CONSENT FOR CANCER RESEARCH

Project Title: Phase II Study of Pembrolizumab plus SurVaxM for glioblastoma at first recurrence

Cleveland Clinic
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Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at Cleveland Clinic

KEY INFORMATION

This study is a phase II study to test the effects of the two study drugs combined with your cancer. The two study drugs are SurVaxM and Pembrolizumab.

The study drug Pembrolizumab (PEM) is a chemotherapy drug and (SurVaxM) is a cancer vaccine that stimulates your immune system to kill glioblastoma cells that contain survivin. How this works is, during the two weeks after you complete radiation and chemotherapy and if you are eligible, you will receive the two drugs; (SurVaxM) as an injection under your skin (in your arm) in addition to your chemotherapy drug PEM, which will be given intravenously.

The SurVaxM vaccine and PEM will be given to you in a series of 4 doses with approximately 2 weeks between each dose (500mcg) and then every 3 months.
The combination of these study drugs is to test to see how your tumor will response.

1. Introduction

We invite you to take part in this study because you have been told you have a recurrent brain cancer called glioblastoma. All patients will receive the study drug combination consisting of SurVaxM and PEM with no randomization, stratification or dose escalation. The combination of PEM and SurVaxM will be tested in patients with recurrent or progressive glioblastoma following failure of standard therapy.

Please ask any questions you may have about the study or this consent form before signing it. Please take your time to make your decision. You will be given a copy of the signed and dated informed consent form prior to participation in the study for you to keep.

What should I know about a research study?

- Someone will explain this research study to you.
- You can choose whether or not to take part.
- You can agree to take part and then later change your mind.
- Your decision whether or not to participate will not be held against you.
- You can ask all the questions you want before you decide.

2. Purpose

The purpose of this study is to find out what effects, (good and bad) the combination study drugs PEM and SurVaxM study drug has on your cancer.

PEM is a chemotherapy drug approved by the FDA to treat certain skin cancers. SurVaxM is a cancer vaccine and considered to be an investigational drug that is not approved by the FDA.

What is SurVaxM (also called SVN53-67/M57-KLH)?

Cancer cells make proteins that are not usually produced by most normal cells. Because of this, your body sends certain white blood cells to attack tumors that contain these proteins. Experiments have shown that the immune system can be helped to kill tumors by vaccinating with small pieces of these proteins. SurVaxM is a cancer vaccine being investigated to treat glioblastoma by activating the immune system to fight the cancer. Most glioblastomas contain a protein called survivin. The purpose of SurVaxM is to stimulate your immune system to kill glioblastoma cells that contain survivin.

This research study is designed to test whether SurVaxM given with PEM treatment improves the survival of patients with glioblastoma.

This study will include about 49 patients nationally. We expect to enroll up to 15 patients at Cleveland Clinic over 2 years. It is expected that this study will take about 3 years and will continue until the needed number of participants are enrolled.

What is **PEM** (also called **Keytruda)**
PEM is a medicine that may treat certain cancers by working with your immune system. PEM can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended.

CONFLICT OF INTEREST

One of the Investigators conducting this was involved in the development of the vaccine that makes products used in this study. As compensation he received equity interest in the company. If you have any questions regarding conflicts of interest, please ask you study doctor or call the Cleveland Clinic Institutional Review Board at (216) 444-2924.

3. Study Procedures
If you qualify and agree to be in the study, you will undergo an evaluation to see if you meet the requirements to be included in the study. Many of the procedures that will be performed during the course of the study and that are described in this section, such as routine blood tests, tumor evaluations, physical examinations, and vital signs, would normally be performed as part of your standard care regardless of study participation. However, some of these may be performed more frequently than might normally be done.

