that may affect your willingness to start or continue in the study as it becomes available.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION
Signing this document means you allow us, the researchers in this study, and other working with us to use some information about your health for this research study.

This is the information we will use and include in our research records:

- Demographic and identifying information like your name, address, telephone number, and email address.
- Related medical information about you like family medical history, allergies, current and past medications or therapies, information from physical examinations such as blood pressure readings, heart rate, temperature, and lab results.
- All tests and procedures that will be done in the study

How we will protect and share your information:
We will do everything we can to keep you information private, but we cannot guarantee this. The research records will be kept in a secured manner and computer records will be password protected. We may need to disclose information about you as required by law.

Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this information as part of the regular treatment, payment, and health care operations of the hospital.

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.

In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:

- Members of the research team and University of Utah Health Sciences Center
- The University of Utah Institutional Review Board (IRB), who reviews research involving people to make sure the study protects your rights;
- BMS, the drug supplier of nivolumab, and its authorized agents

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- Takara, the drug supplier of HF10, and its authorized agents
- Government agencies responsible to confirm research accuracy such as the United States Food and Drug Administration (FDA), and the National Cancer Institute (NCI) which is a part of the National Institute of Health (NIH)
- Governmental agencies in other countries where the study drug may be considered for approval.

If we share your identifying information with groups outside of the University of Utah Health Sciences Center, the groups may not be required to follow the same federal privacy laws that we follow. They may also share your information again with others not described in this form.

What if I Decide Not to Take part After I sign the Consent and Authorization Form?
You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

This authorization does not have an expiration date.

You have a right to information used to make decisions about your health care. However, your information from this study will not be available during the study; it will be available after the study is finished.

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OPTIONAL RESEARCH (Making your choice about having optional procedures)

We would like to perform optional biopsies and collect extra blood for optional research. You do not need to participate in the optional research, and you also don't have to choose to participate in both. If you choose not to participate, it will not affect your ability to participate in the main study nor exclude you from it.

Tumor Tissue

The researchers would like to collect fresh tumor tissue from you by performing a biopsy a few different times in the study. These will be collected from some of your tumor lesions or your lymph nodes. These will be collected at day 42 and then again if your cancer returns. Please ask your study team for any questions you may have about this prior to making your choice. Please mark your choice:

___ YES, I will allow the optional biopsies to be done and my tissue to be used for optional research.

___ NO, I will not allow the optional biopsies to be done and my tissue to be used for optional research.

Additional Blood Collection

We would like to collect additional blood from you. These will be collected prior to every nivolumab injection throughout the study. Please ask your study team for any questions you may have about this prior to making your choice. Please mark your choice:

___ YES, I will participate in the optional additional blood sample collection.

___ NO, I will not participate in the optional additional blood sample collection.

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CONSENT

I have been given adequate time to read and consider the information in this consent form prior to signing (or it has been read to me). All my questions about the study and my participation in it have been answered and I will be given a copy of this signed and dated consent form for my records and continued reference.

My signature below indicates that I voluntarily agree to take part in this research study. By signing this consent form, I do not release the study doctor or his study staff, the institution or the sponsor from their professional and legal duties.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

I agree to take part in this research study and authorize you to use and disclose health information about me for this study, as you have explained in this document.

_____
Participant's Name

_____ _____ _____
Participant's Signature Date Time

_____
Name of Person Obtaining Authorization and Consent

_____ _____ _____
Signature of Person Obtaining Authorization and Consent Date Time

WITNESS STATEMENT: (For Non-English Speaking Participants Only)

Consent was obtained from the participant using a short form for non-English speakers. The short form used was in the participant's native language. This full consent form was used as the written summary of the oral presentation of the study with the use of an interpreter.

As a witness, I confirm that I was present for the complete consent process for this study. I confirm that the participant named above was informed of the information in this consent document in a language he/she understands and that the participant has agreed to take part in the research study. The participant's questions were answered to their satisfaction before they signed the short form.

_____
Name of Witness

_____ _____ _____
Signature of Witness Date Time

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Information requested for federal grant reporting purposes *(optional)*

Sex/Gender

- ❑ **Male**
- ❑ **Female**

Ethnicity

Do you consider yourself to be Hispanic or Latino? (see definition below)

Hispanic or Latino. A person of Mexican, Puerto Rican, Cuban, South or Central American, or other Spanish culture or origin, regardless of race.

Select one:

- ❑ **Hispanic or Latino**
- ❑ **Not Hispanic or Latino**

Race

What race do you consider yourself to be?
SELECT ONE OR MORE OF THE FOLLOWING:

- ❑ **American Indian or Alaska Native.** A person having origins in any of the original peoples of North America (including, Central or South America) who maintains cultural identification through tribal affiliation or community recognition.
- ❑ **Asian.** A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.
- ❑ **Black or African American.** A person having origins in any of the black racial groups of Africa.
- ❑ **Native Hawaiian or other Pacific Islander.** A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
- ❑ **White.** A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.
- ❑ **Unknown.**

❑ **Check here if you do not wish to provide some or all of the above information.**

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