If you are determined to be eligible for the study, you will receive the SurVaxM vaccine and PEM. If the study doctor determines that your tumor has grown at any time during the study, or if you experience serious side effects, you will stop the study treatments. You and your study doctor will decide what future treatment, if any, is right for you and you may receive alternate treatments at that time. As part of the study, even after you discontinue study treatment and start alternate treatment, your study doctor and/or study staff will still contact you every three months to see how you are feeling.

Screening
Before you begin the study, the study doctor or study staff will talk to you about the study to determine whether you are willing to participate. The study doctor or study staff will not be able to begin the study procedures until you give your permission by signing this consent form.

After you sign this form, the study doctor or study staff will do the things listed below when you come in for study visits. If you would like more information about the tests and procedures that will be done, ask the study doctor or study staff.

During the screening phase, the following examinations, tests or procedures will be done to find out if you can be in the study:

- You will be asked information about your medical history and the medications that you are taking, including natural or herbal products.
- You will be asked a series of questions to test your memory.
- You will have a physical examination (including blood pressure, pulse, temperature, height, and weight) and a neurological examination.
- Blood (about 5 teaspoons) will be drawn for routine clinical laboratory tests to evaluate liver, bone marrow, metabolic and kidney functions.
- Your blood (about 1 teaspoon) will also be tested to see if your white blood cells have a certain type of Human leukocyte antigen (HLA) proteins. These proteins or markers -- found on most cells in your body. Your immune system uses these markers to recognize which cells belong in your body and which do not.If this information is already available to the study doctor, it will not have to be repeated
- A sample of your urine will be collected for testing.
- If you are a woman capable of having children, your blood (about 1 teaspoon) will be tested to make sure you are not pregnant.
- Any brain imaging (MRI or CT scan) performed after your surgery, but before you start standard radiation and chemotherapy, will be collected by the study team to verify that your tumor did not grow during radiation therapy.
- Additional brain imaging (MRI or CT) will be performed. If the imaging suggests that your tumor has recurred or grown since your surgery, you will not be eligible to start the study.
- Your study doctor will obtain a sample of your brain tumor (saved from your surgery). This sample will be sent to a laboratory that will test whether your tumor contains survivin.
- A sample of your brain tumor (saved from your surgery) will also be tested for IDH-h, MGMT,EGFRvIII and PDL-1 status
- If you sign this consent document prior to starting radiation and chemotherapy, the study doctors may perform additional imaging and blood tests specifically for the purpose of this study.

Registration (During the two weeks after you complete radiation and chemotherapy):
If you are determined to be eligible for the study, you will be registered into the study and you will receive SurVaxM as an injection under your skin in addition to your chemotherapy drug PEM, which will be given intravenously.

If you qualify and agree to participate, the study will start with you receiving a dose of SurVaxM every two weeks, for a total of four doses. This is called the "priming phase" of vaccination. The priming phase will begin with the first dose of vaccine given about 7-28 days after the completion of standard-of-care chemo or radiation

Study drug injections may continue every 3 months (boosting or "maintenance phase") after you finish the initial four injections of the priming phase, provided that you have no serious side effects and your tumor has not grown

Vaccine Priming Phase:
The SurVaxM vaccine and PEM will be given to you in a series of 4 doses with approximately 2 weeks between each dose (500mcg) and then every 3 months. Each dose will be injected with a small needle subcutaneously (just under the skin of your arm). Immediately afterward, a dose of sargramostim will be injected a short distance (about one inch or less) from the first injection site. Dosed every two weeks for 4 doses (100 mcg) and then every 3 months.

Sargramostim helps your bone marrow make new white blood cells, which help to fight infections.

Montanide ISA 51, 1 ml per dose dosed every two weeks for 4 doses and then every 3 months. Montanide helps to stimulate the immune system and keep the SurVaxM-confined to the injection site.

Table 1 Trial Treatment

Drug	Dose/Potency	Dose Frequency	Route of Administration	Regimen/Treatment Period	Use
PEM	200 milligram	Q3W	IV infusion	Day 1 of each 3 week cycle	Experimental
SurVaxM	500 microgram	Q 2 weeks x 4 then Q 12 weeks	Subcutaneous	Q 2 weeks x 4 then Q 12 weeks	Experimental
sargramostim (GM-CSF)	100 microgram	Q 2 weeks x 4 then Q 12 weeks	Subcutaneous	Q 2 weeks x 4 then Q 12 weeks	Experimental
Montanide ISA 51	1milliliter (ml)	Q 2 weeks x 4 then Q 12 weeks	Subcutaneous	Q 2 weeks x 4 then Q 12 weeks	Experimental

We will use the opposite arm for the next injection and will alternate arms thereafter.
If there is swelling, redness or discomfort at the injection site remaining from the previous vaccine injections, your study doctor may give the remaining injections on the front surface of your thigh.

Before each priming vaccine injection is given, the following assessments will be performed:

- A review of any medications that you are taking and how you are feeling will be conducted.
- Physical examination (including blood pressure, pulse, temperature, and weight) and a neurological examination will be performed.
- Karnofsky Performance Status (KPS) will be assessed to evaluate your ability to perform ordinary tasks.
- You will be asked a series of questions to test your memory.
- Blood (about 6 tablespoons) will be drawn for routine clinical laboratory tests, CBC/diff and CMP to evaluate liver, bone marrow, metabolic and kidney functions, and to test your immune response to the vaccine.
- A sample of your urine will be collected for routine testing.
- If you are a woman and able to have children, your blood and/or urine will be tested to make sure you are not pregnant

Vaccine Maintenance Therapy:
These vaccine visits will occur every 12 weeks after the vaccine priming phase starting 12 weeks after the completion of the vaccine priming phase (4 doses of vaccine given every 2 weeks) for as long as you receive the study drug. The following will be performed at these visits:

- Blood (about 6 tablespoons) will be drawn for routine clinical laboratory tests, including routine tests to evaluate liver, bone marrow, metabolic, immunologic and kidney functions.
- Karnofsky Performance Status (KPS) will be assessed to measure your ability to perform ordinary tasks.
- You will be asked about any medications you are taking and how you are feeling.
- You will then be given an injection of the study drug into your skin and will be looked after by the study staff for at least an hour to make sure that you don't have any bad effects from the injections.

Measurement of Local Skin Reaction:
The most common side-effect of the vaccine is likely to be a local skin reaction with redness, itching, pain and possibly swelling at the injection site occurring soon after injection. You or your caregiver will be asked to monitor any local skin reaction that may occur once you leave the clinic. You will be asked to measure the area of local reaction between 24 and 48 hours after administration of the vaccine using the diameter of a U.S. quarter – approximately 1 inch – as a reference. The study coordinator will contact you, or your caregiver, within 3 to 5 days after the injection to obtain your measurement of the reaction.

Disease Assessment Visits:
These visits will occur every 9 weeks. The following will be performed at these visits:

- Physical examination (including blood pressure, pulse, temperature, and weight) and a neurological examination.
- You will be asked a series of questions or tasks to test your memory.
- A brain MRI scan will be performed.
- You will be asked about any medications that you are taking and how you are feeling.

End of Treatment/Study Termination
When it is decided to stop your treatment with SurVaxM and PEM, you will discontinue study treatment and will have the following tests and procedures done within 30 days of your last treatment date:

- Optional bloods draw for additional analysis. If you agree, and additional blood samples will be drawn (about 1 tablespoon) for testing to determine your molecular profile. This may help the study sponsor to determine how future patients might respond to this treatment. This will not affect your treatment
- A brain MRI will be performed.
- You will be asked about any medications that you are taking and how you are feeling

Follow-up Period
If there comes a time that your disease gets worse and you are no longer receiving treatment under this study, someone at the study site will contact you by telephone every 12 weeks to assess for survival status until death, withdrawal of consent, or the end of the trial, whichever occurs first.

4. Risks

While you take part in this study, you may be at risk for side effects. You should discuss these with your doctor.

The drugs/procedures used in this study may cause all, some, or none of the side effects listed. There may be other side effects of the drugs/procedures that we do not know of yet.

The side effects may be mild, moderate, or severe. Many side effects go away shortly after the treatment stops, but occasionally, side effects can be serious, long lasting, may be permanent, and can even be fatal. It is not possible to tell which side effect will affect you or how mild or severe the side effect might be. We can only tell you what other people have experienced. Please talk with your doctor about these side effects.

It is very important that you notify your doctor right away about **any** side effects, problems, or unusual experiences you may have while taking this medication. This will decrease the chance that the side effects continue or become worse. Sometimes there are other medications that we can give you to make the side effects better or make you more comfortable. If severe side effects do develop, you and your doctor may decide it is in your best interest to stop taking part in the study.

Risks of SurVaxM
The study drug has been assessed in a single study in humans in which the risks and side effects of this vaccine were all minor. Nevertheless, additional side effects that are as yet unknown could occur. In the previous phase I clinical trial, the following side effects were observed:
• Injection site redness, swelling or tenderness 6/9 patients (all mild)
• Low leukocyte counts 4/9 (mild to moderate)
• Fatigue 3/9 patients (all mild)
• Muscle aches 2/9 patients (mild to moderate)

Based upon this and what is known about the drug, a list of possible side effects includes:

Likely side effects - those that occur in 15% - 30% of persons who receive this drug:

• Minor pain at the injection site
• Swelling of skin at the injection site
• Itching at injection site
• Redness at injection site
• Bruising at injection site
• Thickening of skin at injection site
Less likely side effects - those that could occur in approximately 10%-14% of persons who receive this drug:
• Low white blood cell counts
• Flu-like symptoms including muscle and joint aches.

Unlikely side effects - those that occur in approximately 5%
It is possible that the vaccine could cause an immunologic reaction against normal tissues in the body. This is called autoimmunity. To date, such a reaction has not been observed, but remains possible.
• An immunologic reaction to normal tissues in the body could have a number of possible effects that are unknown at the present time, including mild, moderate or severe side effects. These could be reversible or irreversible.

Rare but serious side effects - Those that occur in less than 5% of persons who receive this drug:
• A skin reaction could occur at the injection site that is severe enough to cause skin ulceration
• The preparation of SVN53-67/M57-KLH is sterile; however, infection at the injection site is a possible risk of any injection. An infection could cause:
• Pain at injection site
• Redness at injection site
• Warmth of skin surrounding injection site
• Fever
• Drainage from injection site
• An allergic reaction could occur. These could be minor or serious. An allergic reaction could produce any or all of the following side effects:

- Rash or hives
- Itching
- Wheezing
- Coughing
- Shortness of breath
- Low blood pressure
- Swelling of vocal cords
- Death

You will be monitored closely for possible allergic reactions to the vaccine. If they occur, you may need to stop treatment. In the event that this occurs, other possible treatments for your cancer will be discussed with you.

Treatment could cause a type of immune response against the tumor that could lead to brain swelling. To date, no cases of vaccine related brain swelling have occurred; however, such a reaction could cause any, some, or all of the following side effects:

- Seizures
- Weakness or paralysis
- Changes in sensation
- Speech problems
- Loss of vision
- Headache
- Changes in thinking or memory
- Permanent or irreversible brain damage
- Death

Risks of Montanide

SurVaxM is given together as an injection with a drug called Montanide ISA 51. These two drugs are mixed and then injected under the skin. Montanide helps to stimulate the immune system and keep the SurVaxM confined to the injection site so it can work locally on the immune system. Montanide ISA 51 has been used extensively in clinical trials of vaccine treatments and its risks are minor. These risks include:

Likely side effects - those that occur in approximately 15% - 30% of persons who receive this drug:

• Pain at injection site
• Itching at injection site
• Local skin swelling at injection site
• Redness at injection site

Less likely side effects
those that occur in approximately 10%-14% of persons who receive this drug:
• Flu-like symptoms including muscle and joint aches

Risks of PEM

Likely side effects
• Shortness of breath
• Chest pain
• Cough
• Pneumonitis
• Rash
• Itching
• Blisters, peeling, or skin sores
• Painful sores or ulcers in your mouth or nose, throat or genital area
Infusion (IV) reactions that can sometimes be severe and life-threatening
• Chills or shaking
• Dizziness
• Fever
• Feeling like passing out

Pembrolizumab is a medicine that may treat certain cancers by working with your immune system. Pembrolizumab can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended

Risks of Sargramostim

In addition to injections of SurVaxM, patients will receive separate injections of sargramostim within 1-3 cm (about one inch) of the peptide/Montanide injection site. Sargramostim also stimulates the immune system. Most of the side-effects of sargramostim have been seen when the drug has been injected by vein (intravenously). In the current clinical trial, sargramostim will be injected into the skin (subcutaneously) only.

Likely side effects - those that occur in approximately 15% - 30% of persons who receive this drug:
• Tiredness
• Headache
• Bone, joint and muscle pain
• Skin rash
• Itching
• Skin redness at injection site

Less likely side effects - those that occur in approximately 10%-14% of persons who receive this drug:
• Fluid retention
• High or low white blood cell or platelet counts
Unlikely side effects - those that occur in approximately 5% to 9% of persons who receive this drug:
• Fainting

• Fever
• Flushing
• Nausea
• Vomiting
• Sweating
• Back pain
• Leg spasms
• Shortness of breath

Rare but serious side effects - those that occur in less than 5% of persons who receive this drug:
• Allergic reaction, including anaphylaxis (anaphylaxis is a serious and potentially life threatening allergic reaction)
• Pericarditis (irritation of the covering of the heart)
• Pericardial effusion (fluid around the heart)
• Low blood pressure
• Rapid heart beat

Treatment regime could cause a type of immune response against the tumor that could lead to brain swelling. To date, no cases of vaccine related brain swelling have occurred; however, such a reaction could cause any, some, or all of the following side effects:
• Seizures
• Weakness or paralysis
• Changes in sensation
• Speech problems • Loss of vision • Headache • Changes in thinking or memory

Risks of MRI

If you take part in this research, you will have an MRI (magnetic resonance imaging and/or magnetic resonance spectroscopy). MRI uses a magnet and radio waves to make images

(pictures) of the inside of the head and/or body. There have been no ill effects reported from exposure to the magnetism or radio waves used for these studies; however, it is possible that harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal that may cause injury to you. We will ask you about metal within your body (this includes certain dyes used in tattoos and body piercings). If there is any question about potentially hazardous metal within your body, you will not be able to participate in this research study. We will also keep the MRI room locked so that no one carrying metal objects enters the room while you are having this scan performed. In addition, the MRI scanner makes a loud buzzing noise that could affect hearing ability. You will be provided with earplugs and assistance in their use in order to protect your hearing. You will be able to communicate with the scanner technologist using an intercom and/or signaling device. The technologist will try to help you feel as comfortable as possible in the scanner. You can ask to stop the scan and be removed from the scanner at any time by using the intercom or signaling device.

There is a very slight risk of an allergic reaction if contrast material is injected. Such reactions usually are mild and easily controlled by medication. If you experience allergic symptoms, a radiologist or other physician will be available for immediate assistance.

Gadolinium-based contrast agents (dyes) may increase the risk of a rare but serious disease called nephrogenic systemic fibrosis in people with poor kidney function. Nephrogenic systemic fibrosis triggers thickening of the skin, organs and other tissues. There is no effective treatment for this debilitating disease.

Blood draw Risk
The insertion of the needle to draw blood is painful; however, the discomfort is brief. For most people, needle punctures to get blood samples do not cause any serious problems; however, they may cause bleeding, bruising, discomfort, infections, dizziness, or fainting.

Injection Site Reactions
Mild and moderate injection site reactions such as swelling, redness and/or pain may occur, but should resolve without any further complications. Topical corticosteroids are permitted to treat injection site reactions at the discretion of the investigator.

Reproductive Health/Sexual Activity

The effect of SurVaxM and PEM on human sperm and eggs and the fetus has not been studied. The effects on a developing child from using SurVaxM and PEM during pregnancy and the risk of birth defects are unknown.

This study may involve risks to you or your unborn child that are not known at this time. Therefore, you should not become pregnant or father a baby while you are participating in this study. Also, you should not nurse your baby while on this study. Women of childbearing potential will be required to take a pregnancy test before being allowed to take part in this study. You may also be asked to take pregnancy tests while receiving the study treatment. The pregnancy test must be negative before you enter this study.

You will be asked to practice an effective method of birth control while you are on this study and for a time after your treatment ends. This includes, but is not limited to, oral birth control pills, an IUD, condoms with spermicide, or abstinence. In women of childbearing potential, birth control should continue for 6 months after the last treatment to ensure the drug/treatment has cleared from the body. Since interactions between the study drug and oral birth control pills cannot be ruled out, a "barrier" method of contraception (condom, diaphragm) must be used as well.

In certain cases, oral birth control pills cannot be used for birth control. Please discuss this with your doctor.

When you sign this consent form, to the best of your knowledge, you are not pregnant and do not plan to become pregnant while taking part in this study. Should you become pregnant during this study, you need to immediately tell your study doctor and obstetrician. If you wish you may request a referral for counseling or ask about counseling (such as, genetic counselor, social worker, or psychologist.) to discuss this further.

Male patients must use an effective method of birth control. This can include, but is not limited to, condoms with spermicide, abstinence, or having a vasectomy. When taking part in this study, you should continue use of birth control for six months after receiving the last dose of the drug to be sure the drug has cleared from the body. Males who are receiving treatment should not donate sperm for at least six months after the study is completed. Discuss birth control measures with your doctor.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), effective May 21, 2010, generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.

- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

NEW INFORMATION

You will be told about any significant new findings regarding SurVaxM and PEM that become known during the course of this research study that might reasonably affect your willingness to participate in this study. You may be asked to sign a new consent form if this occurs.

5. Benefits

It is not known if this treatment will help you or not. Addition of SurVaxM and PEM to standard therapy may slow or stop the growth of the cancer in your brain. If the treatment is successful, you might also see a decrease in your symptoms and improvement in your quality of life. It is also possible that the investigational treatments may prove to be unhelpful or even harmful to you. You understand that there is no guarantee that being on the study will help you. Future patients may be helped from the results and information gained from this study.

There is no claim that the investigational compound is safe or effective

6. Alternatives to Participation

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Usual/standard treatment for your disease or condition may be appropriate. This may include treatment with other drugs, drug combinations, surgery, radiation therapy, or possibly other research programs here or at other centers which may be testing new drugs for your type of cancer
- Taking part in another study

- Getting no treatment
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Talk to your doctor about your choices before you decide if you will take part in this study.

7. Costs and Compensation

In addition to the tests and procedures that will be done as part of your conventional medical care (routine medical treatments), certain tests and procedures will be done only if you are a participant in this study (non-routine medical treatments). The costs of your routine medical care will be billed to you or to your health insurance company or government insurance program in the usual way.

Costs for non-routine medical treatments conducted as part of this study will not be billed to you or your insurance company. These are listed below. Except for the items below, you are responsible for payment of all charges related to the medical care you receive, including charges that your insurance company may refuse to pay. Insurance companies or government health care programs may refuse to pay for non-routine or experimental medical treatments or the consequences of such treatments.

The following will not be charged to you or your insurance company:
• SurMaxM, PEM, Montanide and Sargramostim
• Laboratory tests and procedures required only for this study

You will not be paid for your participation in this study.

This study is part of the development of a potential new drug. If the results of this study are positive or if the study is successful and the drug is eventually sold commercially, you will not be compensated in any way for taking part in this study.

This study could be ended before the entire study protocol is completed for various reasons. You will be responsible for any health care costs that arise after the study ends.

For more information on clinical trial and insurance coverage, you can visit the National Cancer Institute's (NCI) website at
http://cancer.gov/clinicaltrials/understanding/insurance-coverage
You can print a copy of the 'Clinical Trials and Insurance Coverage' information from this website. Another way to get information is to call 1-800-4-CANCER (1-800-422-6237) and ask NCI for a free copy.

8. Research-Related Injury

Despite all safety measures, there is a chance that you might experience a medical injury or illness from being in this study. A research-related injury is a physical injury or illness that is directly caused by the proper administration of the study drug, or the proper performance of any procedure that is required only for this study and is not part of your routine medical care.

The Sponsor will not pay for co-pays, deductibles or medical expenses if you, your study doctor, or the study center failed to comply with instructions relating to the study, or if your injury is the result of your medical condition prior to entering the study. The Sponsor will not pay for routine medical treatment, and will not pay such things as lost wages, disability, or discomfort due to any medical problem or injury.

By signing this consent form, you are not giving away any legal rights, including your right to seek payment for any harm you receive while participating in this study.

If you experience physical injury or illness as a result of participating in this research study, medical care is available at the Cleveland Clinic or elsewhere; however, the Cleveland Clinic has no plans to provide free care or compensation for lost wages.

Further information about research-related injuries is available by contacting the Cleveland Clinic Institutional Review Board at (216) 444-2924

9. Privacy and Confidentiality

Federal regulations require that certain information about individuals be kept confidential. This information is called "protected health information" (PHI). PHI includes information that identifies you personally, such as your name, address and social security number, or any medical or mental health record, or test result that may have this sort of information on it. By signing this consent form, you are authorizing your study doctor, study staff, and personnel at the hospital, medical center, or location where the study is conducted, to use or disclose your PHI.

We may share your information with others, such as those who planned, pay for, or work with us on this study, or to whom we are required to share information by law. Your PHI and other health information will be disclosed to the Sponsor and its representatives, and may be disclosed to other parties, such as the U.S. Food and Drug Administration, the Department of Health and Human Services, and other government agencies; contract research organizations or service providers hired by the Sponsor to help perform the study; data safety monitoring committees and other committees providing study guidance; the Institutional Review Board; and any other person or entity to whom we are required to make disclosures by law. These parties are not obligated by law to protect PHI, so absolute confidentiality of your PHI cannot be guaranteed. Once your PHI is released, it may be re-released, at which point your PHI will no longer be protected by federal privacy regulations.

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to David Peereboom M.D. and the research staff at Cleveland Clinic for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition..

Some of the tests and procedures done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record.

In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the Cleveland Clinic Institutional Review Board and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to:

- Study sponsors and their agents
- The Food and Drug Administration;
- The Department of Health and Human Services;
- The National Cancer Institute (NCI);their Institutional Review Boards;
- Data Safety and Monitoring Boards;

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to:

David Peereboom M.D.

Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside the Cleveland Clinic cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic will not use your information collected in this study for another research purpose without your written permission; unless the Cleveland Clinic Institutional Review Board (IRB) assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

10. Voluntary Participation

Your participation in this research study is voluntary. Choosing not to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

11. Termination of Participation

Your participation in this research study is voluntary. You may choose not to participate, or you may withdraw from this study at any time. Your decision will not affect your current or future medical care. If you decide to withdraw from this research study, you must inform the study doctor. For safety reasons, you will be asked to return to the clinic for a final study visit.

The study doctor or sponsor may end your participation in this study without your consent if you do not follow the study doctor's instructions, if the study doctor or the sponsor feels the study drug is ineffective, harmful or has medically unacceptable side effects, or for other reasons at the discretion of the study doctor or the sponsor. If you are withdrawn from the study, you will be asked to return to the clinic for a final study visit

Questions About the Research
If you have any questions, you can ask the Principal Investigator and/or research staff.
David Peereboom M.D. at [redacted]

Emergency and After-hours Contact Information.

If you are a Cleveland Clinic patient, you should contact the page operator at (216) 444-2200 or toll free at (800) 223-2273, and ask for the oncologist (cancer doctor) that is on call.

If you have questions about your rights as a research subject, you may contact the Institutional Review Board (IRB) at Cleveland Clinic IRB 216-444-2924

Where Can I Get More Information?

You may call the National Cancer Institute's Cancer Information Services at:
1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may also visit the NCI website at http://cancer.gov

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo

You will get a copy of the signed and dated informed consent form prior to participation in the study for you to keep. If you want more information about this study, ask your study doctor.

US National Institutes of Health (NIH) Clinical Trial Database

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.

Optional Testing

TISSUE/BLOOD/OTHER SPECIMEN AND DATABANK
DO YOU HAVE TO GIVE TISSUE, BLOOD OR OTHER SPECIMEN TO TAKE PART IN THIS STUDY?

Consenting to give an extra blood sample and have it stored is not needed to take part in the rest of the study. If you decide not to join in this part of the study, you can still join the rest of the study.

If you agree, an additional blood sample will be drawn (less than 1 tablespoon) for testing to determine your molecular profile. Molecular profiling is a method of testing that looks at each person's cancer tumor and studies the genetic characteristics as well as any unique biomarkers. The information gathered is used to identify and create targeted therapies that are designed to work better for a specific cancer tumor profile. This may help the study sponsor to determine how future patients would respond to this treatment. This will not impact your treatment.

If you give permission for the sample now and change your mind later, you will need to write to the doctor listed on the first page of this form and let him/her know that you changed your mind. If we have not already used the sample, it will be destroyed and not used. If you have any questions, please ask your doctor.

My blood can be taken and kept for use in research to learn about, prevent, treat, or cure cancer.

PLEASE CHECK ONE BOX

□ YES □ NO (I may still be in the study if I mark "NO")

Initials____

I agree that someone from Roswell Park Cancer Institute (RPCI)may contact me in the future to ask me to take part in more research.

PLEASE CHECK ONE BOX

□ YES □ NO (I may still be in the study if I mark "NO")

Initials____

Roswell Park Cancer Institute (RPCI) staff may use my clinical data (not personal identifiers/PHI) associated with the study/specimen/tissue to do other research

PLEASE CHECK ONE BOX

□ YES □ NO (I may still be in the study if I mark "NO")

Initials_____

12. Signature

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

Signature of Participant	***Date***	***Printed Name of Participant***

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

Signature of Person Obtaining Consent	***Date***

Printed Name of Person Obtaining Consent

Treatment beyond radiologic disease progression (to be used in selected patients):

This portion is specially created in patients where the physicians will chose to treat patients beyond progression on MRI imaging,

The patient acknowledges that this practice is not considered standard in the treatment of cancer using chemotherapies. However when patients are treated with immunotherapy sometimes imaging changes are seen which may look worrisome for progression, however these may arise due to inflammation due to the immune system in response to immunotherapy or vaccine.

My physician / treating team spoke to me about alternative treatment options, including any available approved therapies and participation on alternative clinical trials.

Signature

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

_____	_____	_____
Signature of Participant	***Date***	***Printed Name of Participant***

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____ _____

Signature of Person Obtaining Consent ***Date***

_____

Printed Name of Person Obtaining Consent